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Editorial

"KMC Practices During COVID-19 Pandemic"

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EDITORIAL

KMC Practices During COVID-19 Pandemic

Md. Mahbubul Hoque

Preterm and low birth weight newborns are highly vulnerable population for whom high quality care from health services is imperative. More than 80% of the world's annual neonatal deaths (2.5 million) occur in babies with a low birth weight (LBW, <2500 g), among which two-thirds are preterm (<37 completed weeks of gestation) and one third are small-for-gestational-age.[1-3] To achieve NMR target of SDG it is mediatory to reduce death from prematurity as the complications of prematurity are the leading cause of death in neonates and children aged <5 years.[4]

Kangaroo mother care (KMC) involves continuous skin-to-skin contact between a newborn and a caregiver (usually the mother). It is a model of care that is an alternative to the incubator for preterm newborns. The World Health Organization (WHO) has recommended this type of care in both developed and developing countries as soon as the premature neonate is clinically stabilized.[5] Kangaroo mother care includes early and continuous skin-to-skin contact, breastfeeding, early discharge from the health-care facility and supportive care. The clinical efficacy and health benefits of kangaroo mother care have been demonstrated in multiple settings. In low birth weight newborns (< 2000 g) who are clinically stable, kangaroo mother care reduces mortality and if widely applied could reduce deaths in preterm newborns.[6,7]

However, in spite of the evidence, KMC practices have been interrupted by the COVID-19 pandemic. Owing to the high contagion and fatality rate of the virus and the WHO declaration of COVID-19 as a pandemic, routine medical care has been impacted and thus the rate of KMC has suffered consequently. The COVID-19 pandemic is disrupting facility-based care. Further, mothers in facility settings are more frequently being separated from their newborns.

As clinical evidence shows KMC is highly effective in the management of preterm baby - development partners, professional bodies and countries set together several times and discussed how to sustain KMC practices during the COVID-19 pandemic. Different countries made their own guidelines on the management issue of neonate and child during COVID-19 pandemic. Initially there were conflicting global guidelines on mother-newborn care during the pandemic, particularly regarding skin-to-skin contact, and few such guidelines specifically for low- and middle-income countries (LMIC). A systematic review of 20 clinical guidelines from 17 countries found that one third of them recommended mother-newborn separation.[8] However, Bangladesh continues to promote KMC amidst COVID-19 pandemic to prevent prematurity related complications and deaths, which was possible by combined efforts from DGHS of GoB, WHO, UNICEF, USAID, Save the Children and professional bodies' like Bangladesh Neonatal Forum (BNF), Bangladesh Paediatric Association (BPA), Bangladesh Perinatal Society (BPS).

The WHO recommended that mothers and newborns should not be separated. The dyads should enable the practice of KMC even in cases of suspected or confirmed COVID-19 by using personal protective equipment and the disinfection of used surfaces.[9]

A newly published study using the British Paediatric Surveillance Unit reported 66 cases of SARS-CoV-2 among neonates receiving inpatient care in the UK between March and April 2020, of whom 17(26%) were born to mothers with perinatal infection. Seven of these 17 neonates became infected despite being separated from their mother immediately after birth, supporting WHO and other development partners and professional bodies guidance to keep mother and baby together even when maternal COVID-19 is suspected or confirmed.[10]

A recent study showing the comparative risk analysis of maximum neonatal lives saved by KMC, versus maximum lives lost due to COVID-19, and

Correspondence to: Prof. Md. Mahbubul Hoque, Professor, Department of Neonatal Medicine, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital. Cell: 01729290121, E-mail: mahbubulhoque2013@gmail.com

incremental deaths caused by reduced KMC coverage in facilities.[11] In this research they modeled two scenarios over 12 months. Scenario 1 compared the survival benefits of KMC with universal coverage (99%) and mortality risk due to COVID-19. Scenario 2 estimated incremental deaths from reduced coverage and complete disruption of KMC. Projections were based on the most recent data for 127 LMICs (~90% of global births), with results aggregated into five regions. Hence, the benefit of KMC is 65-fold higher than the mortality risk of COVID-19 and estimated 2·3-4·6% increase in neonatal mortality across the 127 countries.[11]

Preterm newborns are at risk, especially in LMICs where the consequences of disruptions are substantial. As the survival benefit of KMC far outweighs the small risk of death due to COVID-19 we urge policymakers and healthcare professionals to protect services for preterm and as such consider KMC in the neonatal wards, with the use of all related precautions, even if the mother is SARS-CoV-2-positive.

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LEADING ARTICLE

Clinical Presentation and Outcome of Multisystem Inflammatory Syndrome in Children in Dhaka Shishu (Children) Hospital

[a]Shireen Afroz, [a]Tahmina Ferdaus, [b]Abdul Jabbar, [a]Umme Tanjila, [a]Abu Hasnat, [a]Sabrina Akter, [a]Tarannum Khondoker, [a]Tanjina Haque Silvi, [a]Jannatul Ferdous, [b]Rezoana Rima, [b]Mohammad Abdullah Al Mamun, [a]Jonaki Khatun

Abstract

Background: *The increasing trend in multisystem inflammatory syndrome in children (MIS-C) during Covid-19 pandemic is alarming. Understanding the clinical course and outcome will give the clinical and public health implications of this syndrome.*

Objectives: *This study was conducted to find out the clinical presentation, course of the disease and outcome of the children and adolescents of MIS-C.*

Methods: *This observational study was conducted in the department of Pediatric Nephrology, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh, from August 2020 to October 2020. Total 12 children of MIS-C diagnosed according to WHO diagnostic criteria of MIS-C were included after taking written informed consent from the parents. Mean, median and standard deviation were calculated for the continuous variables.*

Results: *The age ranged from 17 days to 13 years, 56% were male, 17% were positive for SARS-CoV-2 by RT-PCR and 4(33%) had history of the COVID-19 exposure. Organ-system involvement included bilateral pneumonia in 92%, myocarditis in 78%, swollen hands and feet in 67%, mucocutaneous involvement in 50%, diarrhea in 50%, musculoskeletal involvement in 50%, acute kidney injury (AKI) in 33% patients and acute pancreatitis in 25% patients. The median duration of hospitalization was 11 days and ICU stay was 5 days. Mean duration of fever was 8.66 days. Kawasaki's disease-like features were documented in 50% patients and 4 of them had elevated level of procalcitonin and troponin I. Markedly elevated C reactive protein (CRP), Ferritin and D dimer in all patients were present. All patients with cardiac involvement had left ventricular dysfunction and ejection fraction was as low as 38.5%. Coronary-artery dilatation was documented in 33%. About 67% received intensive care with oxygen support by low flow nasal cannula or face mask, 33% received vasoactive support and systemic glucocorticoid, 50% received intravenous immunoglobulin (IVIG) plus methyl prednisolone. Antiplatelet and anticoagulant therapy was given in 75% and 33% patients respectively. Out of 12 patients 2 died, the contributing cause of death included complications like hypotension, shock, myocarditis, coagulopathy and AKI.*

Conclusion*: MIS-C led to serious and life-threatening complications especially when there are cardiac involvement, hypotension and acute kidney injury.*

Keywords: *Multisystem inflammatory syndrome, children, Kawasaki like disease, COVID-19.*

Introduction

During this COVID-19 pandemic an alarming increase in children presenting with fever, hyper inflammation and multiorgan dysfunction frequently requiring intensive care have been observed.[1-3] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections may result in multisystem inflammatory syndrome in children (MIS-C). The clinical presentation of MIS-C includes fever, severe illnes and the involvement of two or more organ systems, in combination with laboratory evidence of inflammation and laboratory or epidemiologic evidence of SARS-CoV-2 infection. Some features of MIS-C resemble Kawasaki disease, toxic shock syndrome, and secondary hemophagocytic lympho-histiocytosis/macrophage activation syndrome.[1] The

[a]Department of Paediatric Nephrology, Dhaka Shishu (Children) Hospital.
[b]Department of Paediatric Cardiology, Dhaka Shishu (Children) Hospital.
Correspondence to: Prof. Shireen Afroz, Professor of Critical Care Nephrology & Dialysis, Department of Paediatric Nephrology, Bangladesh Institute of Child Health (BICH) and Dhaka Shishu (Children) Hospital. Cell: 01715054239, E-mail: safroz1@live.com
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illness resembles Kawasaki disease (KD), with coronary dilatation and aneurysms occurring in some children, the cardiovascular manifestations were typically on the severe end of the KD spectrum with cardiogenic shock a common presentation together with other features. However, few patients present without the cardiovascular manifestations with other similar extra cardiac features; shows prompt recovery compared to those with cardiac manifestations.[1] So we need to pay special emphasis on those who presents with severe symptoms and KD spectrum with cardiogenic shock a common presentation together with other features. Recently a new definition has been given by WHO that define a unique syndrome named multisystem inflammatory syndrome in children (MIS-C). The clinical presentation of MIS-C includes fever, severe illness and the involvement of two or more organ systems, in combination with laboratory evidence of inflammation and laboratory or epidemiologic evidence of SARS-CoV-2 infection. The relationship of MIS-C to SARS-CoV-2 infection suggests that the pathogenesis involves post-infectious immune dysregulation.[1,3] Patients with MIS-C should ideally be managed in a pediatric intensive care environment since rapid clinical deterioration may occur.[1] Specific immunomodulatory therapy depends on the clinical presentation. In this study we have evaluated the clinical and biochemical profiles of children with MIS-C and their outcome in a tertiary care children hospital.[1]

Materials and Methods

This observational study was conducted in the department of Pediatric Nephrology, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh, from August 2020 to October 2020. Total 12 children of MIS-C diagnosed according to WHO diagnostic criteria of MIS-C were included after taking written informed consent from the parents. The case definition included 5 criteria: serious illness leading to hospitalization, an age of less than 21 years, fever that lasted for at least 24 hours, laboratory evidence of inflammation, multisystem organ involvement, and positive RT-PCR or exposure to persons with COVID-19 in the past month. Their detail history, demographic information, clinical characteristics, laboratory values, hospital course, treatment, and outcomes were evaluated. Patients were treated with supportive measures; vasoactive support, intra venous immunoglobulin (IVIG) and pulse methyl prednisolone were given when there were echocardiographically detected cardiac abnormalities; anti-platelet agent and anti-coagulant were given in patients with raised D dimer.

We defined values for tachycardia, tachypnea, hypotension, lymphopenia, neutropenia, and elevated levels of D dimer, ferritin (all during the first 24-72 hours of admission) on the basis of age standards. Clinical myocarditis was defined as cardiac dysfunction on echocardiography with an elevated troponin level; when troponin levels were not tested, clinical myocarditis was defined as cardiac dysfunction (defined as any ventricular dysfunction or hypokinesia or decreased contractility or ejection fraction). Coronary artery aneurysm was reported on the basis of echocardiographic findings.

Presenting signs and symptoms were classified as constitutional (fever temperature more than 100°F, or subjective fever with chills), cardiovascular (chest pain), gastrointestinal (abdominal pain, nausea, vomiting, or diarrhea), dermatologic (rash or swelling of fingers, hands, toes, or feet), mucocutaneous (conjunctival injection or mucosal changes), neurologic (headache, altered mental status, or confusion), lymphadenopathy, musculoskeletal (myalgia or arthralgia), upper respiratory (congestion or sore throat), or lower respiratory (cough, shortness of breath, or wheezing).

Patient's age was grouped into 3 categories: less than 1 year, 1 year to 5 year and >5 year. Mean, median and standard deviation were calculated for the continuous variables.

Results

Among 12 patients 6 is were male and 6 were female age ranged from 17 days to 13 years. Half of the patients presented with cardiac involvement (Table-I).

Table I
Characteristics of the Patients

	Overall n=12	With cardiac involvement n=6	Without cardiac involvement n=6
Gender			
Male	6	3	4
Female	6	3	2
Age			
<1 year	2	0	2
1 year to 5 year	3	1	2
>5 year	7	5	2
Range 17 days to 13 years			

Amongst 12 patients 2 were COVID-19 RT-PCR positive and rests were negative. One patient aged 9 year was hospitalized following a road traffic accident and 1 month following admission became COVID-19 +ve and developed features of MISC Another COVID-19 + ve patient of 7 year was obese and among the rest none had any coexisting conditions or chronic illnesses. History of COVID-19 exposure was found in 4 patients and all of them were >5 years of age. All of the study patients presented with fever, 92% (n=11) of the patients presented with respiratory symptoms, 58% (n=7) with chest pain and cardiovascular system involvement and 6 of them were older than 5 year, 50% (n=6) with gastrointestinal system involvement, 25% (n=3) with abdominal pain and biochemically confirmed acute pancreatitis, dermatological involvement in the form of rash was found in 5 patients, swollen hands and feet were noticed in majority of the patients 8(67%), mucocutaneous involvement in 6(50%) patients, renal involvement as acute kidney injury (AKI) in 4(33%) patients, musculoskeletal involvement in 6(50%). None of the study patients had lymphadenopathy and neurological symptoms (Table II).

Table II

Clinical characteristics of the patients according to age group

Characteristics	Overall n=12	<1 year n=2	1 year to 5 year n=3	>5 year to 13 year n=7
Positivity for COVID 19 RT-PCR	2 (17%)	0	0	2
Coexisting condition	2 (17%)			2
Any (Road traffic accident)				
Chronic disease				
Obesity				
COVID 19 exposure prior to the onset	4 (33%)	0	0	4
Fever	12 (100%)	2	3	7
Cardiovascular: Chest pain(myocarditis)	7 (58%)		1	6
KD or atypical KD	6 (50%)	0	1	5
Gastro intestinal: n= 6(50%)				
Abdominal pain	4	0	1	3
Nausea	5	1	1	3
Vomiting	5	1	1	3
Diarrhea	6	1	2	3
Acute Pancreatitis n=3(25%)	3	0	0	3
Dermatological n=8 (67%)				
Rash	5	0	1	4
Swollen hands or feet	8	0	2	6
Mucocutaneous n=6(50%)				
Conjunctivitis	5	0	1	4
Mucosal change	6	1	1	4
Respiratory n= 11(92%)				
Lower respiratory	11	2	3	6
Bilateral pneumonia	11	2	3	6
Cough	11	2	3	6
Shortness of breath, wheezing	11	2	3	6
Musculo skeletal n=6(50%)				
Muscle ache n=6	0	0	0	6
Joint pain n=2	0	0	0	2
Lymphadenopathy (n=0)	0	0	0	0
Neurological(n=0)				
Headache	0	0		0
Altered mental status or confusion	0	0		0

All ptients were tested for SARSCoV-2 RT PCR; 2 (20%) patients showed positive RT PCR for COVID-19. None underwent antibody serologic testing due to unavailability. Four (33%) of the patiens had COVID-19 like illness 6 weeks before MIS-C symptoms appeared. Amongst 12 patients 11 had tachycardia and tachypnea, 7 presented with hypotension, 11 had temperature >100°F, none had oxygen saturation below 95%. Median WBC was 14,400 per cubic millimeter, median lymphocyte was 23.5%, median neutrophil count was 69.5%, median platelet count was 2, 65,000/ cubic millimeter. Most patients (12) had marked elevation of 3 biomarkers: CRP, Ferritin and D dimer, 8 had hypo-albuminemia. Four of the 6 patients with cardiac involvement had elevated troponin I levels. Elevated procalcitonin level was also found in 4 of 6 MISC patients. Chest radiograph of 11 patients showed features of pneumonia with bilateral opacities and 5 had mild to moderate pleural effusion. Ultrasonography of abdomen showed hepato-splenomegaly in 5 patients and only hepatomegaly in 4 patients, ascites was evident in 4 patients (Table III).

Table III

Vital signs and laboratory values of the patients

Vitals & lab parameters	Overall	<1 year	1 year to 5 year	>5 year to 13 year
Tachycardia	11	2	2	7
Tachypnea	11	2	2	7
Hypotension	7	0	1	6
Temperature >100°F	11	1	3	7
Oxygen saturation <92%	0	0	0	0
Median WBC per cubic millimeter	14,400	—	—	—
Median Lymphocyte (%)	23.5	—	—	—
Median Neutrophil (%)	69.5	—	—	—
Median Monocyte (%)	6			
Median platelet per cubic millimeter	2,65,000	—	—	—
Elevated Troponin level (n=4)				
Not done =8	4	0	1	3
Elevated CRP(mg/L)(n=12)		109±65	114.63±111.11	203.38±134.65
5-100	2	0	1	1
>100 to 200	4	2	1	1
>200 to 350	6	0	1	5
Elevated Ferritin level (ng/ml)(Mean ±SD, n=12)		1467±264.45	4008.33±6087.35	2763.14±3312.05
300-1000	5	0	2	3
>1000-5000	4	2	0	2
>5000	3	0	1	2
Elevated Procalcitonin level (ng/ml) (n=6)				
Done 6 (elevated n=4)Not done 6	4		1	3
Elevated D dimer (ng/L) (Mean±SD, n=12)		5.4±6.5	5.7±3.74	6.52±4.27
Elevated	10	1	3	6
Normal	2	1	0	1
Serum albumin level				
Low (<25 g/L)	8	1	2	5
Normal	4	1	1	2
Elevated level of SGPT n=2	2	1	0	1
Elevated Lipase n=3	3	0	0	3
Chest radiograph				
Bilateral opacities.	11	2	3	6
Mild to moderate pleural effusion	5	0	0	5
Ultrasonography of abdomen				
Hepatomegaly-splenomegaly	5	1	1	3
Hepatomegaly	4	0	1	3
Ascites	4	0	1	3

Left ventricular dysfunction was found in 6/12 (50%) patients with ejection fraction as low as 38.5% (Table IV). Coronary-artery dilatation was documented in 3 patients (33%) and brightness of coronary arteries in 2 patients, severe pulmonary hypertension (PHTN) in 5 patients and mild PHTN in 1 patient. Kawasaki's disease like features were documented in 6 (50%) patients. But none had lymphadenopathy or typical mucocutaneous features meeting the criteria for complete Kawasaki disease (Table IV).

The median duration of hospitalization was 7.75 days (range, 3 to 30 days). Mean duration of fever was 8.66 days; range 3 days to 30 days. Amongst 12 patients, 8 received intensive care (67%) and oxygen support by low flow nasal cannula or face masks but none of the surviving patients needed high flow oxygen or mechanical ventilation, 4 (33%) received vasoactive support,4 received methyl prednisolone only, 6 received IVIG plus methyl prednisolone. Nine (75%) patients received antiplatelet therapy and 4 patients received anticoagulant therapy. One patient received hemodialysis (Table V).

Table IV
Echocardiographic findings and KD like features

S/L	Age in year	Gender	Ejection fraction (EF %)	LV dysfunction	Coronary artery dilatation	Pulmonary hypertension	KD like features
1	13	M	40	yes	Brightness of coronaries	Severe PPHN	yes
2	9	F	45	yes	Perivascular brightness of right coronary artery with pericardial effusion	Severe PPHN	yes
3	9	M	38.64	yes	No coronary dilatation	Severe PPHN	yes
4	7	F	43	yes	Coronary artery dilatation	Severe PPHN	yes
5	9	F	44	yes	Left coronary artery dilatation	Severe PPHN	yes
6	3 1/2	F	55	yes	Dilated coronaries, with perivascular brightness	Mild PPHN	yes

Table V
Clinical course and treatment

Clinical course	
Mean duration of fever	8.66 days (Range 3 days to 30 days)
Median time from symptom of onset to hospitalization (days)	7.75 days (Range: 3 days to 30 days)
Mean duration of ICU stay (n=7)	4.8 days (Range 32 days to7 days)
Median time to ICU entry days	10 days (Range 32 days to 33 days)
Median length of hospital stay	11 days (Range 37 days to 30 days)
Therapy	
Oxygen support through low flow nasal cannula	8(67%)
Vasoactive support Inj. Dopamin+ Dobutamin	4(33%)
Systemic glucocorticoid	4(33%)
Systemic glucocorticoid + IVIG	6(50%)
Anti-platelet therapy	9(75%)
Anticoagulant therapy	4(33%)
Dialysis	1(8 %)

Table VI
Complications and outcome according to age groups

	Overall (n=12)	< 1 year	1-5 year	>5 year
KD or atypical KD	6	0	1	5
Myocarditis	7	0	1	6
Shock	1	0	0	1
Hypotension	1	0	0	1
Coronary artery dilatation	5	0	0	5
Acute kidney injury	4	0	0	4
Pancreatitis	3	0	0	3
Death	2	0	0	2

Most of the children older than 5 years developed life threatening complications; KD or atypical KD was found in 5 children older than 5 years and in only 1 child aged 3 and half year. Myocarditis was seen in 7 children and 1 of them presented with hypotension and another 1 with shock. Four patients presented with AKI amongst them 3 improved with supportive treatment, but 1 needed hemodialysis (HD). Out of the 12 patients 2 (17%) died, both had coronary artery dilatation. One had hypotension and another had shock, both of them had hyponatremia and AKI, one needed hemodialysis (HD) support. Three patients older than 5 years had abdominal pain and markedly elevated serum lipase with hyperglycemia and subsequently being improved. Out of 12, 10 patients were discharged with normal level of inflammatory markers with low dose oral corticosteroids for the next 6 weeks and was kept under regular follow up. On follow up all the patients showed normal echocardiographic findings during the next 2 months following discharge along with normal level of inflammatory laboratory markers (Table VI).

Discussion

As in previous studies in New York[2] and Italy[4], MIS-C cases in this series in Bangladesh followed the peak of the COVID-19 pandemic (August 2020 to October 2020) which supports geographic association between COVID-19 and MISC. Amongst 12 patients with MIS-C, 50 % were male, similar male preponderance (54%) was observed by previous authors.[2] In our series' we did not get patients older than 13 years of age, most of the patients (58%) were in between 5 to 13 years of age, which was comparable to 42% in New York study.[2] A neonate in this series was diagnosed as MIS-C, the presenting features were high fever, bilateral pneumonia and markedly raised inflammatory markers with normal echocardiography, sterile blood and urine cultures and negative RT-PCR for COVID-19 in both baby and mother. MIS-C in newborn although rare, but suspected case has been reported by previous authors.[2] In this study 2 (20%) patients showed positive RT-PCR for COVID-19, none underwent antibody serologic testing due to lack of facilities. Four patients (33%) had COVID-19 like illness 6 weeks before MIS-C symptoms appeared. Majority of the children and adolescents of New York report were COVID-19 positive[2] compared to only 2 patients (17%) in our cohort, which is much lower than other MIS-C studies.[1-3,5-12] It is possible that the seronegative patients in this cohort were either never infected with SARS-CoV-2 or their antibodies declined rapidly following mild or asymptomatic infections, similar possibilities has also been suspected in previous studies.[1,13]

Of the 12 patients in this series no one was admitted with a preexisting condition, only 1 had history of recent road traffic accident and was admitted for surgery and subsequently became COVID-19 positive. All the patients had fever at admission. The prevalence of respiratory symptoms was highest (92%), followed by cardiovascular, dermatologic, gastrointestinal, renal. We found variations in presenting symptoms and manifestations according to age. The prevalence of myocarditis (5/6), musculoskeletal symptoms (67%), AKI (33%) and acute pancreatitis (25%) was highest amongst

children older than 5 years of age. All the patients (12) underwent chest radiograph and[11] had features of bilateral pneumonia, severe clinical presentation was marked in patients with all age groups. Ultrasonography of abdomen showed hepatosplenomegaly in 5 patients and only hepatomegaly in 4 patients, ascites were evident in 4 patients. Overall, the clinical features of our cohort are comparable to those previously reported in the MIS-C literature.[2, 5-12,14,15]

A total of 6 patients presented with Kawasaki disease like symptoms with cardiac manifestations and most of them (5) were older than 5 years of age and echocardiogram of all of them had variable degrees of left ventricular dysfunction with ejection fraction as low as 38.5%. Coronary-artery dilatation was documented in 3 patients (50%) and brightness of coronary arteries in 2 patients (33%), severe pulmonary hypertension (PHTN) in 5 patients (83%). Of these 6 patients elevated level of troponin I was seen in 4(67%). Kawasaki disease like features with MIS-C has recently been described in New York and in few other countries but little in Northeast Asian countries, such as Japan, despite the prevalence of SARS-CoV-2 in this region.[15, 16] The median age of our cohort which was comparable to the median ages reported previously in the MIS-C literature[7,9,11] was considerably older than that of Kawasaki disease, where the peak incidence is 1-3 years of age.[16-19]

Death occurred in two children one aged 7 year and another was 9 year old both were female and presented with hypotension, shock and AKI. Both were admitted with abdominal pain and fever, had tachycardia and hypotension on presentation, and during the course of their hospitalization received vasopressor support and underwent intubation; one received IVIG, HD, another could not afford IVIG, but both received systemic glucocorticoids and vasoactive supports. The contributing cause of death for both children included complications like hypotension, shock, myocarditis, coagulopathy and AKI.

In addition, our MIS-C cohort appears clinically distinct from Kawasaki disease, none of our patients within our MIS-C cohort meeting the criteria for complete Kawasaki disease. Gastrointestinal symptoms and myocardial dysfunction are uncommon in Kawasaki disease, both of which were more prevalent in our MIS-C cases with cardiac involvement. The acute phase was characterized by increased levels CRP and ferritin (Table III), confirming acute inflammation. Raised troponin is indicative of myocardial dysfunction and injury.[12,15] Raised D-dimer in the acute phase suggests a procoagulant state. Although acute inflammation is common in Kawasaki disease, the procoagulant state seen in MIS-C patients is not a common feature of Kawasaki disease.[3,16-19] Immunologically, our MIS-C cohort appears distinct from Kawasaki disease as we did not observe neutrophilia and raised monocyte counts, which are features of Kawasaki disease, which is consistent with previous study reported by Carter MJ et al[3]. Amongst 12 patients, 67% needed ICU support but only 2 death cases needed mechanical ventilation. Complete recovery has been observed in 83% cases. In this study, patients were commonly treated with IVIG, glucocorticoids, and vasopressors. This constellation suggests an inflammatory vasculopathy with some similarities to Kawasaki disease. Our findings are consistent with those of other studies.[2,4,5] Previous investigators have also been suggested that patients with MIS-C should ideally be managed in a pediatric intensive care environment since rapid clinical deterioration may occur. Specific immuno-modulatory therapy depends on the clinical presentation. The relationship between the immune response to SARS-CoV-2 vaccines in development and MIS-C requires further study.[1-3]

Conclusion

Multiorgan dysfunction and systemic inflammation was clearly evident with MISC in children and appears distinct from Kawasaki disease. Multi-system inflammatory syndrome in children led to serious and life-threatening complications especially when there is cardiac involvement, hypotension and acute kidney injury. Patients with MIS-C should ideally be managed in a pediatric intensive care environment since rapid clinical deterioration may occur.

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DS (Child) H J 2020; 36(2): 95-100

ORIGINAL ARTICLE

A Study On Clinical and Laboratory Profile of Children with COVID-19 Attending A Tertiary Care Hospital in Bangladesh

Kazi Iman[1], Sharmin Mahbuba[2], Farhana Rahat[3], Morsheda Khanam[4], Azmeri Sultana[5], Md. Fazlul Haque[6]

Abstract

Background: *An outbreak of COVID-19 caused by 2019 novel coronavirus started first in Wuhan, Hubei province of China. Thereafter it spreaded to different countries of the world. Cases among children has been increasing day by day. Despite taking all measures of prevention virus spreading is uncontrolled.*

Objectives: *To determine the clinical features and laboratory profile of children with COVID-19.*

Methods: *This was a cross sectional study conducted in Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka. Clinical and laboratory profile were analyzed among the children (aged 0-16 years) admitted between 1st May 2020 to November 2020 with positive RT-PCR for COVID-19. Data were analyzed by using SPSS.*

Results: *Total 159 cases were included in the study. The most common symptom was fever (97.5%), then the second most common was cough (80.5%), other symptoms were diarrhea (28.3%), vomiting (17%), anorexia (30.8%) and weakness (30.2%). WBC count was within normal limit, leucocytosis was found in 5% cases and leucopenia in 3% cases. Few cases were reported with neutropenia and lymphopenia. Few cases were reported as thrombocytosis. ESR and CRP were high. Chest X-ray showed opacities in 62.9% cases. In most of the cases it was bilateral, few cases showed unilateral. In 37.1% cases it was normal. The disease category of all infected children remained same all through the hospital stay and no mortality was seen.*

Conclusion: *Children with COVID-19 had distinct clinical features. Fever and cough were the most common symptoms. WBC count was found within normal limit but ESR and CRP were high. Chest radiograph showed opacities in majority cases. The outcome of COVID-19 in children was good.*

Keywords: *COVID-19, clinical and laboratory profile, children, Bangladesh.*

1. Registrar, Department of Paediatrics, Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka.
2. Assistant Professor, Department of Paediatrics, Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka.
3. Assistant Professor, Department of Paediatrics, Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka.
4. Assistant Professor, Department of Paediatrics, Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka.
5. Associate Professor, Department of Paediatric Nephrology , Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka.
6. Professor, Department of Paediatrics, Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka.

Correspondence to: Dr. Kazi Iman, Registrar, Department of Paediatrics, Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka. Cell: 01711317493, E-mail: kaziiman28@gmail.com

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Introduction

The pandemic disease COVID-19 first started in Wuhan, Hubei Province, China in December 2019, caused by corona virus manifested as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).[1] On 30th January 2020 World Health Organization (WHO) declared that COVID-19 a public health emergency of international concern (PHEIC).[2]

COVID-19 infection is a highly contagious to all age group. It spreads mainly through droplets of discharge from nose or saliva when an infected person sneezes or coughs.[3] COVID19 transmits from human to human though initially it had been thought that transmission occurs through animal to human.[4] Transmission to children may occur from asymptomatic cases.[5] In some cases this RNA virus was detected in faecal mater, so there is every possibility of faucal-oral transmission.[6] The vulnerability of the spread of this new coronavirus is more and this pandemic has been found to have spread throughout Asia and across the world. The number of deaths is rising quickly.[7] In Bangladesh first case of COVID19 has been reported on 8th March 2020.[8,9]

Despite taking all measures, virus spreading remains uncontrolled. Recent literature indicate that the mean incubation period of this disease is 3 to 5 days but it may range from 0 to 24 days.[10-12] The incidence of COVID-19 in children is not known due to very few cases in children.[13] It is uncertain why there are few pediatric cases considering that children have developing immune systems, and thus should be more vulnerable to the virus. In addition, pregnant mothers were also advised to stay indoors, as the long-term and short-term consequences of the virus on the fetus and whether there can be mother-to-child vertical transmission is unknown.[14]

Clinical scenario of COVID-19 varies, it may be asymptomatic or critically ill. Some data shows that adult patients with corona virus infections manifest with fever, cough, respiratory distress, easy fatigue ability and lymphopenia. Elderly with co morbidities may develop severe pneumonia which may turn to severe acute respiratory syndrome and even death may occur.[15-18] According to multiple studies it seems that children usually present milder symptoms than adult.[19,20] However there are limited reports about clinical manifestation and laboratory profile of paediatric patients both nationally and internationally. Due to the dearth of evidence and information on COVID-19, WHO has encouraged more research, particularly those involving children and pregnant women to give a better understanding and outline the clinical characteristics and natural history of the illness.

On the basis of clinical features and epidemiological factors all the suspected cases should be tested. When someone had contact with a patient with COVID-19, PCR testing should be done of asymptomatic to symptomatic contacts. Screening tests should be done according to local situation demands. Rapid collection of sample and testing of specimens from suspected patients should meet the case definition for COVID-19. Suspected cases should be tested for the corona virus with nucleic acid amplification tests (NAAT), such as RT-PCR for COVID-19. Outbreak can be minimized by this way.[21]

Supportive investigations that can be done includes: CBC, decrease WBC count (9-25%), decrease lymohocyte count (83%), increase WBC count (24-30%) and decrease platelet count. Poor prognosis was found in patients with lymphopenia at the beginning of the outbreak. Neutrophil to Lymphocyte ratio more than 3.5 is a poor prognostic factor. C reactive protein (CRP): Most of the patients with COVID-19 have significantly increased levels of CRP. It indicates a possibility of secondary bacterial infection. Procalcitonin: Maximum patients have normal level of procalcitonin. D-dimer: In severe cases D-dimer levels are also found significantly elevated with, bad prognosis. Liver and kidney function test, Serum Ferritin, Arterial blood gas analysis, S. LDH and D-dimer all are suggestive to detect multi organ failure.[22] To address this emerging current issue, we aimed to go through both clinical and lab profile of hospitalized children.

Materials and Methods

This was a cross sectional study conducted in Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka from 1st May to November 2020. A total of 159 children (aged 0-16 years) admitted with positive RT-PCR for COVID-19 were enrolled in the study. Nasopharyngeal swab was taken for RT-PCR test. Patients who were RT PCR for COVID was positive with any chronic disease like Cerebral palsy, Congenital heart disease, Chronic kidney disease etc. were excluded from the study.

Detailed history and clinical examinations were done. Hematological profiles (Hb%, TC, DC of WBC, ESR, Platelet count) and other test like CRP was done in all patients. Chest radiograph was also taken in all patients. Clinical and laboratory data were collected and analyzed by SPSS version 21. Informed written consent were taken from the parents. Ethical clearance from the ethical committee of Dr. MR Khan Shishu Hospital and Institute of Child Health was also taken before enrollment in the study.

Results

A total of 159 children presented with positive RT-PCR for COVID-19 were included in the study. Among them 61 (38.36%) were male patient and 98 (61.64) were female patient (Fig 1). Male female ratio was 1:1.6. Most of the patients were from Dhaka city, few were from outside Dhaka city (Fig 2).

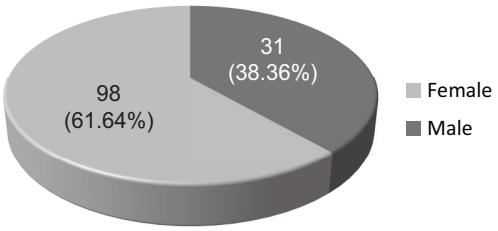

Fig 1 *Distribution of male and female children with COVID-19*

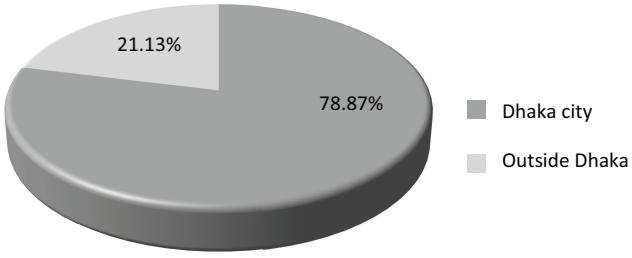

Fig 2 *Category of COVID-19 patients according to the residence*

Children of all age groups were affected, among them most commonly affected age group was 1-5 year (42.1%) (Table I).

Symptoms of the infected children were fever, cough, loose motion, vomiting, anorexia and weakness. Fever was the most common reported symptom in 97.5%(155) of cases. The second most common symptom was cough in 80.5%(128) of cases. Most of the patients presented with dry cough. Diarrhoea was seen in 28.3%(45) and vomiting in 17%(27) cases. Other symptoms such as anorexia was noticed in 30.8%(49) and weakness in 30.2%(48) patients (Fig 3).

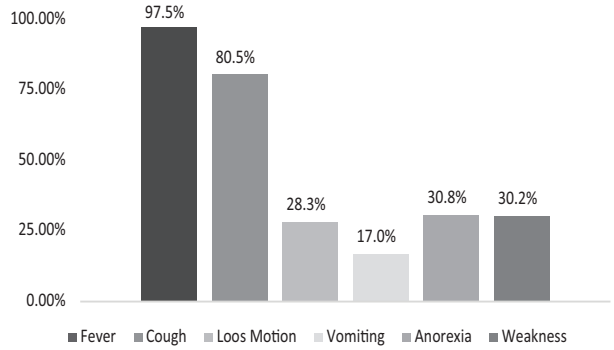

Fig 3 *Clinical features in study population*

Table I
Distribution of age in study population

	Frequency	Percent
Day 1 to <12 month	41	25.8
1 year to <5 years	67	42.1
5 years to <10 years	32	20.1
10 years to <16 years	19	12.0
Total	159	100.0

Table II
Laboratory profile of children with COVID-19

	Mean	Std. Deviation
Hb	11.3579	1.60164
WBC	9030.00	3154.733
Neutrophil	52.59	13.743
Lymphocyte	39.43	14.981
Platelet	315603.77	111957.950
ESR	24.11	22.162
CRP	83.9616	201.80763

All the patients were well nourished according to weight for age CDC growth chart. Mean weight was 17.24 kg and height was 92.6 cm. Mean temperature was 100°F. Oxygen saturation of the children was measured by pulse oximeter. Average range of oxygen saturation was from 80% to 90% without oxygen inhalation in maximum patients. Chest examination was done in all patients. Auscultation findings were different in different patients. Crepitation was the most common finding 87(54.7%).

Ronchi was present in 21(13.2%) and both crepitation and ronchiwas present in 13(8.2%) cases.

Laboratory profile showed normal while blood cell (WBC) count. Differential counts were within normal range. Thrombocytopenia was not reported rather thrombocytosis was seen in some cases. Marked incrase level of CRP was found (Table II). Chest X-ray was done in all cases. It showed opacities in 62.9% cases. Most of the cases it was bilateral few cases showed unilateral. In 37.1% cases it was normal (Table III). The disease category of all infected children remained same all through the hospital stay and no mortality was seen.

Table III
Radiological findings of children with COVID-19

	Frequency	Percent
Pneumonia	100	62.9
Normal	59	37.1
Total	159	100.0

Discussion

The number of COVID-19 in children has increased in Bangladesh as well as worldwide. In a study showed 2.2% of 44,672 confirmed cases were corona virus infected children and they were under 19 years old.[23] The great interest of the study is that there was low mortality in children in comparison to other pandemic or outbreak of viral illness. Cao et al[24] reported that children act as silent carriers or spreaders. This was a hospital based study whereby all the information was collected from the parents. Details history was taken from the parents and clinical examination of the patients were done and some related investigations were also done. Our study added the clinical and lab profile of hospitalized children with COVID-19.

In our study we found that the disease may present in any age group but most commonly affected age group was one to five years of age, Sarangi et al[25] showed similar result. In a literature review they found fever and cough were the main symptoms in children with COVID-19.[26] In our study we found similar result fever was present in 97% cases and cough in 80.7% cases. A literature showed malnutrition a risk factor in adult in COVID-19.[27] We noticed all the children were well nourished as per weight for age and it was similar to other studies.

Recently some experimental studies added that, like the severe acute respiratory syndrome coronavirus which is also called SARS-CoV and the novel coronavirus 2019 (2019-nCoV) both uses the same receptor; angiotensin converting enzyme II (ACE-II).[28,29] So there is a possibility that the activity or may be function of ACE-II in children is not like that as in adults.

Nasopharyngeal swab was taken for RT-PCR for COVID-19 in all suspected cases and all positive cases were included in this study. Yang et al[30] reported that sputum and nasal swabs have potential to achieve a positive rate of 88.9% and 73.3% respectively. As a result, there is every possibility of false negative reports and there is a chance of silent spread of infections from one children to others.

The laboratory profile of adults with COVID-19 has demonstrated low WBC count with associated neutrophilia, eosinopenia, lymphopenia, and thrombocytopenia. Also, higher NLR, LMR and PLR have been associated with severe disease and used for prognostication.[31] In this study WBC count was normal in the majority of the cases. Few cases showed leucopenia but no evidence of thrombocytopenia and this was similar to some other literatures. CRP was high in adults with sever COVID-19 in adults. We also found elevated CRP in children with COVID-19.

Chest X-ray was done in children with COVID-19. We found opacities in 62.9% cases. Xia et al[32] found opacity on chest radiograph in 50% (n=20) of the paediatric patients. Literature review provide evidence that children and adult present differently. Future studies are needed to explain these differences.

COVID-19 claimed many lives in adults than in children.[33] Impaired immunity in adult patients may be possible cause of death. The co-morbidities such as diabetes, cancer and cardiovascular diseases increased prevalence of COVID-19 in adult and elderly. As a result, these patients are more prone to develop organ damage following coronavirus infection.[33] Children suffered less as they do not have comorbidities but co infection was common in one third of the patients. Typhoid fever, meningitis, urinary tract infection and acute viral hepatitis were seen in our study cases. There are many literatures which showed co infection in children with COVID-19.[34-40]

The scientific communities most urgent priorities are to pick and support the best therapies and to prevent and tackle the COVID-19 pandemic. As there was no specific treatment, study population got supportive and symptomatic treatment. This study also added that the prognosis of the children were good.

Results of this study confirmed that children with COVID-19 is not a severe disease, however severe presentation in selected population of paediatric patients may also occure. Evidence need to be generated to further establish the incidence of severe presentation of COVID-19 in infants and children with pre-existing disease.

Conclusion

Children are disproportionately affected by COVID-19 and severe symptoms are less common in children. Symptoms include fever, cough, diarrhea, vomiting, anorexia and weakness. Lab profile showed normal WBC count, high ESR and CRP. Chest X-Ray revealed opacities. Most of the patients were from Dhaka city few were from outside Dhaka city. Further experimental trials would be beneficial to provide robust evidence for development of treatment protocol to reduce morbidity in children with COVID-19.

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ORIGINAL ARTICLE

COVID-19: Is It Rare in Neonate?

Maksudur Rahman[1], Nishat Jahan[2], Liton Chandra Saha[1], Kinkar Ghosh[3], Kanta Chowdhury[2], Md. Mahbubul Hoque[4], M Monir Hossain[4], Mahfuza Shirin[1], MAK Azad Chowdhury[4]

Abstract

Background: *The Global pandemic COVID-19 affects mainly adult population with serious devastating effects in some of them, particularly those with chronic comorbidities. It is less common in children and rare in neonates.*

Objectives: *The aim of study was to identify the COVID-19 in neonates so that we can give proper emphasis on neonatal COVID-19.*

Methods: *This cross sectional study was conducted from April 2020 to August 2020 at Dhaka Shishu (Children) Hospital in Bangladesh. Neonates with suspected COVID-19 were tested for SARS-CoV-2 virus by RT- PCR and positive cases were included in the study. Data were collected and statistical analysis was done by SPSS version 26.*

Results: *Out of 1714 admitted neonates, 32 (2%) cases were COVID-19 positive. Male were 21(67%) and female were 11 (33%). Majority of the cases (28,88%) were at term. Twelve (38%) cases were from Dhaka and 20 (62%) cases came from outside Dhaka. Only 4(13%) cases were found positive for SARS-CoV-2 virus by RT- PCR within 3 days, among them 2 (6%) cases were within 24 hours of age. Nine cases (28%) were RT-PCR test positive within 4-7 days and 19 cases (59%) were RT-PCR positive within 8-28 days. Most of the cases belonged to neonatal medicine (24,75%) and 8(25%) cases were associated with surgical diseases. Sepsis was present in 17(53%) cases, perinatal asphyxia in 8(25%) and pneumonia in 6(19%) cases. Fourteen cases were discharged after improvement, 12 were referred to COVID-19 designated hospital, 2 cases were transferred to corona unit and 4 cases died.*

Conclusion: *In this study a good number of neonates were affected with COVID-19. Perinatal asphyxia, sepsis and pneumonia were common association with COVID-19. So for proper management and prevention of transmission of this disease, it should be properly addressed in neonates.*

Keywords: *COVID-19, neonate.*

1. Associate Professor, Department of Neonatal Medicine, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Bangladesh.
2. Registrar, Department of Neonatal Medicine, Dhaka Shishu (Children) Hospital, Bangladesh.
3. Epidemiologist, Dhaka Shishu (Children) Hospital, Bangladesh.
4. Professor, Department of Neonatal Medicine, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Bangladesh.

Correspondence to: Dr. Maksudur Rahman, Associate Professor, Department of Neonatal Medicine, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Sher-e-Bangla Nagar, Dhaka- 1207, Bangladesh. Cell: 01715315462, Email: maksuddr@gmail.com

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Introduction

There was an outbreak of viral pneumonitis in Wuhan, Hubei, China in December 2019.[1-3] This global pandemic disease is caused by a novel beta coronavirus species, the 2019 novel coronavirus (2019-nCoV).[1-3] It was finally renamed as SARS-CoV-2 (severe acute respiratory syndrome corona virus 2) and the disease was named as COVID-19 (coronavirus disease 2019).[1-3]

The disease is less common in children and rare in neonate.[4,5] The first case in neonate with covid-19 was found in china on first February 2020.[3] Then 3 cases of neonatal COVID-19 were identified in china up to February 2020.[2] In Iran first neonatal case was also identified in the month of February.[6]

Due to enhance surveillance of COVID-19 and availability and accessibility of rapid genetic amplification assays, a growing number of pediatric cases with COVID-19 was confirmed in Wuhan and other areas.[1,5,7] Now the number of neonates with COVID-19 are increasing in different areas of the world.[2,8,9]

The SARS-CoV-2 causes variety of clinical symptoms especially in respiratory system like mild upper respiratory tract infection, pneumonia, severe pneumonia. Sometime this infection rapidly spreads causing acute respiratory distress syndrome (ARDS), shock and death.[1,2,10] Most of the children are asymptomatic and have mild clinical manifestations unlike adults. Neonates with COVID-19 have less clinical manifestations.[2,5]

As increasing the publications, it is found that newborns are susceptible to this disease from COVID-19 positive mother and community, and viruses are detected for a prolonged period; therefore, newborns might play a role in community transmission.[1]

So it is important to see the incidence of neonatal COVID-19, so that management of the disease can be taken more appropriately and transmission to heath personnel as well as family members can be prevented.

Materials and Methods

This cross sectional study was conducted from April 2020 to August 2020 at Dhaka Shishu (Children) Hospital (DSH), one of the largest children hospital in south Asia. This is a multidisciplinary tertiary care hospital which is not designated for COVID-19. An isolated corona unit was started at the middle of July in this hospital. Appropriate written consent was taken before each intervention from the parents of neonates. All neonates who were admitted at this hospital for different reasons were assessed for any suspicion of COVID-19. Clinical suspicions were made by baby born to suspected or confirmed COVID-19 mother, exposed to relatives infected with COVID-19, related with cluster outbreak and with abnormal clinical course such as respiratory distress, fever, not responded with conventional treatment and abnormal chest X-ray. Neonates with suspected COVID-19 were tested for SARS-CoV-2 and it is our hospital protocol to do RT-PCR before going for any operation. Nasal swab was taken with a swab stick by heath technologist with all aseptic precautions and wearing PPE (Personal protective instrument). The Swab stick, named COPAN FLOQSwabs (503CS01; COPAN Diagnostics, Brescia, Italy) was introduced into nose at a length similar to half way between ear lobule to same side ala nasi of nose. Then proximal broken swab stick was put into a tube (Falcon tube) filled with 1 mL of 1X RNA shield (D7005; Zymo, Irvine, CA). Finally, RT-PCR (Reverse transcription-polymerase chain reaction) was done for detection of nucleic acid of virus. The method used for this test was real time PCR for SARS-CoV-2 using the TaqPath COVID-19 RT-PCR Kit (A7817; Thermo Fisher Scientific, Waltham, MA). All tests were done in a government approved laboratory. Then all the positives cases were evaluated and cases were either discharged who had features of improvement or referred to COVID-19 designated hospital or transferred to corona unit of Dhaka Shishu (Children) Hospital. The discharged neonates were given proper counselling for breastfeeding, isolation care of baby and also isolation for attendants.

In this study main outcome variable was number of test positive cases for SARS-CoV-2. Data regarding gender, birth weight, gestational age, resident, and associated diseases were collected. The data were entered and analyzed using Statistical Package of Social Science SPSS, version 26. The descriptive statistics such as frequencies, percentages were calculated to summarize nominal and ordinal data, while mean and standard deviation to describe numerical variables.

Results

During this study period total 1714 neonates were admitted. Among them 32(2%) cases were COVID-19 positive (Fig 1).

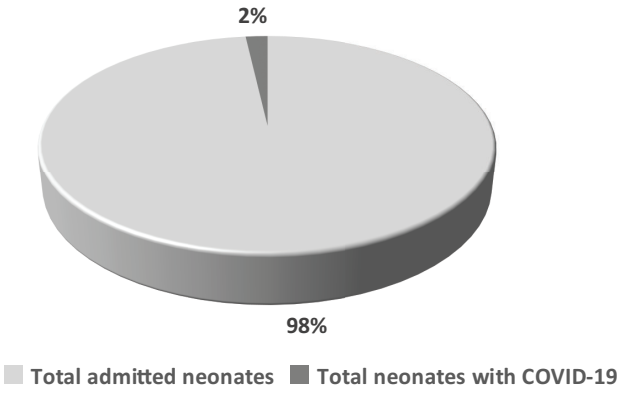

Fig 1 *Hospital incidence of neonates with COVID-19*

Among the cases male were 21(67%) and female were 11 (33%). Male and female ratio was 1.9:1. Term baby was 28(88%) and preterm was 4(12%). Mean weight was 2698±294 g. Twelve (38%) cases were from Dhaka and 20(62%) cases were from outside of Dhaka (Table I).

Table I
Distribution of cases according to gender, gestational age, weight and resident (N=20)

	Number	Percentage
Male	21	67
Female	11	33
Term	28	88
Preterm	4	12
Weight in g (mean±SD)	2698±294	
Dhaka (capital)	12	38
Outside Dhaka	20	62

Only 4 (13%) cases were positive for SARS -CoV-2 virus by RT- PCR within 3 days, among them 2 (6%) cases were within 24 hours of age. Nine (28%) cases were test positive within 4-7 and 19(59%) cases were positive within 8-28 days (Table II).

Table II
Days at which test positive for SARS-CoV-2 by RT-PCR (N=20)

Age of the cases (day)	Number of cases	Percentage of cases
1-3	4	13
4-7	9	28
8-28	19	59

SARS = severe acute respiratory syndrome; COV- 2 = corona virus 2; RT-PCR = reverse transcription-polymerase chain reaction.

Most of the diseases associated with COVID-19 belonged to neonatal medicine department (24,75%) and 8 (25%) cases were associated with surgical diseases. In neonates two or more diseases coexisted in same cases. Sepsis was present in 17(53%) cases with COVID-19. Perinatal asphyxia was present in 8(25%) and pneumonia in 6(19%) cases (Table III). Among 32 positive cases, 14 cases were discharged after improvement, 12 cases were referred to COVID-19 designated hospital and 2 cases were transferred to corona unit of DSH, which was finally discharged with advice. Four cases died at our hospital (Table IV).

Discussion

This cross sectional study was conducted from April 2020 to June 2020 at Dhaka Shishu (Children) Hospital. All admitted neonates with COVID-19 were taken as cases. During this study period total 1714 neonates were admitted. Among them 32 (2%) cases were COVID-19.

The first case of COVID-19 was detected in Bangladesh at 8th March 2020 who was adult.[11] We started RT-PCR for COVID-19 at this hospital in the month of April in this year.

Worldwide the incidence of covid19 in children is very few in contrast to adult and it is rare in neonates.[12] The first children affected by COVID-19 was in china on January, 2020.[13] Liu et al[14] showed in their study that the incidence of COVID-19 in paediatric age group was 1.6% among the hospitalized children with respiratory tract infection. Another study conducted by Tu et al[15] showed that the incidence of COVID-19 in children was 0.6% among the confirmed cases of all age group. In the month of February several study showed that neonates were also affected by COVID-19.[3,16] The first neonate with COVID-19 was identified in first February 2020 which was published by Wang et al.[3] Then 3 neonates with COVID-19 were identified in that month which was published by Choi et al.[1] At that time in different countries neonates were also affected with COVID-19. In Iran first case of neonatal COVID-19 was found in this month.[6] Different publications on neonates with COVID-19 showed that the number of neonate with COVID-19 is increasing in the world.[1,6] But still it is very few unlike adult.[7] The cause of less neonatal COVID-19 may be the presence of less number of ACE2 receptor in their respiratory tract and their more stronger innate immunity than adult.[17,18] Surprisingly we see more

Table III
Associated diseases with COVID-19 (N=32)

Name of the Diseases	Admission age of cases (day)	Number of cases	Percentage of cases[#]
Term, Perinatal Asphyxia HIE II[a] with	1	3	9
Pneumonia[c]	4		
	15		
Perinatal Asphyxia	22	4	13
HIE II[a] with sepsis[b]	18		
	13		
	4		
Perinatal Asphyxia HIE III with sepsis[b],	6	1	3
Term, IUGR, Jaundice			
Neonatal Jaundice with sepsis[b]	5	4	13
	6		
	9		
	11		
Pneumonia[c] with sepsis[b]	20	2	6
	18		
Term AGA with EONS	8	2	6
	2		
Term AGA with LONS	20	4	13
	17		
	11		
	14		
*Pneumonia[c] with CHD with syndromic Baby	20	1	3
*Congenital Heart disease	23	1	3
AKI	8	1	3
PUV with B/L TEV	15	1	3
*Occipital Encephalocele	2	1	3
Mylomylengocele	5	4	13
	1		
	4		
	4		
ARM with sepsis[b]	5	1	3
*ARM	22	1	3
Hypertrophic pyloric stenosis	17	1	3

HIE: Hypoxic Ischemic Encephalopathy; IUGR: Intra Uterine Growth Retardation; AGA: Appropriate for Gestational Age; EONS: Early Onset Neonatal Sepsis; LONS: Late Onset Neonatal Sepsis; CHD: Congenital Heart Disease; AKI: Acute Kidney Injury; PUV: Posturetral Valve; B/L: Bilateral; TEV: Telipes Equenovarus, ARM: Anorectal Malformation; *late preterm; [a] perinatal asphyxia 8 cases, [b] sepsis 17 cases, [c] pneumonia 6 cases. [#] percentage expressed in round figure.

Table IV
Outcome of Neonates with COVID-19 (N=32)

Variable	Number (Percentage#)
Discharged with advice	14(44)
Transferred to corona Unit*	2(6)
Referred to COVID-19 designated hospital	12(38)
Death	4(12)

*which finally discharged with advice; # percentage expressed in round figure.

number of neonates with COVID-19 (2%, 20 cases) in this study. The neonatal COVID-19 is increasing. It may be due to increase community transmission, and household contact including mother. Though the transmission of SARS- CoV- 2 virus through placenta and breast milk is still unidentified.[19-21]

Among the cases with COVID-19 male were 21(67%) and female were 11 (33%). Male and female ratio was 1.9:1. Term baby was 28(88%) and preterm was 4(12%). Mean weight was 2698±294 g. It was found that in this study male was predominantly affected by COVID-19. The cause of this finding is still unknown. In this study it was found that term and normal weight neonates were affected more. But regarding gender and gestational age, no statistical comparison was done. In one study, it was found that there was no significant sex predominance in children.[5] In this study Twelve (38%) cases with covid19 lived in Dhaka and 20(62%) cases in outside of Dhaka. This implies that only in Dhaka (capital of Bangladesh) affected cases were more as a single city than rest of the districts. In another study it was found that COVID-19 affected cases were more in city.[5]

In our study only 4(13%) cases were positive for SARS -CoV-2 virus by RT- PCR within 3 days, among them 2(6%) cases were within 24 hours of age. Nine (28%) and 19 (59%) cases were test positive within 4-7 days and 8-28 days respectively. It may imply that most of the cases were affected from community or from family members. In one study it was found that children were affected from community or household contact.[16]

It was found in this study that most of the diseases associated with COVID-19 belonged to neonatal medicine department (24,75%) and only 8(25%) cases were associated with surgical diseases. In neonates two or more diseases coexisted in the same case. Sepsis was present in 17(53%) cases with COVID-19. Perinatal asphyxia was present in 8(25%) and pneumonia in 6(19%) cases.

This hospital is not a COVID-19 designated hospital and all patients were out born.An isolated corona unit was started at the middle of July in this hospital, initially all patients were admitted in another hospital and later referred to this hospital. Newborns with any conditions or diseases was admitted. In this study it was not found whether associated conditions like sepsis and pneumonia were caused by COVID-19 or these conditions were associated with neonatal COVID-19. Several study showed COVID-19 presented with respiratory distress, sepsis like manifestation etc.[5,10]

In this study among 32 positive cases, 14 cases were discharged after improvement, 12 cases were referred to COVID-19 designated hospital and 2 cases were transferred to our corona unit which was finally discharged with advice. Four cases died at our hospital. In this study exposer history could not be evaluated properly.

We have found significant number of neonates with COVID-19 in this study. These neonats may be a source of transmission of this disease. So, we should give proper emphasis on test, tracing and management of neonatal COVID-19 like adult.

Conclusion

In this study a good number of neonates were affected with COVID-19. Perinatal asphyxia, sepsis and pneumonia were common association with COVID-19. So for proper management and prevention of transmission of this disease, it should be properly addressed in neonates.

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Conflict of interest

There was no conflict of interest.

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ORIGINAL ARTICLE

Effects of Intermittent Kangaroo Mother Care in Preterm Low Birth Weight Babies: A Randomized Controlled Trial

Nishat Jahan[1], Md Mahbubul Hoque[2], MAK Azad Chowdhury[3]

Abstract

Background: *Prematurity is the largest cause of neonatal mortality. They need incubators or radiant warmers which are expensive and very difficult to arrange in a resource constraint country. Kangaroo mother care (KMC) had been proposed as an alternative to conventional neonatal care for low birthweight (LBW) babies.*

Objectives: *To observe the benefits of Kangaroo mother care in preterm low birth weight babies.*

Methods: *This randomized controlled trial was conducted over 6 months in Dhaka Shishu Hospital. Neonates who were <1800 gm and hemodynamically stable were enrolled. Total 80 neonates were enrolled and divided into 2 groups: Kangaroo mother care group and conventional method care group (incubator/warmer). The mother or caregiver were taught for KMC, supervised by trained nurses round the clock. KMC was given at least 2 hours at a time and at least 12 hours in a day. When the baby was not in KMC at that time the baby was placed in cot with adequate coverings. During hospital stay both the groups were monitored.*

Results: *In KMC group 25% and conventional care group 40% neonates became hypothermic. Among the study population 35% neonates in KMC and 65% neonates in conventional care groups developed sepsis (p= 0.007). More KMC babies were exclusively breastfed at the end of the study (95% vs 60%). The KMC babies had shown better growth: weight gain per day (18.35±7.81 grams vs 13.55±4.89 p<0.001) and length (0.99±0.70 vs 0.71±0.44 cm, p = 0.03). KMC babies were discharged earlier than conventional care baby.*

Conclusion: *KMC provides significant improvement in exclusive breast feeding, reduction of infection, decrease hospital stay and gaining weight of the babies. It also helps in maintaining temperature better than conventional care.*

Keywords*: Kangaroo mother care, conventional care, exclusive breast feeding, growth, thermal control.*

Introduction

Birth weight is a significant determinant of newborn survival. Prematurity is the largest direct cause of neonatal mortality.[1] In Bangladesh reported rate of neonatal mortality and morbidity varies from 31-50%.[2] One of the main reasons that LBW/premature babies are at a greater risk of illness and death because of their lack of ability to control body temperature; they become hypothermic very quickly.[3] Prematurity and low birth weight are associated with increased bacterial infections[4] and vulnerable to develop respiratory distress syndrome

1. Registrar, NICU, Department of Neonatal Medicine, Dhaka Shishu (Children) Hospital.
2. Professor, Department of Neonatal Medicine, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital.
3. Former Head, Department of Neonatal Medicine, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital.

Correspondence to: Dr. Nishat Jahan, Registrar, NICU, Department of Neonatal Medicine, Dhaka Shishu (Children) Hospital. Cell: 01711977095, E-mail: shimee.nishat@gmail.com

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(RDS), necrotizing enterocolitis (NEC), patent ductus arteriosus (PDA), intra-ventricularhaemorrhage (IVH) and long term sequelae such as retinopathy of prematurity, chronic lung disease and developmental disabilities. Well thermal control, monitoring of heart rate and respiratory rate, oxygen therapy, maintenance of fluid and electrolyte, special attention to nutritional support and safeguard against infection are the corner stone of management of these neonates.[5] Neonatal intensive care of LBW babies is difficult in developing countries due to high cost, difficulty in maintenance and repair of equipments, intermittent power supply, inadequate cleaning of instruments and shortage of skilled staff. For sharing the incubator, risk of infection is very high.[6] There is an alternative approach for providing thermal care and improving survival of LBW infants that is both effective and affordable-namely, Kangaroo Mother Care, or KMC.[1] The introduction of Kangaroo mother care has resulted in improved preterm infants outcome including decreased infant pain sensation and stress, improved breast-feeding success as well as improved development and growth in the neonatal Intensive Care Unit (NICU). The KMC has been associated with improvements in short and long-term neonatal care health outcome to date.[7] The length of KMC should be up to 20+ hours a day. But as Bangladesh is hot and humid country it was very difficult to continue KMC for 20 hours for this we recommend short session of KMC also known as intermittent KMC which can be started during medical treatment, each session of KMC should be minimum 2 hours and at least 12 to 16 hours a day. It is one of the government's four priority neonatal interventions. To achieve Sustainable Development Goal (SDG) we need to significantly reduce preterm deaths. The socio economic, cultural and environmental context of our country is different from many other countries in Europe, Africa where most of the studies have been done. Very few studies have been done on KMC in Bangladesh. So we proposed to do a study in our setting to see its efficacy and its acceptance by our mothers and other caregivers, so that it helps to motivate the policy makers, stake holders and the professional people to implement the method for better care of our preterm babies.

Materials and Methods

This prospective randomized controlled trial was conducted in a tertiary hospital, Dhaka Shishu (Children) Hospital (DSH) over 6 months period from August 2016 to January 2017. Eighty neonates were enrolled according to the inclusion (stable neonate with birth weight 1250 to 1800 gm, gestational age between 30 to 35 weeks) and exclusion criteria (major congenital malformation, severe perinatal asphyxia, babies requiring ventilator or ionotropic support, critically ill mother, caregiver not interested to give KMC, having birth weight <1250 gms or >1800 gms, gestational age <30 weeks or >35 weeks).

They were divided into 2 groups: Case (K) kangaroo mother care group and control (C) conventional method care group. Randomization was achieved by simple randomization and allocation was concealed by sealed envelope. KMC was initiated as soon as the baby was stable. In KMC group mother or caregiver, father and other family members were counseled at a time explained about what is KMC, the benefits of KMC in terms of feeding, weight gain, temperature maintaining and control of infection. They were also counseled how to maintain household work during KMC. The baby was provided skin to skin contact with mother or care giver in upright position dressed with a cap, socks and diaper and supported in bottom with a sling/binder. Mother was provided with front open gown. Adequate privacy was ensured. Comfortable bed or chair was provided to mother or caregiver practicing KMC in ward. KMC was given at least 2 hours at a time and at least 12 hours in a day. All the babies were on breast milk either through nasogastric tube or by cup spoon later on breast feeding was started. The KMC chart was maintained by doctor and KMC nurses in the ward. In between KMC session babies placed in cot with adequate cloths and coverings. Neonates with conventional method (CMC) group were managed under radiant warmer and incubator.

During hospital stay both the groups were monitored. Regular follow up of temperature, apnoea, gastrointestinal symptoms, feeding, growth parameter and septic screening were done for both groups.

After discharge, the neonates were followed weekly up to 40 weeks of corrected gestational age at DSH in a follow up room and babies weight, length, OFC were measured. Every time mother were counseled about feeding practice and danger sign.

Ethical permission was taken from Ethical Review Board of Bangladesh Institution of Child Health. Data were compiled and analyzed with the help of SPSS version 21.0. Comparison was done by unpaired student's 't' test and chi square (χ^2) test. A probability value (p) of less than 0.05 was considered to indicate statistical significance.

Results

Total 80 neonates were enrolled, 40 in each group. Two neonates in KMC group and three in conventional care group died during hospital stay so 38 patients in KMC and 37 in control group were completed follow up to 40 weeks of corrected gestational age. There were no significant difference in age on admission, sex, birth weight, mode of delivery, H/O PROM, first cry between two groups (Table I).

Table I

Distribution of the patients according to age, sex birth weight and delivery events

Variables	Case (K) n=40 No (%)	Control (C) n = 40 No (%)	p value
Age on admission (days, mean±SD)	1.80±1.09	2.10±1.19	0.244^{ns}
Sex			
Male	24(60.0)	28(70.0)	
Female	16(40.0)	12(30.0)	0.348^{ns}
Birth weight (gm)			
1250-1499	23(57.5)	22(55.0)	
1500-1800	17(42.5)	18(45.0)	0.821^{ns}
Mode of delivery			
NVD	26(65.0)	22(55.0)	0.361^{ns}
LUCS	14(35.0)	18(45.0)	
PROM			
Yes	20(50.0)	24(60.0)	0.369^{ns}
No	20(50.0)	16(40.0)	
First cry			
Immediate	5(12.5.0)	2(5.0)	0.235^{ns}
Delayed	35(87.5.0)	38(95.0)	

Unpaired 't' test was done in quantitative variables and χ^2 test was done in qualitative variables

There were no significant difference between case and control group inoccurrence of hypothermia, apnoea and hypoglycemia. This table also shows that 14(35%) neonates of case (K) and 26(65%) neonates of control (C) were diagnosed as suspected sepsis which was statistically significant and 4(28.6%) neonates of case and 8(30.8%) neonates of control group was diagnosed as culture proven sepsis (Table II).

Table II

Comparison of complications between two groups during hospital stay

Variables	Case (K) (n-40) No (%)	Control (C) (n-40) No (%)	p value#
Hypothermia			
Yes	10(25.0)	16(40.0)	0.152^{ns}
No	30(75.0)	24(60.0)	
Apnoea			
Yes	10(25.0)	14(35.0)	0.329^{ns}
No	30(75.0)	26(65.0)	
Hypoglycemia			
Yes	16(40.0)	12(30.0)	0.348^{ns}
No	24(60.0)	28(70.0)	
Suspected sepsis			
Yes	14(35.0)	26(65.0)	0.007**
No	26(65.0)	14(35.0)	
Culture proven sepsis			
Yes	4(28.6)	26(65.0)	0.884 ^{ns}
No	10(71.4)	14(35.0)	

#χ^2 test, n=Total number of subjects, *=Significant; **=Highly significant; ns=Not significant

The mean days to reach full enteral feeding was 9.35±3.95 days and 14.35±6.06 days in case and control group respectively and was statistically significant. Exclusive breast feeding rate was 95% and 60% during discharge from hospital in case and control group respectively and that was statistically significant. There was no significant difference in feeding intolerance between two groups (Table III).

Table III
Distribution of two groups related to feeding

Hospital course	Case (K) (n=40) No. (%)	Control (C) (n=40) No. (%)	p value
Start of first feed on			
1st day	14(35.0)	8(20.0)	0.133ns
2-3 days	20(50.0)	20(50.0)	1.00ns
4-5 days	6(15.0)	12(30.0)	0.108ns
Time (days) to achieve full enteral feeding	9.35±3.95	14.35±6.06	<0.001*
Episode of feed intolerance			
Yes	8(20.0)	12(30.0)	0.302ns
No	32(80.0)	28(70.0)	
Exclusive breast feeding (at discharge)			
Yes	38(95.0)	24(60.0)	<0.001**
No	2(5.0)	16(40.0)	

Unpaired 't' test was done in quantitative variables and χ^2 test was done in qualitative variable. n=Total number of subjects, *=Significant, **=Highly significant, ns=Not significant

In case group mean days of weight gain started was 6.60±1.74 and it was 8.45±2.14 in control group. The mean (days) ± SD to regain birth weight was 10.35±3.09 and 13.50±3.70 in case and control group respectively (Table IV).

Table IV
Comparison of weight gain pattern in two groups

Variables	Case (K) (n=40)	Control (C) (n=40)	p value
Weight gain started (Days) (mean±SD)	6.60±1.74	8.45±2.14	0.001**
Birth weight regain (Days) (mean±SD)	10.35±3.09	13.50±3.70	0.001**

Data were expressed as Mean ± SD. Statistical analysis were done by Unpaired 't' test. **=Highly significant

This table shows that mean weight gain (grams) of case group and control group were 18.35±7.81 and 13.55±4.89 respectively. Head circumference increase (cm/wk) 0.77±0.47 and 0.48±0.28 and length increase (cm/wk) 0.77±0.47 and 0.48±0.28 in case and control group respectively which were statistically significant (Table-V).

Table V
Distribution of changes in rate of growth parameter between two groups at 40 weeks corrected ages

Growth parameter	Case (K) (n=38)	Control (C) (n=37)	p value
Weight gain (gm/day) (mean±SD)	18.35±7.81	13.55±4.89	<0.001**
Head circumference increase (cm/wk) (mean±SD)	0.77±0.47	0.48±0.28	0.001**
Length increase (cm/wk) (mean±SD)	0.99±0.70	0.71±0.44	0.035*

Data were expressed as Mean ± SD. Statistical analysis were done by Unpaired 't' test. *=Significant, **=Highly significant, ns=Not significant

22 babies in KMC care were discharged within 14 days of admission and 16 patients after15 days of admission. In conventional method care 7 patients were discharged within 14 days and 30 patients after 15 days of admission which was statistically significant (Table-VI).

Table VI
Distribution of the patients by outcome on hospital stay and mortality

	Case (K) (n=40) No. (%)	Control (C) (n=40) No. (%)	p value
Outcome			
Improved and discharge	38(95.0)	37(92.5)	0.644ns
Death	2(5)	3(7.5)	
Hospital stay			
14 days	22(57.89)	7(18.9.0)	<0.001**
≥15 days	16(42.11)	30(81.0)	

Statistical analysis were done by χ^2 test. *=Significant, **=Highly significant, ns=Not significant

Discussion

Four million newborn die each year in the world, among them 99% are from developing countries. Twenty eight percent of newborn deaths are attributed to low birth weight (LBW) and

prematurity.[8] Low birth weight (LBW) infants particularly for those weighing <2000 gm at birth are the major issues of concern in child and maternal care services.[7] As the conventional care for low birth weight babies in hospital are very costly procedure for developing countries KMC can be an alternative care for low-birth-weight infants. So to evaluate the efficacy of KMC for management of preterm low birth weight neonate a randomized controlled trial was conducted in neonatal ward of Dhaka Shishu (Children) Hospital. Neonates in both groups were found to be non-comparable in birth weight, sex, mode, place of delivery.

Incidence of hypothermia was less in KMC than conventional care group. During the hospital stay 25% neonates in KMC group became hypothermic and in conventional care group 40% became hypothermic which was not statistically significant (p=0.152). This finding was comparable with a study done in Australia by Kathryn L. Roberts et al, where temperatures remained stable or rose by 0.2° - 0.4°F (0.1°–0.2°C) for both groups.[9] A study had done at Nepal found that 3.1 % babies in KMC group and 12.6% babies in control group developed hypothermia (p<0.0481) which was statistically significant.[10] Fluctuation of temperature is more common in incubator care which is more detrimental for babies. Hypothermia were found more often in conventional care group than kangaroo mother care group (47% vs 27%), and p=0.05 and this randomized control trial was done in Indonesia.[11] Sumon Rao et al[12] also had found significantly higher number of babies in incubator care group suffered from hypothermia.

A large portion of neonates (65%) in conventional care group developed sepsis during the study period. In KMC group, the rate of sepsis was 35%. The difference in rate of sepsis in two groups were statistically significant (p=0.007). Charpak et al[13] found that the frequency of nosocomial infections was significantly higher in the control group (6.8%; KMC: 3.4%; rate ratio: 2.01; 95%CI: 1.04-3.87).

A metaanalysis showed KMC decreased risk of neonatal sepsis (RR 0.53, 95% CI 0.34, 0.83).[14] Cochrane review by Conde-A A, concluded that KMC reduces the incidence of sepsis.[15] It can be said that in KMC care incidence of sepsis is less as there is minimum handling by mother or by caregiver.

Apnoea occurred in 10(25%) neonates in KMC group and 14(35%) neonates in Conventional method care group which was not statistically significant. Similar result was found in Nepal where none of the baby developed apnoea in KMC and 3 babies developed apnoea in conventional care group which was not statistically significant (p=0.08).[10]

This study had shown that first feed could start in 50% of babies in both the groups by 2-3 days which was not statistically significant (p= 0.16). Similar result found in another study done in Pakistan regarding the starting of feeding between KMC and CMC.[16]

In this study mean days to reach full enteral feed was 9.35±3.95 and 14.35±6.06 days in KMC group and conventional care group respectively and this difference is statistically significant (p= 0.001). Rao et al[12] had found less time required to reach full enteral feeding in KMC group (5.71± 5.65 and 4.85±4.94 in KMC and conventional care group respectively but the result was not statistically significant (p= 0.25).

During discharge exclusive breast feeding rate was 95% for KMC and 60%conventional care which is statistically significant (p=0 .001). Another comparative study by Sumon Rao where he also had found higher rate of exclusive breast feeding in KMC group.[12] Similar study had done in Pakistan, Iran and result were similar to us.[15-17]

In this study, KMC had shown significant effect on weight gain and regaining birth weight. In KMC group mean 6.60±1.74 days was required to start weight gain and 8.45±2.14 days for control group. To regain birth weight it was needed 10.35 ± 3.09 and 13.40± 3.70 days in KMC group and conventional care group respectively and both the differences were significant statistically. A study had done in Indonesia and found median duration of birth weight regain was 5 days in KMC group and 6 days in CMC group and p= 0.4 which was statistically not significant.[11]In another study the mean postnatal age at which the babies regained their birth weight was significantly less in the KMC group, 15.7± 6 0.7 days, compared to the control group, 24.6 ±3.8 days (p =0.001) like our study.[18]

In this study at 40 weeks of corrected gestational age, KMC neonates showed significantly higher daily weight gain than conventional care group. In KMC

group rate of weight was 18.35±7.81 gms and in conventional care group 13.55±4.89 gms, p=<0.001, which is statistically significant. Head circumference increased (cm/wk) 0.77±0.47 and 0.48±0.28 and length gain (cm/wk) was 0.99±0.70 and 0.71±0.44 in KMC group and conventional care group respectively and both the differences were significant statistically. Gathwala et al had done a comparative study and result showed similar to us that were mean weight gain in the KMC group was 21.92+1.44 compared to 18.61 +1.28 gm/day in the control group (p=0.05). The mean length gain in cm/week was1.03+0.5 in the KMC group compared to 0.74+0.05 in the control group (p=0.05). The mean OFC increase in cm/week was 0.59+0.04 in the KMC group compared to 0.47+0.03 in the control group (p= <0.05).[19] Similarly in another study had done by Sumon Rao and found that KMC babies achieved significantly better growth. It revealed that KMC babies had better average weight gain per day (KMC 23.99 gm vs CMC 15.58 gm, p<0.0001). The weekly increment in head circumference (KMC: 0 .75 cm vs CMC 0.49 cm, p<0.02) and length (KMC: 0.75 cm vs CMC 0.49 cm, p<0.02) were higher in KMC group.[12]

During hospital admission mean weight was 1426 gms in KMC group and 1427 gms in conventional method care group having no statistical significance. But at 40 weeks of corrected age weight was 2105 gms in KMC group and 1946 gm in conventional method care. Achieving a better early growth pattern in neonates of KMC due to the reduced energy expenditure during KMC.[20]

As regards to hospital stay, kangaroo mother care reduced hospital stay significantly .Fifty seven percent neonates discharged within 14 days of hospital stay in KMC group, in case of conventional care group 18.9% of neonates discharged within 14 days but 80% of neonates need >5 days for discharge and p value is 0.001 which is statistically significant. Early attainment of full enteral feeding, fewer infection episodes possibly contributed to shorter hospital stay in KMC group. Mishra et al[21] showed, average duration of hospital stay was longer in CMC (14-18 days) than the KMC group (6-8 days) (p=0.038). Like our study in Ethiopia Ninety-one per cent and 88 per cent of babies in KMC and CMC were discharged from the study in the first 7 days of life, respectively.[22]

Conclusion

This study conclude that KMC has found significantly effective in weight gain, exclusive breast feeding, reduction of infection and reduction of hospital stay. Thermoregulation control was better in KMC than CMC though it was not statistically significant.

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ORIGINAL ARTICLE

Surgical Outcome of Right Ventricular Outflow Tract Reconstruction Using Bicuspid Pulmonary Valve in Tetralogy of Fallot Repair: A Single Centre Experience

Mohammad Rokonujjaman[1], SM Shaheedul Islam[2], Nawshin Siraj[3], Nusrat Ghafoor[4], Syed Tanvir Ahmad[5], Md. Atiqur Rahman[6], Md. Ibrahim Khalilullah[7], Abdullah-Al- Shoyeb[8], Mahfuza Begum[9], Md. Golam Saklayen[10]

Abstract

Background: *Tetralogy of Fallot (TOF) is one of the most common congenital cardiac defect. In patients with small PV annulus, it has to be augmented to certain diameter by cutting annulus. In these cases, transannular patch is used free PR is inevitable. Free PR with transannular patch ultimately leads to RV dilatation, dysfunction, arrhythmia and failure with time. Monocuspid reconstruction of PV is commonly practiced in many centers but its long-term outcome is poor though it helps to achieve a less stormy ICU course. Modified monocusp or bicuspid PV reconstruction is a good choice where 0.1mm PTFE patch is used.*

Objectives: *We are presenting the results of bicuspid PV reconstruction using a 0.1mm PTFE patch as a method of RVOT reconstruction in repair of TOF with transannular patch.*

Methods: *A total, 42 patients diagnosed as TOF were treated from January 2016 to October 2020. Age range 18 months to 35 years, weighing 10 kg to 70 kg. 38 patients had TOF, 4 had DORV with PS. The transannular patch was followed by implantation of a 0.1-mm PTFE modified monocusp valve using posterior fixation.*

Results: *Among total patients 28 were male and 14 were female. Mean age 9.58±5.6 yrs. Bypass time was 187±31 min, cross-clamp time 123.63±25.42 min. Out of 42 patients, PR gradient was trivial in 7(16.67%), mild in 31(73.1%), moderate in 4(9.52%) patients. First, a follow-up echocardiogram revealed no significant deterioration of PR gradient. ICU stay was 89±32.6 hours and mean hospital stay 11.48±2.1 days.*

Conclusion: *Initial results using a transannular patch with a modified monocusp valve to repair the outflow tract in cases of Tetralogy of Fallot were excellent. There were only a slight pressure gradient and mild regurgitation in most of the cases.*

Keywords: *Tetralogy of Fallot, transannual patch, pulmonary valve gradient, regurgitation.*

1. Associate Professor & Consultant, Cardiac Surgery, Ibrahim Cardiac Hospital & Research Institute, Dhaka.
2. Associate Professor & Consultant, Cardiac Surgery, Ibrahim Cardiac Hospital & Research Institute, Dhaka.
3. Associate Professor & Sr. Consultant, Radiology & Imaging, Ibrahim Cardiac Hospital & Research Institute, Dhaka.
4. Associate Professor & Consultant, Radiology & Imaging, Ibrahim Cardiac Hospital & Research Institute, Dhaka.
5. Assistant Professor & Associate Consultant, Cardiac surgery, Ibrahim Cardiac Hospital & Research Institute, Dhaka.
6. Registrar & Specialist, Cardiac Surgery, Ibrahim Cardiac Hospital & Research Institute, Dhaka.
7. Assistant Professor & Associate Consultant, Cardiac Anesthesiology, Ibrahim Cardiac Hospital & Research Institute, Dhaka.
8. Registrar & Specialist, Cardiac Surgery, Ibrahim Cardiac Hospital & Research Institute, Dhaka.
9. Registrar & Specialist, Cardiac Surgery, Ibrahim Cardiac Hospital & Research Institute, Dhaka.
10. Assistant Registrar, Cardiac Surgery, Ibrahim Cardiac Hospital & Research Institute, Dhaka.

Correspondence to: Dr. Mohammad Rokonujjaman, Associate Professor & Consultant, Department of Cardiac Surgery, Ibrahim Cardiac Hospital & Research Institute, Dhaka, Bangladesh. Cell: 01711311200, Email: drselim74@gmail.com
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Introduction

It has been more than five decades since the first total surgical correction of Tetralogy of Fallot (TOF) done. Treatment of this defect varies from MBT shunt to total repair. Universally the choice and outcome of repair depends on the age, body weight and complexity of the lesion. But the maturity of the team largely matters to get optimum outcome with same characteristic of the patient. Outflow tract enlargement is a basic concept in surgical correction of heart diseases with Right ventricular outflow tract obstruction (RVOTO) like TOF. In patients with borderline PV annulus, transannular patch enlargement of RVOT ends up with inevitable free pulmonary regurgitation and chronic RV volume overload. Ventriculotomy, pulmonary insufficiency with chronic RV volume overload, leads to progressive RV dilatation and dysfunction and arrhythmias associated with impaired functional capacity in the long term.[1] So every surgeon has an attempt to reconstruct the of RVOT to avoid the long term complication and decreasing the probability of early and late interventions. This reconstruction can be done in many ways like using prosthetic valves, homografts or xenografts in pulmonary position.[2-9] One of the important problem with biological and artificial valves are tissue degeneration, subsequent stenosis and regurgitation with time. Use of artificial valves has many limitations including anticoagulation, redo surgery and cost involvement. With this view, onocuspid reconstruction of the pulmonary valve is practiced for a long time but it became less popular due to the early development of pulmonary regurgitation though it provides good support in the early postoperative period.[3,7] More over,for a country like Bangladesh, cost and management of artificial valve is a big deal. To overcome this issue, implantation of an expanded poly tetra fluoro ethylene (PTFE) bicuspid valve is a good option for the reconstruction of RVOT fater TOF surgery for the patients who require trans annular patch augmentation of PV annulus. This kind of reconstruction facilitates early recovery after surgery and also gives medium to long term benefits.[2,5-8,10,11] In our centre, we are also practicing the bicuspid pulmonary valve reconstruction using 0.1 mm PTFE patch in pulmonary position and we are following the system proposed by Nunn et al[10].

Materials and Methods

In total, 42 consecutive patients who needed enlargement of the right outflow tract with a trans annular patch (TAP) were treated between Jan 2016 and October 2020. Of these, 38 had TOF and 4 double outlets right ventricle (DORV) with PS. Four patients had previously undergone palliative treatment with a modified Blalock-Taussig shunt. The ages of patients ranged from 18 months to 35 years and weight from 10 kg to 70 kg. Pre-operative workup was common for all cases. Transthoracic echocardiogram and CT aortopulmonary angiogram were routine for all cases. CT scan was used for proper evaluation of main pulmonary arteries and branch PAs. Cardiac catheterization was used only for cases with MAPCA's-for evaluation and coiling. Three patients required MAPCA coiling preoperatively. Pre-operative Mc Goon ratio and Nakata index were a very good guide for probable trans annular patch augmentation of RVOT. Moreover, this technique also implemented if post-operative RV: LV pressure ratio more than 0.5 and significant RVOT gradient (25 mmHg) at the level of the pulmonary valve in cases where the pulmonary valve was preserved initially. After surgical correction, epicardial echocardiography was performed (as TEE was not available before 2019) to determine infundibulum morphology and the degree of pulmonary regurgitation and stenosis, classified as mild, moderate, or severe. The pressures were determined by direct puncture of the right ventricular infundibulum, right ventricle proper, and main pulmonary artery. All the patients under went echocardiography before discharge to determine the pulmonary gradient and the degree of pulmonary neovalvular regurgitation.

Pulmonary atresia and major coronaries crossing RVOT cases were excluded from this study. Patients below 10 kg were not included as the long term efficacy of valve function is not clear among the patients with small pulmonary artery diameter.

The surgical technique includes standard cardiopulmonary bypass. Mild hypothermia with bicavalcanulation and aortic cross clamping. Deaeration was facilitated by CO_2 insufflation into the operative field. Following transatrial closure of the ventricular septal defect (VSD), the outflow tract

was enlarged with a TAP (Fig 1). The pulmonary neo valve was a 90°-120° semicircle of 0.1 mm PTFE whose radius equaled the distance between the commissure of the native pulmonary valve and the lower vertex of the ventriculotomy incision. Its fanlike shape its most characteristic feature offers a very generous free edge compared to classic monocusp valves.

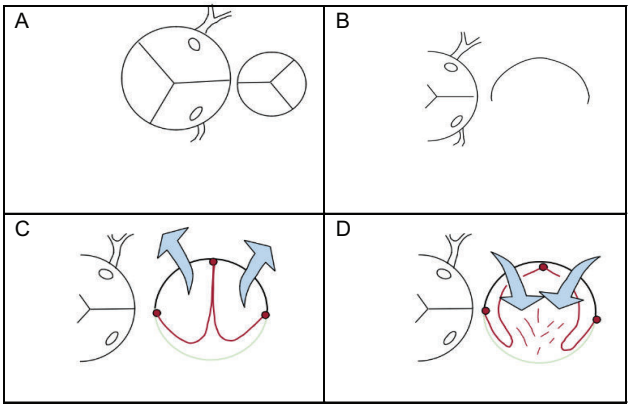

Fig 1 *A: Relative sizes of aortic and pulmonary valves in tetralogy of Fallot. B: Pulmonary artery, open and flat. C: Expanded polytetrafluoroethylene (PTFE, red) fixed at the central point and edges (in the shape of a 3) with a transannular patch (green) in systole (arrows, blue). D: PTFE valve (red) in diastole (arrows, blue), moving toward the perimeter of the pulmonary neo artery (native artery shown in black and patch of pericardium shown in green).*

The central point of the curved free edge (circular) is sutured to the posterior side of the native pulmonary artery in the commissural plane. The vertex of the patch is tied to the vertex of the ventriculotomy incision and the two ends of the suture are used to join the straight sides of the patch to both edges of the ventriculotomy incision. Finally, the TAP (glutaraldehyde treated autologous pericardium or commercially available bovine pericardium) is fixed to the edges using an independent suture, thereby covering the pulmonary neo valve which is shown diagrammatically in Fig 1. Both the pleurae left open with large bore drains. Two RV pacing wires were fixed with prolene sutures. Delnido cardioplegia solution used in all cases and repeated after 70 minutes. Milrinone used in every patient in the theatre and ICU. Overnight ventilation maintained in all cases.

Results

Among the 42 patients, 28(66.67%) were male and 14(33.33%) were female. The mean age of the patients was 9.58±5.6 yrs and the mean BSA was 0.90±0.34 kg/m^2. In respect of the blood group, 12 were O+ve, 1 was A-ve, 8 were A+ve, 1 was A-ve, 11 were B+ve, 3 were B-ve and AB+ve were 4. The mean total cardiopulmonary bypass time was 187±31 minutes and the mean aortic occlusion time was 123.63±25.42 minutes. The mean total operation time was 6.06±0.65 hours. Out of 42 patients, 9(21.43%) had a PV gradient 0-10 mm/Hg, 24(57.14%) had 10-20 mm/Hg, and 9(21.43%) had >20 mm/Hg in the post-operative echocardiogram (Table I). PR gradient was trivial in 7(16.67%), mild in 31(73.1%), moderate in 4(9.52%) patients. First, a follow-up echocardiogram revealed PR gradient remained trivial in 4 (10%) patients, augmented from trivial to mild in 3(7.5%), stationary to mild in 25(62.5%), and mild to moderate in 5(12.5%) patients. It remained moderate in 3(7.5%) patients (Table II).

Table I
Gradient across the reconstructed pulmonary valve

Gradient (mmHg)	Number (%)
0-10	9(21.43)
10-20	24(57.14)
>20	9(21.43)

2(4.76%) patients required peritoneal dialysis in the ICU. Among them, one expired on the 3rd POD and another rescued. The rescued patient required total of 10 cycles of peritoneal dialysis.

Re-exploration and reintubation were required in 2(4.76%) patients. Total 2(4.76%) patients developed low output syndrome which was managed medically.

Table II
Quantification of pulmonary regurgitation after surgery and follow-up after 3 months

Gradient	After surgery/During discharge n (%)	Gradient	After 3 months n (%)
Trivial	7(16.67)		4(10%)
Mild	31(73.1)	Trivial to mild	3 (7.5)
		Mild	25 (62.5)
Moderate	4 (9.52)	Mild to moderate	5(12.5)
		Moderate	3(7.5)

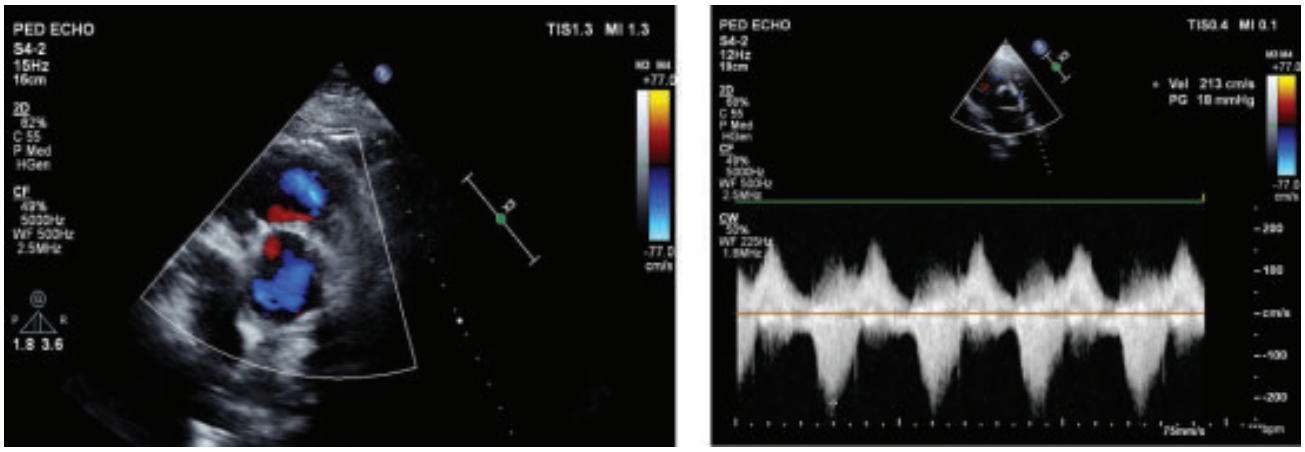

Fig 2 *Echocardiogram finding of reconstructed PV with minimum gradients across the neo valve*

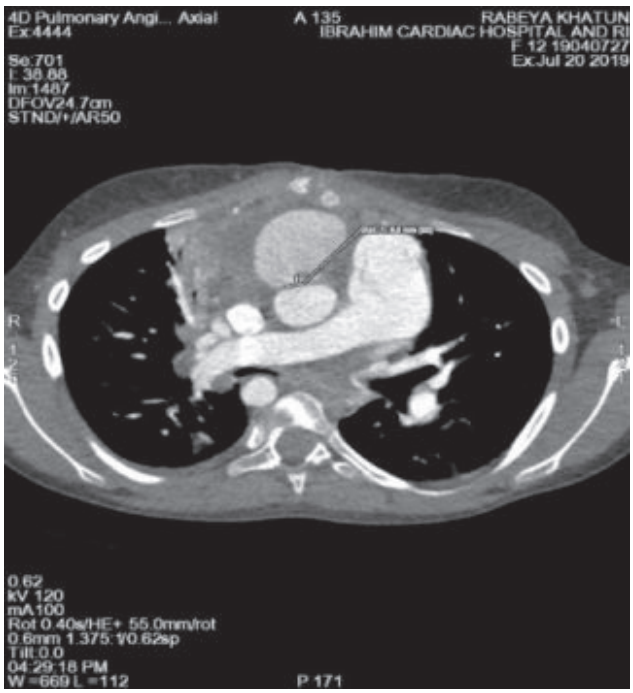

Fig 3: *Post-operative computed tomographic image of PV reconstruction showing well dilated RVOT and line of neo pulmonary valve*

Neurological symptoms in the form of hemiplegia developed in 3(7.14%) patient which were improved later. The mean total ICU stay time was 89±32.6 hours and the mean total hospital stay was 11.48±2.1 days. Total two patients died in the whole series.

Discussion

TOF is a common CHD and most of the cardiac centers are practicing the repair of this lesion according to the capability of the team. In the initial days, outcome of TOF repair was not excellent in maximum centres. Staged surgery was a common practice in smaller children and with narrow PV annulus. Now a days, the results of repair are considered excellent irrespective of timing and surgical technique.[1,2,10] Transannular patch augmentation is randomly used in TOF repair where the PV annulus is small and post operative RV:LV pressure ratio is more than 0.5. The use of transannular patches dramatically reduced the death but of course at the cost of severe pulmonary insufficiency. After the repair of TOF, the physiology of RV changes. After the relief of RVOTO, RV turns into a volume overloaded chamber. This changes

along with ventriculotomy usually leads to acute response early after surgery.[1] This response is well tolerated in most patients but some patients develop right ventricular failure. This free PR causes progressive RV dysfunction, long term re intervention and even sudden death.

RVOT reconstruction in TOF correction has two benefits. Firstly, excellent ICU course and secondly, it reduces the rate of pulmonary insufficiency in the medium and long term. PTFE valve can be implanted in many ways in the pulmonary position. In our study we are presenting our experience by using the technique proposed by we can choose the size and shape of neovalve according to the need of the patient in this technique.

In the field of congenital heart surgery, a 0.1mm PTFE membrane is widely used as a valve substitute in pulmonary valve position. It has good biocompatibility and its microporus structure is expected to impede cellular penetration and subsequent calcification. So, in our study, we used a 0.1mm PTFE patch. The material is thin enough to give a shadow similar to natural pulmonary valve which is found in post operative CT scan (Fig 3).

Optimization of the closure mechanism is mandatory to achieve the optimum outcome from this neovalve. Here we fix the central point of the curved edge to the commissural plane to get optimum closure during diastole.[10] The total length of the patch, and subtraction amount of tissue taken up by the suture line. A circular sector with an angle close to 120° showed good outcomes in our series and others.[10] As the free edge is kept generous, it aroused a question of whether it will create an obstruction to outflow. But, this did not occur due to the elasticity of the extremely thin material used (0.1 mm). Moreover, the material is so thin that oral platelet aggregation inhibitors were not required.[10,11]

The distal fixation of the neovalve takes the shape of a three or double-arched vault, its operation resembling that of a bileaflet prosthesis with anteroposterior orientation. It is specifically the bileaflet configuration that halves the time it takes for the free edge to move over the perimeter of the pulmonary artery compared to the classic monocusp valves. This mechanism optimizes the opening and closing of the neovalve in systole and diastole, respectively (Fig 1).[10]

Prevention of valve incompetence is the major challenge in hand sewn pulmonary valves, so the shape and placement of the free edge of the PV leaflet carries an important role. If we place the free edge as distal as possible in the main pulmonary artery it will increase the competence of the valve without prolapse. Leaflet area is also important and the addition of a fixation suture at the free edge of the leaflet posteriorly increases the leaflet area. If we look at other advantages, it will reduce the wall stress in the leaflet, forces the free edge to coapt without prolapse, and decreases the time it takes the two halves of the free edge to move from fully closed to fully open positions. It also allows a greater degree of over correction in size in the RV outlet because the valve can be crafted to fill any outlet. The hinge point in the leaflets changes as the two leaflets move from fully open to fully closed position. It may prevent a buildup of fibrinous material at a hinge point.[2] Blood in each RV systole, not only is ejected through the valve but also empties the volume of blood on the pulmonary arterial side of the leaflets. That volume is added to the pulmonary flow for that systole and returns from there to the pulmonary arterial side of the valve when it closes. This is how the RV systolic volume is delivered to the pulmonary arterial tree.

During echocardiogram, we could see some regurgitation at the origin of the pulmonary branches instead of the infundibulum. Echocardiography may overestimate the degree of regurgitation in these patients but this is beyond the aims of this study. Post operative echocardiogram is depicted in Fig 2 which shows RVOT gradient and pulmonary regurgitation.

It is always possible to implant an oversized pulmonary neovalve according to the need of the patients. Larger sized valves were associated with a longer duration of valvular competence. In cases of post-procedural pulmonary regurgitation in young adults, prosthetic pulmonary valve should be considered.[10,11] Study by Nunn et al demonstrated excellent late results in 93% and only trivial or mild pulmonary regurgitation compared to 50% in the Indianapolis group.[10] In our series, regurgitation was also mild in most of the cases (more than 90%). It is observed in many studies that, the bicuspid PTFE valves in the pulmonary position as a RVOT reconstruction technique is durable in the medium term, could maintain its competency in the follow-up period, and not resulted in significant obstruction in the RV outlet.[10]

Conclusion

RVOT reconstruction in case TOF repair with TAP is essential to achieve optimum post operative outcome. Bicuspid valve or modified monocusp reconstruction of RVOT with a 0.1mm, PTFE membrane could retain its competency in 93% of cases which is simple and replicable. The initial results are appreciating. Only mild regurgitation and a slight pressure gradient were observed during the follow-up period. A medium or long-term follow-up study is required to acknowledge these findings. It can be applied safely in TOF repair where transannular patch is used.

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ORIGINAL ARTICLE

Acid-base and Electrolyte Disturbances in Children Presenting with Acute Watery Diarrhoea in Emergency Observation and Referral Unit of Dhaka Shishu (Children) Hospital

Md. Abu Tayab[1], Md. Ariful Hoq[2]

Abstract

Background: *Acute watery diarrhoea (AWD) is a leading cause of illness and death amongst children in developing countries. Electrolyte and acid-base disturbances play an important role in the associated morbidity and mortality.*

Objectives: *To observe the acid-base and electrolyte changes in moderate and severe dehydration in AWD in children.*

Methods: *This cross sectional study was carried out in the Observation and Referral Unit of Dhaka Shishu (Children) Hospital from July 2018 to December 2018. Children below five years of age who came with acute diarrhoea with moderate to severe dehydration were included in the study. After admission 2ml of whole blood was collected with all aseptic measures at the time of insertion of intravenous cannula before giving intravenous fluids to measure serum levels of Na and K while arterial blood was also taken for analysis. The data was analyzed by using SPSS version 20.*

Results: *Total 125 AWD cases were admitted among them 98(78.4%) had moderate dehydration whereas 27(21.6%) had severe dehydration. Hyponatremic dehydration was present in 41(32.8%) cases. Among them 30(30.6%) had moderate dedydration and 11(40.4%) had severe dehydration, hypernatremic dehydration was present in 11.11% cases, hypokalemia was present in 54(43.2%) cases. Among them 42(42.86%) had moderate dedydration and 12(44.44%) had severe dehydration. Metabolic acidosis was present in 38(30.4%) cases [28(28.57%) in moderate dedydration and 10(37.04%) in severe dehydration]. The comparison of mean serum sodium and potassium value of the children with moderate and severe degrees of dehydration did not attain statistical significance, but there was a significant difference in bicarbonate concentration among moderate and severe dehydration cases (p=0.02).*

Conclusion: *Hyponatremia and hypokalamia was the commonest electrolyte abnormality among moderate to severe dehydration with AWD. Mean serum sodium and potassium of the children with moderate and severe degrees of dehydration did not attain statistical significance, but bicarbonate concentration was significantly low among severe dehydration cases.*

Keywords: *Acute watery diarrhea, electrolyte and acid-base disturbances.*

1. Associate Professor, Department of Emergency, Observation and Referral Unit, Bangladesh Institute of Child Health & Dhaka Shishu (Children) Hospital, Dhaka.
2. Assistant Professor, Department of Paediatrics, Sher-E-Bangla Medical College and Hospital, Barisal.

Correspondence to: Dr. Md. Abu Tayab, Associate Professor, Department of Emergency, Observation and Referral Unit, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital. Cell: 01714305833, E-mail: mddrtayab@gmail.com

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Introduction

Acute Watery Diarrhoea (AWD) is a public health problem in many regions of the world, especially where poverty prevails. It is defined as sudden onset of excessively loose stools of >10 mL/kg/day in infants and >200 g/24 hr in older children which lasts <14 days.[1] According to World Health Organization (WHO) the definition of diarrhoea is three or more loose stools per day, or as having extra stools than normal for that person.[2] It is a leading cause of illness and death in children of developing countries.[3-5] Worldwide, an estimated 1.7 billion cases of acute diarrhoea and nearly 700,000 deaths occur each year in children under 5 years.[6]

In early childhood, the clinical problem of diarrhea arises from the loss of water and electrolytes in the stool in excess of their intake. The main cause of death in acute diarrhea is dehydration, which results from the loss of fluid and electrolytes in diarrheal stools.The clinical manifestations of acute diarrhea are related to the severity of water deficit and the type of electrolyte disturbances. Often laboratory facilities are not available or, even if available, there is a considerable time lag in obtaining the results. Consequently, clinical recognition of water and electrolyte disturbances becomes important, particularly Hyponatremic dehydration, due to its serious neurological consequences. Electrolytes are ionized molecules found in the blood as well as in various tissues and cells of the body. The main serum electrolytes are sodium, potassium, and bicarbonate with varying distribution and functions.[7] In the extracellular fluid, sodium and chloride are the dominant cation and anion, respectively. Potassium is the most abundant cation in the intracellular fluid and contributes to the maintenance of intracellular tonicity and the resting cell membrane potential. These molecules which are either positive or negative ionic charge conduct an electric current and help to balance pH and acid-base levels in the body. Bicarbonate is the main anion in the extracellular fluid and helps to regulate blood acidity (pH). The increase or decrease in bicarbonate concentration results in acid-base disorder.[7] Since extracellular fluid osmolality and volume are determined by sodium content, this ion plays a key role in water and electrolyte regulation. In this regard, the biochemical derangement in children with dehydration may be hyponatraemic, isonatraemic or hypernatraemic.[8] Other biochemical disturbances observed include hypokalaemia and metabolic acidosis. Electrolyte disturbances are established risk factors for diarrhea-related deaths.[9] Serum electrolyte measurement is usually unnecessary in children with mild to moderate dehydration. However, laboratory measurements of serum electrolytes are recommended in patients with severe dehydration.[10] Electrolytes also facilitate the passage of fluid between and within cells and play a part in regulating the function of the neuromuscular, endocrine and excretory systems. Abnormal electrolytes with acute diarrhoea are common, it may be unrecognize and results in morbidity and mortality. Presence of different types of electrolyte disorders is associated with significant increase in mortality rates among children with diarrhea.[11] A study conducted in 2010 in Dhaka Shishu(Children) Hospital showed that electrolyte disturbances in AWD was associated with increased morbidity, with hyponatremic dehydration in 15% cases.[12] Electrolyte disorders may remain unrecognized and result in increased morbidity and mortality. Timely recognition, a high index of suspicion, and a thorough understanding of common electrolyte abnormalities is necessary to ensure their correction.[13]

No recent studies from this hospital exist regarding the electrolyte and acid-base disturbances occurring in a child suffering from AWD with moderate to severe dehydration. The present study was undertaken to ascertain the frequency of different types of electrolyte and acid-base disorders among the children with diarrhea having moderate and severe dehydration.

Materials and Methods

This cross sectional study was carried out in Observation and Referral Unit of Dhaka Shishu (Children) Hospital from June 2018 to December 2018. Children below five years of age who came with acute diarrhoea having history of loose motion at least three episodes in 24 hours of less than 14 days were included in the study after their parent's consent. Those children who have diarrhoea lasting more than 14 days and those having associated other diseases such as protein energy malnutrition were excluded. Each child with acute diarrhoea was then assessed by taking history from mother/caregiver, performing physical and systemic examination.

Dehydration status was assessed and moderate and severe dehydration was included in the study. After admission, 2ml of whole blood was collected after aseptic measures at the time of insertion of cannula before giving intravenous fluids. Electrolyte analyzer using ion selective electrodes were used to measure serum levels of Na and K while arterial blood was also taken for blood gas analysis. The data was analyzed statistically through SPSS version 20.0.

Results

Total 125 cases of AWD with moderate to severe dehydration was analyzed and among them 35.2% were below 1 year of age, 44.8% were 1-2 years of age and 20% were 3-5 years of age (Table I).

Table I

Distribution of the study patients by age (N=125)

Age (in years)	Number	Percentage
<1	44	35.2
1-2	56	44.8
3-5	25	20

Among the AWD cases 98(78.4%) had moderate dehydration whereas 27(21.6%) had severe dehydration. Hyponatremic dehydration was present in 41(32.8%) cases among them 30.6% in moderate dedydration and 40.4% in severe dehydration cases. Hypokalemia was present in 54(43.2%) cases among them 42.86% in moderate dedydration and 44.44% in severe dehydration cases. Metabolic acidosis was present in 38(30.4%) cases among them 28.57% in moderate dedydration and 37.04% in severe dehydration cases (Table II).

Mean serum sodium in moderate dehydration was 135.22±7.51 and 132.86±4.26 in severe dehydration. Mean serum potassium was 3.52±0.47 in some dehydration and 3.36±1.15 in severe dehydration. The comparison of mean serum sodium and potassium of the children with moderate and severe degrees of dehydration did not attain statistical significance, p=0.38 and p=0.57, respectively. However, there was a significant difference in bicarbonate concentration among moderate and severe dehydration cases (p=0.02) (Table III).

Table II

Electrolyte and acid-base status according to different stages of dehydration (N=125)

		Moderate Dehydration (n=98) (%)	Severe Dehydration (n=27) (%)	Total (%)
Na	Normal	59(60.20)	13(48.15)	72(57.6)
	Hyponatremia (<135 mmol/L)	30(30.61)	11(40.74)	41(32.8)
	Hypernatremia (>145 mmol/L)	9(9.19)	3(11.11)	12(9.6)
K	Normal	54(55.10)	13(48.15)	67(53.6)
	Hypokalemia (<3.5 mmol/L)	42(42.86)	12(44.44)	54(43.2)
	Hyperkalemia (>5.5 mmol/L)	2(2.04)	2(7.41)	4(3.2)
Metabolic acidosis	Absent	70(71.43)	17(62.96)	87(69.6)
	Present	28(28.57)	10(37.04)	38(30.4)

Table III

Mean electrolyte and acid-base level in moderate and severe dehydration (N=125)

Patient data	Total	Moderate dehydration n=98	Severe dehydration n=27	p value
Serum Sodium (mEq/l)	134.08±5.88	135.22±7.51	132.86±4.26	0.38
Serum Potassium (mEq/l)	3.44±0.81	3.52±0.47	3.36±1.15	0.57
Bi-carbonate (mEq/l)	16.3±4.32	17.60±4.12	15.06±4.52	0.02

Data was expressed as Mean±SD; p value <0.05 is considered as significant

Discussion

This study included 125 patients for electrolyte and acid-base disturbances who presented with AWD with moderate to severe dehydration in less than five years of age. Most of the patients were below 24 months of age. Incidence of diarrhea is higher in this age group. Jotsna et al[12] also found higher incidence at age group of 6-11 months in Bangladesh. We found mean serum sodium 134.08±5.88 mEq/l, while potassium was 3.44±0.811 mEq/l. Nowrouzi et al[14] found mean sodium 137±10.3 mEq/l, while the mean serum potassium was 4.4±1.2 mEq/l. Mean serum sodium in moderate dehydration was 135.22±7.513 mEq/l and 132.86±4.263 mEq/l in severe dehydration. Mean serum potassium was 3.52±0.473 mEq/l in moderate dehydration and 3.36±1.153 mEq/l in severe dehydration. Mean serum sodium and potassium of the children with moderate and severe degrees of dehydration did not attain statistical significance. Okposio et al[15] also did not found statistical significant difference in serum sodium and potassium level among moderate and severe dehydration cases.

The common abnormality was hypokalemia in 42.86%, hyponatremia in 30.61% followed by hypernatremia in 9.6% and hyperkalemia in 2.04% cases. Babar et al[16] found hypokalemia in 43.7%, hyponatremiain 5.7%, hyperkalemia in 4.6% and hypernatremia in 2.9%. Another study in Bangladesh reported frequency of hyponatremia and hypokalemia 27.8% and 47.5% respectfully.[17] This is due to loss of sodium in diarrhoea while potassium loss due to bicarbonate loss in diarrhoea. Pizzoti et al[18] found hyponatremia in 34% of admitted patients. The most common electrolyte abnormality in our study was hypokalemia which was present in 42.86% cases but Greenbaum et al[19] in their study found only 14% case were hypokelemic.

Acid-base disturbances are also common findings in children with acute diarrhoea especially metabolic acidosis. The most common explanations for the occurrence of metabolic acidosis in acute diarrhoea include bicarbonate loss in stool, ketone production from starvation, and lactic acid production from decreased tissue perfusion in hypovolemia. Decreased renal perfusion also causes a decreased glomerular filtration rate, which, in turn, leads to decreased hydrogen (H^+) ion excretion.[20] This study found metabolic acidosis in 28.57% which is comparable with 27.6% metabolic acidosis found by Babar et al.[16] Narchi et al[21] found 59.5% metabolic acidosis, and with increasing levels of dehydration, there was a concomitant reduction in serum bicarbonate concentration. The difference was more significant between moderate and severe but less so between mild and moderate. There was a significant difference in bicarbonate concentration among moderate and severe dehydration cases (p=0.02) in this study. Okposio et al[15] found statistical significant difference in bicarbonate concentration among severe dehydration than moderate dehydration.

Conclusion

Hyponatremia and hypokalamia was the commonest electrolyte abnormality among moderate to severe dehydration with AWD. Mean serum sodium and potassium of the children with moderate and severe degrees of dehydration did not attain statistical significance, but bicarbonate concentration was significantly low in severe dehydration.

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ORIGINAL ARTICLE

C Reactive Protein Response in Severe Acute Malnutrition with Infection

Ahmed Rashidul Hasan[1], Lt Col Kamrun Nahar[2], Salahuddin Mahmud[3], Emdadul Haque[4], Syed Shafi Ahmed[5]

Abstract

Background: *Nearly half of all deaths in children under-five are attributable to malnutrition, translating into the loss of about 3 million young lives a year. The interaction between malnutrition and infection can create a potentially lethal cycle of worsening illness and deteriorating nutritional status. They have altered defense mechanisms during an early infections process, with an increased synthesis of some acute phase proteins including CRP.*

Objectives: *Objective of the study was to identify whether CRP response is helpful in early detection of infection in severe SAM. It may also help to reduce childhood mortality associated with SAM.*

Methods: *This cross-sectional study was conducted with total 50 SAM patients who were admitted in the Gastroenterology Hepatology and Nutrition unit of Dhaka Shishu (Children) Hospital from October 2010 to March 2011. Immediately after admission, clinical evaluation and management was started after sending several investigations along with serum CRP. Re-evaluation of serum CRP was done approximately after 7 days. Data were analyzed by using SPSS version 24.*

Results*: Among the 50 SAM patients, 29 patients were presented with oedema(group-A) and 21 patients were without oedema (group-B). Majority (40) were below 2 years of age with male predominance. Thirty-five patients were partially immunized [69% in group-A and 71.4% in group-B]. During initial assessment, 46% children were hypothermic and 76% were hypoglycemic. Nutritional status (z score) weight-for-age, height/length-for-age, weight for height/length in group-A were -4.56±1.00, -4.27±1.97, -2.71±0.97 and in group-B were -4.65±0.78, -5.06±2.34, -2.58±1.00 respectively. Pneumonia (42%) and diarrhoea (36%) were more common. Increased WBC count was found in 80% patients; and only 10% had low hemoglobin level (<5 gm/dl). Majority (44%) of them had pulmonary infection which was found in their chest X-rays. Immediately after admission serum CRP were high [mean CRP 39.44(±16.04)] in all most all patients, irrespective of their types of malnutrition. After 7 days of management, their CRP became normal [07.24 (± 2.75)], p=<0.001. Mean CRP was less [34.90 (±16.60)] in group-A than in group-B [45.72 (±13.16)] on admission and the finding was statistically significant, p=<0.001.*

Conclusion: *Plasma level of CRP constitute a good screening test for the presence of infection in malnourished children and act as a sensitive indicator of recovery from infection and malnutrition.*

Keywords: *Severe acute malnutrition (SAM), C reactive protein (CRP).*

1. RMO, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Dhaka Shishu (Children) Hospital.
2. Classified Specialist, Paediatric Oncology, CMH Dhaka.
3. Associate Professor, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital.
4. Register, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Dhaka Shishu (Children) Hospital.
5. Professor & Head, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital.

Correspondence to: Dr. Ahmed Rashidul Hasan, RMO, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Dhaka Shishu (Children) Hospital. Cell: 01711949924, E-mail: upal.ah@gmail.com

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Introduction

At least 1 in 3 children under five years of age is not getting the proper nutrition they need to grow well, and 1 in 2 suffers from hidden hunger; particularly in crucial first 1,000 days from conception to child's second birthday and often beyond. An increasing number of children and young people are surviving, but far too few are thriving because of malnutrition, undermining the capacity of millions of children to grow and develop to their full potential.[1] Severe acute malnutrition limits the development potential of a country, and is strongly associated with increased mortality, morbidity, reduced cognitive performance and compromised productivity among its population.[2]

Over the years undernutrition rates remain still alarming; stunting is declining too slowly while wasting still impacts the lives off far too many young children.[3] Even in the year 2020, WHO estimated that globally 47 million children under 5 years of age are wasted, 14.3 million are severely wasted and 144 million are stunted. Around 45% of deaths among children under-5 years of age are linked to undernutrition. These mostly occur in low and middle-income countries.[4] Malnutrition puts children at a greater risk of dying from common infections, increases the frequency and severity of infections, and delays recovery. This interaction creates a potentially deadly cycle of deteriorating health and worsening nutritional status.[3]

The vast majority of malnourished children live in developing regions, mainly in Asia and Africa.[4,5] WHO estimates in 2019 in South-East Asia about 4.7 million under-5 children were moderately and severely wasted (<-2SD) and about 2 million were severely (<-3SD) wasted. About 13.9 million children were moderately and severely stunted (<-2SD) (according to median weight-for-height and height-for-age of the WHO Child Growth Standards).[6] National Guidelines for the Management of Severe Acute Malnourished Children in Bangladesh (July 2017) defined severe acute malnutrition (SAM) by the presence of severe wasting and/or bipedal oedema. A child aged 06-59 months is classified as severe acute malnourished if she/he has one or more of the following: (a) Mid-upper arm circumference (MUAC) <115 mm, (b) Weight-for-length Z score (WLZ) <-3, or Weight-for-height z-score (WHZ) <-3, (d)Bipedal oedema (Kwashiorkor, Marasmic-kwashiorkor, Marasmus). A child less than 6 months old is classified as SAM when one or more of the following: (a) WLZ <-3 (b) Bipedal oedema (c) visible wasting is present.[7]

The scenario of Bangladesh is much frightening as it possesses a major bulk of malnourished children of the developing countries though the situation is slowly improving here from ninties.[8] Severe acute malnutrition affects 450,000 children, while close to 2 million children have moderate acute malnutrition.[9] A great deal has been achieved to improve children's lives; moderate and severe underweight prevalence became 22.6% and moderate and severe stunting became 28% in recent year (2019).[10] In recent (2018-1019) database from National Institute of Population Research and Training (NIPORT) and ICF reported in WHO-UNICEF showing severe wasting 1.5 million, moderate and severe wasting 8.4 million, stunting 30.8millions, 219 million underweight among the 14516.61 million under 5 children of Bangladesh.[11] But still in 2019, child mortality rate for Bangladesh was 30.8 deaths per 1,000 live births; majority reason behind is malnutrition.[12]

In majority cases deaths of malnourished children are associated with infection like pneumonia, septicemia, diarrhoea, particularly mismanagement of diarrhoea with dehydration, sepsis and hypovolumic shock, severe anemia, electrolytes imbalance, vitamin-A deficiency, hypoglycemia, hypothermia etc.[13-15] Among them diarrhoea and pneumonia are very much prone to develop and their incidence of severity, duration of illness, complications are higher in malnourished children.[16-19] Immunodeficiency is common in malnourished children and breaks down the host resistance in large segments. The most existent abnormality detected in various studies has been (1) Impairment in cell mediated immunity (2) Children with SAM are difficult to sensitize by repeated antigens (3) Even delayed hypersensitivity reactions that recall previous sensitization are also delayed. The underlying mechanism include lymphopenia, reduce number of T-lymphocytes in peripheral blood, impaired response to mitogen and antigen, decreases lymphokine production and serum inhibition.[13]

It is well established that nearly every aspect of the body's defense system is damaged by severe malnutrition.[20] But it is not clear whether malnourished infants can mount a comprehensive acute phase protein (APP) response. The characteristic response to an infective stress includes increased plasma concentrations of APP, which play important role in host defense.[21]

Acute-phase protein is defined as a protein whose plasma concentrations increase during certain inflammatory disorders.[22] They are C-reactive protein (CRP), serum amyloid-A, fibrinogen and alpha-1-acid glycoprotein.[23] Perhaps the best known of them is CRP[22], a plasma protein that is produced from liver and its level rises in response to inflammation.[23,24] It is primarily induced by the IL-6 action on the gene responsible for transcription of CRP during the acute phase of an inflammatory/ infectious process.[23] These plasma proteins have role in combating infections, including modulating T-lymphocyte function and the complement system, scavenging haemoglobin and protecting the integrity of healthy tissues against the effect of proteases produced by the pathogens or release from damaged cells.[21,24]

In a study of marasmic children with infection showed that the kinetic mechanism used in mounting an APP response included alterations in both the rate of synthesis and catabolism of protein.[25] Children with kwashiorkor however differ from those with marasmus is having slower rates in whole body protein breakdown, which may reduce the availability of endogenous amino acids for APP synthesis.[26] Manary et al[27] found increased CRP in both oedematous and non-oedematous malnutrition with no significant difference but Amnesty et al[28] found high CRP levels in children with marasmus.

The present study is carried out to determine CRP response in SAM children with infection to see whether they can mount a general APP response and to compare the response between oedematous and non-oedematous SAM. However published evidences in favor of our observation are scanty and we believe it may help in early accurate detection of infection and reduce childhood mortality associated with SAM.

Materials and Methods

This cross sectional study was conducted with severe acute malnlurished patients who were admitted in Gastroenterology Hepatology and Nutrition unit of Dhaka Shishu (Children) Hospital from October 2010 to March 2011. Total 50 patients who fulfilled the following inclusion and exclusion criteria were enrolled in the study. Inclusion criteria were: a) Age: 6 months-59 months b)Irrespective of sex c) Anthropometric measurement fulfill WHO classification when the child present a ratio of - i) W/H <-3 SD with oedema ii) W/H <-3 SD without oedema d) Presence of evidence of infection [Diagnosis of infection required one or more of the following on admission - 1) WBC count >11X10^9/L, 2) Hyperthermia/Hypothermia (body temperature >37°C or <35.5°C) and Hypoglycemia(<3mmol/L or 54 mg/dl), 3) Suggestive Chest X-ray, 4) Positive growth in blood and urine culture, 5) Diagnosis of specific type of infection based on symptoms and signs. Exclusion criteria: a) Patient with secondary malnutrition due to other causes like DM, hyperthyroidism, congenital anomalies or cerebral palsy and b) patient with oedema due to other diseases like CCF, NS, cirrhosis of liver, protein loosing enteropathy.

For each child a semi-structured questionnaire was prepared which included age, sex, nutritional status, birth history, immunization status, previous illness, socio demographic, maternal education, nutrition, psychosocial history like monthly family income of parents. Anthropometric assessments were done immediately after admission. Weight was confirmed by two observers to avoid interpersonal variation. Weight was measured by standard weighing scale, MISAKI (made in Japan), capacity 12 kg (26 Ibs), GRAD = 0-10kg, precision - 50 gm, Accuracy- 5gm. Length/height was measured with locally constructed WHO recommended wooden board (infantometer) in bear leg. Patients <85 cm in length, or children too weak to stand, their length were measured while lying down. If the child was d"85 cm but could not be measured standing, 0.5 cm was subtracted from the supine length. Reference standard was taken as 50th centile of National Centre for Health Statistics (NCHS). Weight for height and height for age was converted into Z score after standardizing with NCHS reference data. Clinical varieties were noted according to WHO classification. Accuracy was carefully maintained and inter-observational error was minimized by involving trained personnel's.

In all children clinical evaluation was done immediately after admission by physical examination then investigation were sent like CBC, RBS, chest X-ray, parasitological examination of smear blood for malaria, serum electrolytes, serum total protein, serum albumin, routine analysis of stool and urine. Blood, urine, stool samples were sent for culture as per need to diagnose infection. Then serum CRP measurement had done to whom infection was suspected on the basis of clinical, biochemical and

radiological criteria before starting nutritional therapy and medical treatment.

Approximately 7 days after admission a new blood sample for CRP was collected. One ml of venous blood was required to determine serum CRP by using CRP reagent. This synthetic particle coated with antibody to CRP, aggregate in presence of CRP in the sample. The increase in turbidity which accompanies aggregation is proportional to the CRP concentration. Accurate result had collected by spectophotometric reading using automatic analyzer machine (Dimension RX max) in clinical biochemistry laboratory in Dhaka Shishu (children) Hospital. A measurement of serum CRP >10 mg/l was considered as infection marker.

For every child after immediate evaluation and collecting blood sample, management has been given according to National Guideline for the severely malnourished children in Bangladesh. For nutrition F-75 formula were started containing 75 Kcal/100 ml,and were treated with antibiotics (Ampicillin ±Gentamycin). All these investigations were done in the pathology, microbiology and radiology department of Dhaka Shishu (Children) Hospital. Informed written consent was taken from parents. Reassurance was given to parents regarding study and all investigations were done at free of cost. Clearance was taken from the ethical review committee and permission of the hospital authority to use the machine. Data entry and analysis was done by using SPSS version-24.

Results

All the 50 severe acute malnourished patients were divided in group-A (n=29) who were severely malnourished with oedema and group-B (n=21) who were severely malnourished without oedema. Majority of study population were below 2 years of age, 25(50%) population from group-A and 15(30%) from group-B and their mean age was11.96 (± 8.93) month in group-A and 16.14(±14.29) month in group-B. Male were predominant in both groups (group-A 58.6% and group-B 71.4%). Most of the children came from slum area and belong to poor family (£5000taka) in both group-A(72.4%) and group-B (66.7%). Majority of children were partially immunized (69% in group-A and 71.4% in group-B) (Table I).

Table I

Socio-economic and socio-demographic characteristic of study population (N=50)

Characteristics	Group-A (Oedematous SAM)	Group-B (Non oedematous SAM)
Age		
6-23 months	25 (50%)	15(30%)
24-59 months	4(8%)	6(12%)
Mean age group (age in month)	11.96 (± 8.93)	16.14 (±14.29)
Gender		
Male	17(58.6%)	15(71.4%)
Female	12(41.4%)	06(28.6%)
Socio-economic status		
Poor (£5000)	21(72.4%)	14(66.7%)
Lower Middle (5000-10000)	05(17.2%)	03(14.3%)
Middle (10000-15000)	03(10.3%)	04(19.0%)
Residence		
Rural	7 (14%)	7(14%)
Urban	8(16%)	4(8%)
Slum	14 (28%)	10(20%)
Immunization		
No immunization	02(6.9%)	03(14.3%)
Partially Immunized	20(69)%	15(71.4%)
Completely Immunized	07(24.1%)	03(14.3%)

During initial assessment of the study population total 23(46%) children were hypothermic; 14(48.3%) from group-A and 9(42.8%) from group-B. Whereas total 10(20%) children of which 4(13.8%) from group-A and 6(28.6%) from group-B were hyperthermic by rectal thermometer (Fig. 1) and similar result were found by axillary thermometer. At admission in group-A hypoglycemia was present in 38(76%) cases, in group-B hypoglycemia was present in 22(76%) cases. Majority of study population were hypoglycaemic in both groups (Fig. 2).

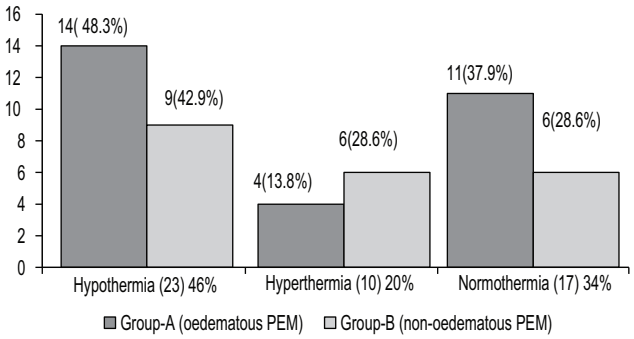

Fig 1 *Distribution of SAM patients by their thermal status (Rectal)*

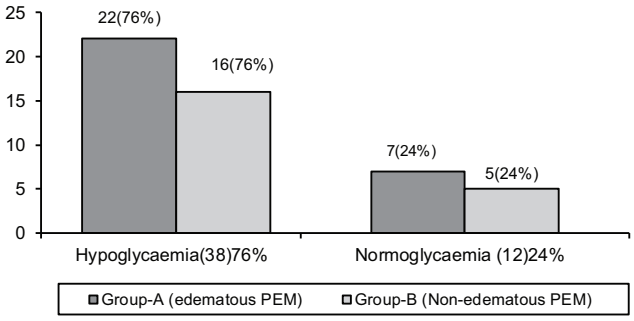

Fig 2 *Distribution of study population by glycaemic status*

In Group-A Z score (weight for age, height/length for age, weight for height/length) were -4.56±1.00, -4.27±1.97, -2.71±0.97 and in group-B were -4.65±0.78, -5.06±2.34, -2.58±1.00 respectively (Table II). Complete blood picture showed that 40 out of 50 study population had WBC count >11000/cu mm; but only 10% had hemoglobin level <5 gm/dl. Majority (44%) of them had pulmonary infection in their chest X-rays (Table III).

Table II

Mean values with standard deviation of anthropometric assessment of study population (N=50)

Study population		Wt for Age %	Wt for Age Z score	Ht for Age %	Ht for Age Z score	Wt for Ht / length%	Wt for Ht /length Z score
Group-A	Mean	59.41	-4.56	84.48	-4.27	73.25	-2.71
(Oedematous SAM)	±SD	±10.96	±1.00	±8.21	±1.97	±20.53	±0.97
Group-B	Mean	51.28	-4.65	83.57	-5.06	84.00	-2.58
(Non-oedematous SAM)	±SD	±9.86	±0.78	±10.59	±2.34	±21.23	±1.00

Table III

Distribution of SAM patients by laboratory findings on admission

Laboratory findings	No of patients	Percentages
Hb (gm/dl)		
<5	5	10
5-10	45	90
WBC(/cumm)		
<12000	10	20
12000-20000	16	32
21000-30000	04	08
>30000	20	40
Chest X-ray findings		
Normal	10	20
Pulmonary infection	22	44
Not done	18	36

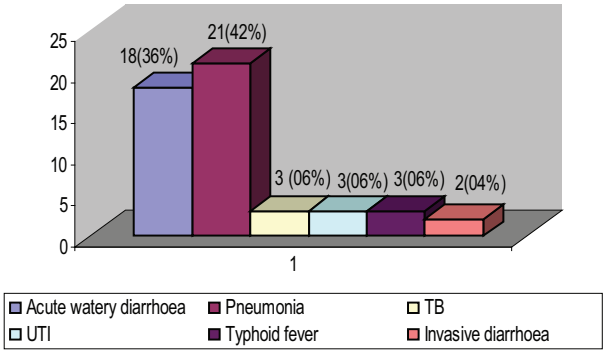

Fig 3 Distribution of SAM patients by types of infection (N=50)

Fig 3 *Distribution of SAM patients by types of infection*

Pneumonia (42%) and diarrhoea (36%) were more common among the study population (Fig 3).

Table IV
Distribution of study population by CRP values on admission and after 7 days (N=50)

CRP value (mg/L)	On admission		After 7 days	
	Group-A (Oedematous SAM) n=29	Group-B (Non-oedematous SAM) n=21	Group-A (Oedematous SAM) n=29	Group-B (Non-oedematous SAM) n=21
0-5	00(00%)	00(00%)	09(31.04%)	11(52.38%)
6-9	01(3.49%)	00(00%)	20(68.96%)	10(47.62%)
10-29	16(55.17%)	00(00%)	00(00%)	00(00%)
30-49	06(20.69%)	06(28.57%)	00(00%)	00(00%)
50-70	06(20.69%)	15(71.43%)	00(00%)	00(00%)

Table V
Mean CRP value of the study population on admission and after 7 days (N=50)

	CRP on admission	CRP after 7 days	p value
Mean (±SD)	39.44 (± 16.04)	07.24 (± 2.75)	<0.001

Table VI
Mean CRP value in two groups of study population on admission (N=50)

CRP	Group-A (Oedematous SAM) Mean (±SD)	Group-B (Non-oedematous SAM) Mean (±SD)	p value
	34.90 (± 16.60)	45.72 (± 13.16)	0.01

During admission out of 29 patients in group-A, 28 had CRP value >10 mg/L and in group-B out of 21 patients all had CRP value >10 mg/L. That is majority of malnourished children had high CRP value on admission irrespective of their type of malnutrition. After 7 days of given management, follow up CRP level done and revealed all patients in both groups had normal CRP value (<10mg/L) (Table IV). Mean CRP value were assessed; on admission it was 39.44(±16.04) and after 7 days (while infection controlled) was 07.24(± 2.75). CRP value was high in severe malnourished child on admission when associated with infection but significantly low on recovery (p <0.001) (Table V). Mean CRP value of group-A was less [34.90 (±16.60)] than in group-B [45.72 (±13.16)] on admission and finding was statistically significant (p=<0.01) (Table VI).

Discussion

Malnutrition is an important public health problem; it is a world health crisis. Millions of people are suffering from different forms of malnutrition. Nutrition is the main cause of death and disease in the world. The developmental, economic, social and medical impacts of malnutrition are serious and lasting.[29]

Globally nearly 47 million children of under-five suffer from severe acute malnutrition and about 45% of under-five death in the world is associated with malnutrition.[4] Nearly half of all deaths in children under 5 are attributable to undernutrition; undernutrition puts children at greater risk of dying from common infections, increases the frequency and severity of such infections, and delays recovery which contributes to an estimated 3 million deaths/year.[3] The prevalence of childhood malnutrition in Bangladesh is among the highest in the world. Even

though we have achieved significant progress in reducing the proportion, the magnitude of the problem still is of great concern.[30,31]

The characteristic response to an infective stress includes increased plasma concentration of CRP, a member of the class of acute-phase reactants, as its levels rise dramatically during inflammatory process in body.[23] This study was unique in its kind which attempted to reveal CRP response in severe acute malnurished children associated with infection to determine whether oedematous SAM child can mount a general acute phase protein (APP) response and also to compare the response in children with oedematous SAM and with non oedematous SAM.

All severely malnourished children are at risk of hypoglycemia and hypothermia; which usually occur together and signs of infection are frequently associated with a high fatality.[32] Present study reflected that hypoglycemia found in majority cases (76%) in both groups of study population; similar to the findings of other authors.[33] Yokoyama et al[34] found 26% of severely malnourished children manifested hypothermia. Present study reflected that hypothermia was found in 48% cases in group-A and 43% cases in Group-B of study population.

This study reflected that diarrhea (36%) and pneumonia (44%) were more common type of infection and frequent association with severely malnourished children. Different study showed diarrhea and pneumonia were very much prone to developed in malnourished children.[16-19] On admission all the children had associated infection which was further supported by an elevated total count of WBC and X-ray findings. Here 32% cases had WBC count between >10,000-20,000)/cumm, and 40% had>30,000/cumm. Ninety percent cases were anemic and maintained Hb level between 5-10gm/dl. About 44% cases had pulmonary infection.

The synergistic malnutrition-infection complex has significant effects on child health.[35] This study revealed 97% cases of group-A and 100% cases of group-B had high CRP concentration on admission in association of infection, which suggests severely malnourished child are capable of mounting an APP response. As shown by Golden et al[35] and Tomkins et al[36] whole body protein synthesis rate is reduced in the infected malnourished children compared with both infected and uninfected well-nourished children, suggesting that the malnourished children may be mounting an APP response through mechanisms other than stimulation of synthesis rate.

Morlese et al[25] suggested that in severe malnutrition APPs increased due to changes in both rate of synthesis and catabolism of these proteins. This study finding of higher APP response of malnourished children is also reported by other authors.[25,37] In the present study after one week of dietary and anti-microbial treatment there was significant drop in the plasma levels of CRP in all cases when the infection had cleared but still malnourished, as like the finding that was previously reported by others.[38] We found mean CRP value was 39.44(±16.04) on admission and after one week 07.24(±2.75),this result was statistically significant (P=<0.001).

Reid et al[38] observed children with oedematous SAM can mount an APP response to infection that is similar with non-oedematous SAM, but the magnitude of the response is less in children with oedematous SAM. The weaker response in oedematous group is not surprising, because other aspect of host defense, relating to immune structure and function, are more compromised in children with oedematous SAM than those with non-oedematous SAM. The present study also reflected that mean CRP value in group-B (non-oedematous) cases were much higher 45.72(±13.16) than in group-A (oedematous) cases 34.90(±16.60) and the result was statistically significant (p <0.01).

Fifty percent of the cases from group-A and 30% cases from group-B were from 06 months to 23 months of age and mean age was 11.96(±8.3) months in group-A and 16.14(±14.29) months in group-B. Amin et al[39] showed majority (77%) of the malnourished children were below 2 years of age. Roy et al[17] showed, age was one of the significant determinants of childhood nutrition. The younger children (<2 years) had significantly higher level of severe malnutrition. As the age of these children grows up the proportion of children with malnutrition decreases. Among study population, male were predominant than female, as like other study.[39] It might be due to the fact that parents were more concerned about male children. Most of the children in this study belonged to poor socio-economic class. Majority of them from urban slum with monthly family income were below 5000 TK. This was in accordance with a similar report from Shakur et al[40] and Awal et al[41] showed that the relationship between malnutrition and poverty

exists in a vicious cycle. Poverty generates malnutrition and malnutrition generates poverty and diseases.

These children's immunization statuses were very poor, only 24% from group-A and 14% from group-B were completely immunized. Islam et al[42] found similar result. Their anthropometric assessment showed that mean nutritional status in Z score (weight for height/length) of group-A was SD-2.71±0.97 and in group-B was SD-2.58±1.00 which found similar like WHO references.[6] This study was a hospital base single centered study, it has chance of over representation which could not reflect general population and may not represent the similar situation in the whole population of the country. This study was a non-randomized cross-sectional study. A broad base longitudinal cohort study could be more meaningful.

Conclusion

In conclusion, plasma level of CRP constitutes a good screening test for the presence of infection in severely malnourished children and that APP is a sensitive indicator of recovery from infection and malnutrition.

Acknowledgement

This study was done free of cost in Gastroenterology Hepatology and Nutrition unit in Dhaka Shishu (Children) Hospital, Dhaka.

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ORIGINAL ARTICLE

Pattern of Burn Injury in Children Presented to Dhaka Shishu (Children) Hospital

Muhammad Rashedul Alam[1], Md. Saif Ullah[2], Prosanto Kumar Biswas[3]

Abstract

Background: *Children are mostly affected in burn injury at our country like other low and middle income countries (LMICs). Approximately 90% of the burns occur in under developed countries, which generally lack the necessary infrastructure to reduce the incidence and severity of burns.*

Objectives: *This study was done to investigate the pattern of burn cases admitted to Dhaka Shishu (Children) Hospital (DSH).*

Methods: *This was a retrospective study conducted over the period of one year from January 2019 to December 2019 at Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh. The data was collected from the patients record section of the hospital. Patients characteristics (e.g. age, sex), causes and severity of injury, outcome, hospital stay and seasonal variation were analized in this study.*

Results: *A total of 91 patients were admitted during study period of one year. This study consisted of 53 male patients (58.24%) and 38 female patients (41.76%) with male to female ratio of 1.3:1. The most frequently hospitalized burn patients were in the age group 3-5 years, which accounted for 30.77% of patients. Burns were more common during winter season followed by autumn season, with 43 cases (47.25%) and 18 cases (19.78%) respectively. The highest number of admissions was during the month of December. Scald burn was the most common cause of burn injury in our study which accounted for 83 cases out of 91 cases (91.2%). Flame burn occured in 3(3.29%) patients. There were 2 cases of electric burn and 2 cases of contact burn during this study period. One patient was with chemical burn. Scald burn was the most common cause of burn injury in this study which accounted for 83 cases out of 91 cases (91.2%). Flame burn occured in 3(3.29%) patients. There were 2 cases of electric burn and 2 cases of contact burn during this study period. One patient was with chemical burn.*

Conclusion: *The most frequently hospitalized burn patients were in the age group 3-5 years and more common during winter season. Most of the burn occured in children are scald in our country due to accidental fall of worm liquid. Superficial epidermal and dermal burns are treated conservatively, but deep burns may require surgical treatment.*

Keywords: *Burns in children, scalds in children, seasonal variation of burn.*

1. Assistant Professor, Burn and Reconstructive Unit, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh.
2. Associate Professor, Burn and Reconstructive Unit, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh.
3. Registrar (Incharge), Burn and Reconstructive Unit, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh.

Correspondence to: Dr. Muhammad Rashedul Alam, Assistant Professor, Burn and Reconstructive Unit, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh. Cell: 0171200577, E-mail: dr.mrapiash@gmail.com

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Introduction

Burn injury is one of the most common injuries around the world. Children are mostly affected in burn injury in our country like other low and middle income countries (LMICs). An estimated 180,000 deaths every year are caused by burns globally in LMICs.[1,2] In the world nearly 90% of burn deaths occur in lower middle or low income countries (LMICs), while only 3% of burn deaths happen in high income countries (HIC).[3] Approximately 90% of burns occur in under developed countries, which generally lack the necessary infrastructure to reduce the incidence and severity of burns.[4] Dhaka Shishu (Children) Hospital (DSH) has a separate 14 bedded burn unit which was started in 1999, is one of the oldest and well-established burn center that serve children. Thus the rationale of this study was to investigate the pattern of burn cases admitted to DSH, to maximize the efficiency of our burn unit to know our defects and to reduce the mortality rates.

Materials and Methods

This was a retrospective study conducted over a period of one year from January 2019 to December 2019 at Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh. The data was collected from the patients record section of the hospital. Patients characteristics (e.g. age, sex), cause and severity of injury, outcome, hospital stay and seasonal variation were examined in this study. The research proposal was presented to the hospital ethical committee and was approved. The data were entered in a Microsoft Excel spreadsheet and analyzed.

Results

A total of 91 patients were admitted in DSH burn unit. The age of burn patients were from neonate to 18 years. Study consisted of 53 male patients (58.24%) and 38 female patients (41.76%) with male to female ratio of 1.3:1. The most frequently hospitalized burn patients were in the age group 3-5 years, which accounted for 30.77% of patients. Only one neonate was found in this study (Table I).

Burns were more common during winter season (December-February) followed by autumn season (September-November), with 43 cases (47.25%) and 18 cases (19.78%) respectively. The highest number of admissions was during the month of December (Table II).

Scald burn are most common cause of burn injury in our study which accounted for 83 cases out of 91 cases (91.2%). Flame burn occured in 3(3.29%) patients. There are 2 cases of Electric burn and 2 cases of contact burn during this study period. One patient with chemical burn (Table III).

Table I
Distribution of age and sex

Age	Male	%	Female	%	Total	%
Neonate	1	1.1	0	0	1	1.10
1-12month	5	5.49	4	4.4	9	9.89
1-3 years	9	9.89	8	8.79	17	18.68
3-5 years	15	16.48	13	14.29	28	30.77
5-10 years	14	15.39	8	8.79	22	24.18
>10years	9	9.89	5	5.49	14	15.38
Total	53	58.24	38	41.76	91	100

Table II
Seasonal variation of burn injury

Season	Month	Number	Percentage
Summer	June-August	5	5.50
Autumn	September-November	18	19.78
Winter	December-February	43	47.25
Spring	March-May	25	27.47

Table III
Causes of burn injury

Type of burn	Male	Female	Number (%)	Average TBSA (%)
Scald	50	33	83 (91.21)	11.4 (10-35%)
Flame	1	2	3 (3.29)	7.1 (5-15%)
Contact	1	1	2 (2.20)	3.3 (4-7%)
Electric	1	1	2 (2.20)	1.7 (1-3.5%)
Chemical	0	1	1 (1.10)	3.2 (3.2%)

Table IV
Management and outcome of burn patient

Management and outcome		Number	Percent
Management	Conservative	89	97.80
	Surgical	2	2.20
Outcome	Improved	88	96.70
	Died	3	3.30
Hospital stay Mean (Range)	Scald (n=83) 9(5-13) days, Flame (n=3) 5(4-9) days, Contact (n=2) 4 (3-5) days, Electrical (n=2) 4(3-5) days, Chemical (n=1) 7(7) days		

In our study the percentage of total burn surface area (% TBSA) ranged from 1% to 35%. Most of them were superficial 84(92.3%) burn and were treated conservatively. Two patients needed surgical treatment due to deep burn. Hospital stay ranged from 4 days to 32 days. The mean hospital stay for scald injury (83 patient) was 9 days, flame burn (3 patients) 5 days, contact burn (2 patients) 4 days, electric burn (2 patients) 4 days and chemical burn (1 patient) 7 days. Among 91 patients admitted in one year 3 patients (3.3%) expired. One patient had 25% of TBSA burn injury aged 4 years 7 months, one patient with 17% of TBSA burn with renal failure aged 9 months, one patient with 15% of TBSA burn with pneumonia and sepsis aged 3years 3 months (Table IV).

Discussion

Burn injury occur over the year but in our study, winter was the most common season for burns which is in agreement with the other studies.[5-7] Some studies reported that summer and spring were the most common season for burn injury.[8] From the findings of our study, a higher incidence of burn patients were found with the low socio-economic condition. In this study, majority of the patients were male, but female were also not rare. Burn injuries represent a major cause of morbidity and mortality throughout the world and its occurrence is not specific to any age group.[3] It was also observed that amongst the paediatric age group, scalds clearly dominate whilst flame burns dominate within the working age group. Similar finding was also reported by the systematic review regarding burns in Nepal and Cosovo.[9] Most of the burn and scald in children in our country is due to accidental fall of hot water, hot milk, hot curry, hot dal, hot water for bathing. Flame burn also occurs but the number is less. Some study shows that flame burn is more in number but is not similar to our study.[10] Analysis of age groups of burn patients show that children are mostly affected by burns which is about 53%. While the age group 0-5 is the most common (41.8%). Data also show that the highest incidence of burns was in the first decade of life (48.4%).[10]

Superficial epidermal and dermal burns are treated conservatively, but deep burns (full thickness) require surgical treatment. The largest number of patients with burns in our clinic were treated conservatively (76.3%), as in South Korea, 80.6%.[11] Although patients with deep burns (third grade) were present in 31% of cases, only 19.3% of our patients were treated surgically.

Burns are preventable public health problem. We believe most of the burn injuries in Bangladesh are caused due to illiteracy, ignorance and lack of effective policy from the government. Medical personnel and government should focus more on prevention program rather than treating the burn patients, identifying the most vulnerable group. Government and health institution should educate people especially in the rural area about burn prevention. We believe the prevention program would be highly beneficial if it can be included in the primary school text book. High-income countries have made a considerable progress in lowering the burn incident, through a combination of educating people and installation of safety measures.

Conclusion

The most frequently hospitalized burn patients were in age group 3-5 years and more common during winter season. Most of the cases of burn found in children are scald in our country due to accidental fall of hot liquid. Superficial epidermal and dermal burns are treated conservatively, but deep burns may require surgical treatment.

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REVIEW ARTICLE

COVID-19 and Children with Congenital Heart Disease: Pandemic Implication

Mohammad Abdullah Al Mamun[1], Manzoor Hussain[2], Rezoana Rima[3]

Abstract

While the global coronavirus crisis worsens, a surprising feature of the disease appears that children might be immune from the worst form of it. Studies suggest that COVID-19 is more likely to infect older adult men, particularly those with comorbidities. There is only limited data detailing the effects of COVID-19 on the pediatric population. Patients with underlying cardiovascular comorbidities are at increased risk of morbidity and mortality from SARS-CoV-2 infection. Certain adult patients with congenital heart disease (ACHD) and with complex congenital heart disease can be considered as high risk for complications related to COVID-19 infection on the basis of decreased functional reserve. While no study on COVID-19 has been included paediatric patients with congenital heart disease, it stands to reason that patients with congenital heart disease can be considered at higher risk for complications from COVID-19. Given the increased risk for severe COVID-19 in adults with underlying cardiac disease, there is concern that patients with congenital heart disease (CHD) may likewise be at increased risk for severe infection, as they are known to have higher risk for complications with viral illnesses including respiratory syncytial virus and influenza.

Keywords: *COVID-19, children, CHD.*

Introduction

An outbreak of pneumonia of an unknown origin developed in Wuhan of Hubei Province, China during December, 2019.[1] By January 7, 2020, Chinese scientists confirmed that the outbreak was caused by a novel coronavirus, renamed as severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2), and the disease is now termed coronavirus disease 2019 (COVID-19).[2-4] On January 30, 2020, WHO declared a public health emergency of international concern (PHEIC) and pandemic on 11 March 2020.[5]

While the global coronavirus crisis worsens, a surprising feature of the disease appears that children might be immune from the worst form of it. Studies suggest that COVID-19 is more likely to infect older adult men, particularly those with chronic comorbidities.[6] There are only limited data detailing the effects of COVID-19 on the paediatric population. A review of 72,314 cases by the Chinese Center for Disease Control and Prevention showed that <1% of COVID-19 cases were in children younger than 10 years.[7] In Bangladesh among confirmed cases 3% of children <10 years were identified as COVID-19.[8] No study described children with congenital heart disease (CHD) and COVID-19, and thus the effect of the virus on this specific patient population is not clear. The mechanism by which children seem less

1. Associate Professor, Division of Neonatal Cardiology, Department of Paediatric Cardiology, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital.
2. Former Head of Paediatric Medicine and Cardiology, Bangladesh Institute of Child Health and Ex-Director, Dhaka Shishu (Children) Hospital.
3. Associate Professor, Department of Paediatric Cardiology, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital.

Correspondence to: Dr. Mohammad Abdullah Al Mamun, Associate Professor, Division of Neonatal Cardiology, Department of Paediatric Cardiology, Bangladesh Institute of Child Health and Dhaka Shishu (Children) Hospital. E-mail: mamundsh@gmail.com
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susceptible to severe infection caused by SARS-CoV-2 has yet to be revealed. It has been theorized that the ACE2 (the binding protein for SARS-CoV-2) in children is not as functional as it is in adults, and thus SARS-CoV-2 is less infectious.[8]

Patients with underlying cardiovascular comorbidities are at increased risk of morbidity and mortality from SARS-CoV-2 infection.[7] Studies so far have not detailed in a granular fashion the risk of individual cardiovascular complications in patients with underlying cardiovascular disease who are infected with SARS-CoV-2. While no studies on COVID-19 have included patients with congenital heart disease, it stands to reason that patients with congenital heart disease could be considered at higher risk for complications from COVID-19. Certain adult patients with congenital heart disease and complex congenital heart disease could be considered high risk for complications related to COVID-19 infection on the basis of decreased functional reserve.[9]

Since this is an emerging infectious disease, there is limited data on the effects of this infection on patients with cardiovascular disease, particularly so for those with congenital heart disease.[10] Importantly, the pandemic has stretched healthcare systems and many care team members are at risk for contracting and possibly transmitting the disease which may further impact the care of patients with congenital heart disease. Despite numerous recently published articles on the topic, understanding of the virus and the disease is incomplete, and robust data specifically in the setting of congenital heart disease are lacking.

Viral effects on the heart and on patients with cardiovascular conditions

Previous coronavirus epidemics (SARS and MERS) showed that they mainly cause pulmonary issues like pneumonia and acute respiratory distress syndrome.[11] They also cause direct myocardial injury and myocarditis caused by both influenza and coronaviruses.[12] Furthermore, patients with underlying heart disease (both congenital or acquired) seem to have increased morbidity and mortality related to viral infections.[13] There are also some data to suggest that patients with underlying heart disease may be more susceptible to contracting coronavirus infection.[14]

COVID-19 and myocardial injury

Mechanism of cardiac injury in COVID-19 and its effects on the cardiovascular system are not fully understood. In some studies, cardiac injury (manifested as an increase in troponin levels) was found in admitted patients and cardiac injury was more common in critically-ill patients.[15-18]

Mechanisms of cardiac injury in COVID-19

- COVID-19 may cause cardiac injury indirectly due to an overwhelming immune inflammatory response and cytokine storm.[19]
- SARS-CoV-2 viral invasion of cardiomyocytes and direct damage via this process, but this has not been proven.[20]
- Severe hypoxia from acute respiratory damage caused by the virus may result in oxidative stress and myocardial injury from increased myocardial oxygen demand in the presence of severe hypoxia due to acute lung injury (ARDS).[10]
- Furthermore, ACE2 is expressed in the heart, and the SARS-CoV-2 virus uses this enzyme as a receptor for entry into the cell.[21] It is unclear that SARS-CoV-2 binding alters ACE2 expression or causes dysregulation of the RAAS (renin-angiotensin-aldosterone system) pathway.

COVID-19 and Kawasaki like disease

Reports of a multisystem inflammatory syndrome (MIS-C) in previously well children temporally associated with COVID-19 infection have emerged.[22] MIS-C shares similarities to severe Kawasaki disease (KD), including the development of giant coronary aneurysms. At least initially, myocardial involvement appears to be reversible and thought to be related to myocardial stunning and edema rather than inflammatory myocardial injury. Thus, although initial cardiac dysfunction may be severe, most of the patients seem to recover their ventricular function. However, the long term prognosis of coronary involvement, and whether the response to therapy is similar to KD, remain to be seen.[23]

COVID-19 and adult congenital heart disease (ACHD)

At present, the number of ACHD patients affected by COVID-19 is unknown. Combining available real-time epidemiological data of confirmed patients with COVID-19[24] with current estimates of CHD prevalence suggests that approximately 4800 ACHD patients currently actively infected in Europe and

about 5600 patients in the USA and Canada as of 22 May 2020. These numbers assume a prevalence of 6.12/1000 adult population (6.16 for the USA)[25,26] and that ACHD patients are infected at a comparable rate as the general population and require confirmation by prospective data. So in Bangladesh we also expect same scenario. Adults with ACHD may be at high risk in the case of COVID-19. Due to the heterogeneity of ACHD and secondary complications, risk profiles are, however, not uniform.

A pragmatic approach is proposed to categorising patients into low-risk, intermediate-risk and high-risk groups.[27]

Infection with SARS-CoV-2 should be suspected in ACHD patients presenting with fever, onset or worsening of dyspnoea, lower than usual peripheral oxygen saturation but also in case of unexplained worsening of ventricular function or new arrhythmia. Rarely these patients may present with overt cardiogenic shock.[28]

Comparison of current and previous oxygen saturations, ECGs, complete blood cell counts, NT-Pro-BNP and troponin may be helpful. A chest X-ray or CT scan may provide additional information in selected patients. Echocardiography should be focused on obtaining information of immediate clinical value such as pericardial effusion or ventricular function in the current situation avoiding prolonged direct physical contact with patients.[29]

Other infections should not be overlooked, and especially endocarditis remains prevalent in ACHD patients.[29]

If ACHD patients are tested positive for SARS-CoV-2, management should be guided by patient risk and clinical status. Parameters of oxygenation, blood pressure, heart rate and ECG should be recorded, and baseline laboratory testing performed. Point of care echocardiographic assessment may be helpful in this situation. Stable patients with low or moderate risk and without signs or symptoms of respiratory or cardiovascular deterioration may be cared at home with supportive measures, instructed to self-isolate and be remotely followed up through teleconsultation. Impairment of lung function is prevalent in ACHD patients and its severity is related to the complexity of the underlying heart defect and the surgical history.[30]

High-risk patients or those with signs of respiratory or cardiovascular impairment require admission ideally at a tertiary ACHD center. Especially patients with complex, cyanotic disease, heart failure and arrhythmias require particular attention. Treatment in patients with cyanotic heart disease should be guided by the relative degree of desaturation compared with baseline and lactate levels rather than absolute oxygen saturation levels. Patients with right heart dilatation or dysfunction are potentially at increased risk of right heart failure as mechanical ventilation and acute respiratory distress syndrome can lead to increase in pulmonary arterial pressures.[27]

COVID-19 and children with congenital heart disease

There are no published studies on COVID-19 in children with congenital heart disease. Thus, all of the current management strategies are extrapolated from what is known about the effect of COVID-19 on adult patients and adult patients with cardiovascular disease. Efforts are under way through the Adult Congenital Heart Association and the International Society of Adult Congenital Heart Disease to gather data on the number of suspected and confirmed cases both in the United States and globally and to better understand outcomes among adult congenital heart disease population.[10] In the absence of data to help guide care it is difficult to make any definitive recommendations.

Risk stratification

Based on observations made in older adults with underlying congestive heart failure, it is likely that patients with underlying CHD may be at risk for more severe disease related to the viral infection. It is important to recognize that there is a broad range of anatomical and physiological abnormalities among patients with CHD, and it is likely that not all are at similar risk for severe disease. In general, patients with impaired ventricular function and those with abnormal pulmonary blood flow/ pulmonary hemodynamics are believed to be at higher risk.[31] Based on anatomy and additional physiological factors including symptoms, exercise capacity, heart failure, pulmonary hypertension and cyanosis, a pragmatic approach is proposed to categorising patients into low-risk, intermediate-risk and high-risk groups.[27,31]

High-risk lesions

- Unpalliated cyanotic CHD.
- Unpalliated shunt lesions with significantly elevated pulmonary blood flow.
- Lesions associated with sequestered lung segments (abnormal venous drainage with arterial supply coming from bronchial vessels).
- Palliated univentricular heart disease.
- Fontan physiology.
- Congenitally corrected transposition of the great arteries (CCTGA).
- Dextro-transposition of the great arteries (d-TGA) palliated by atrial switch procedures (Mustard or Senning).
- Eisenmenger syndrome or pulmonary arterial hypertension (PAH).
- Any lesion with poor systemic ventricular function.
- Heart failure and severe valvular heart disease.

Moderate to low-risk lesions

- Corrected septal defects and other shunt lesions with no residual defect, absence of pulmonary hypertension, and normal systemic ventricular systolic function.
- Palliated tetralogy of Fallot with good ventricular function and competent pulmonic valve.
- D-TGA palliated with arterial switch and normal ventricular function.
- Isolated bicuspid aortic valve (BAV) or valvar pulmonary stenosis (PS) with normal ventricular function and no symptoms.

Management strategy

Shortages of hospital capacity, manpower and supplies are reported even from highly developed countries. Many tertiary cardiac centres and specialized cardiologists had to shift focus of care, postponing or rerouting specialised cardiac procedures to provide adequate resources for general COVID-19 patients. As the focus of the medical community has shifted toward patients suffering from COVID-19, taking care of CHD patients has become extremely challenging. If patients suffer cardiovascular complications from COVID-19 requiring either percutaneous or surgical intervention, each case must be assessed on an individual basis. Each institution should develop protocols for appropriate triage, isolation and treatment of COVID-19 patients who may need such interventions.

Hospital responses in this situation for CHD include[32,33]

- Replacing in-person office visits with telemedicine.
- Implementing universal masking for everyone.
- Practicing social distancing as much as possible in the hospital environment.
- Requiring additional hygiene procedures to protect patients and health care employees.
- Requiring temperature and symptom screenings for visitors and employees. All parents entering the hospital or clinic should be screened for symptoms suggesting SARS-CoV-2 (including cough or fever) as well as for contact with known positive cases.
- Performing routine microbiologic test screening depends on a multitude of factors, including local prevalence. Parents of cardiac patients should follow local guidance in accordance with the CDC guidance.
- Clinical need for imaging, invasive and surgical interventions must be weighed against the risk of infecting healthcare workers.
- Laboratory assessment for cardiac injury is not recommended on a routine basis, patients who show signs and symptoms of myocardial injury (ST-segment changes on an electrocardiogram for example), acute coronary syndrome (chest pain), unstable arrhythmias, or heart failure should be evaluated thoroughly.
- Only a limited goal-directed examination should be performed in emergency life-saving situations, ideally with the transesophageal echocardiography (TEE) probe in a protective sleeve.
- There are reports demonstrating chest CT abnormalities in adults during asymptomatic/pre-symptomatic disease; however, the role of chest CT in relation to COVID-19 in children remains undifferen-tiated at this time. It should be reserved for clinical indication based on symptoms.
- Postponing elective surgeries and procedures which require inpatient resources and preserve those resources for acute needs.

- Preoperatively testing patients for COVID-19. If preoperative testing is required, PCR-based testing of respiratory secretions is the most widely accepted approach.
- Using personal protective equipment (PPE).
- Minimizing the number of personnel. It may become necessary to re-deploy staff to help cover more acute case load if we begin seeing staff become infected with COVID-19.

Prevention of aerosolization and airborne transmission during procedure

The risk of aerosolization and airborne transmission of SARS-CoV-2 during aerosol-generating medical procedures (AGMPs) is especially pertinent to the pediatric cardiac anesthesiologist or intensivist given the high viral loads within the nose and nasopharynx of COVID-19 positive patients.[34]

- Aerosol formation during AGMP may be divided into procedures that induce the patient to produce aerosols (e.g., bronchoscopy, intubation, cough-like force during cardiopulmonary resuscitation) and procedures that mechanically generate aerosols themselves (e.g., bag-mask ventilation, nasotracheal suctioning, tracheostomy tube change, noninvasive ventilation, high-frequency oscillatory ventilation).[35] Among them tracheal intubation was associated with the highest risk of transmission of acute respiratory infections to HCWs.[36] The use of a 3-layered clear plastic drape configuration during extubation in a simulated mannequin model has been shown to limit aerosolization and droplet spray significantly.[37] The first layer was placed under the head of the mannequin, a second torso-drape layer was applied from the neck down covering the chest, and finally, an overhead top drape was placed over the mannequin's head to prevent contamination of the surrounding surfaces, including the HCW.
- For transesophageal echocardiography (TEE) the pediatric cardiac anesthesiologist will be called on to help with placement of the TEE probe in COVID-19 patients because it is considered a significant AGMP.[38] An experienced airway proceduralist, such as a cardiac anesthesiologist, may be the best HCW to pass the echocardiography probe, in full recommended PPE.[39-42]

Care of COVID-19 patients in the cardiac catheterization laboratory[43,44]

- During procedures in the catheterization laboratory, the risk of radiation necessi-tates wearing a protective lead apron and thyroid shield before donning PPE.
- Remove all possible emergency medications that may be required during the procedure from the anesthesia workstation. This will prevent the reopening of the anesthesia workstation and potential contamination of all anesthetic supplies in the workstation. Ideally, the anesthetic workstation should be covered in a plastic sheet as a barrier to reentry to help minimize cross-contamination.
- Catheterization laboratories and cardiac operating rooms use positive ventilation systems and are not designed for infection isolation. Therefore, these rooms will require conversion to an air neutral or negative- pressure room to care for COVID-19 patients safely. In addition, the room will require a terminal clean at the end of the procedure.

Outpatient care of paediatric cardiac patients[23,45-48]

Caring for CHD patients is a shared responsibility and requires a great deal of coordination. The importance of communication between patient and the physicians is paramount so to avoid unnecessary delays in providing appropriate medical or surgical therapy. While CHD patients are inherently a higher risk population, we must weigh the risks of failing to address a cardiac abnormality with that of exposure to COVID-19. Following can be done to help bridge the current gap between patients and hospitals due to the COVID-19 pandemic:

- Utilize telemedicine visits to stay under the care of the pediatric cardiologist and to ensure that timely decisions can be made regarding necessary tests or procedures. The advent of wearable technology and wide availability of blood pressure, heart rate, and oximetry equipment for home use can be a reasonable substitute for in-clinic vital sign measurements.
- Hand-held and easily sterilized echocardiographic equipment can also be a 'handy' substitute for traditional comprehensive

echocardiography, and the inevitably higher rate of exposure in a frequently visited echo lab.

- The clinician must be cognizant of QT prolonging effects of some of the medications like ritonavir/lopinavir that are used in COVID-19 therapy, including hydroxychloroquine and azythromycin. They should be use cautiously especially when combined with hypokalemia, hypomagnesemia, myocarditis, or other QT prolonging medications.
- The WHO and the European Medicines Agency currently approve the use of ibuprofen and NSAIDs in COVID-19. The British Congenital Cardiac Association suggested avoiding NSAIDs to treat fever in COVID-19.
- It is recommended that all cardiac medications, including aspirin, anticoagulants, ACE inhibitors, angiotensin receptor blockers, beta blockers, diuretics and antiarrhythmic medications be continued during COVID-19 illness, unless a clear contraindication develops.
- Coagulation cascade abnormalities and disseminated intravascular coagulation are reported in patients hospitalized with severe COVID-19 disease. So continuing anticoagulation in mild cases with monitoring from the prescribing physician and adjusting anticoagulation can be done as needed in cases of severe COVID-19. Aspirin is commonly used in the pediatric and adult population with CHD for its antiplatelet effects at a low dose of 3 to 5 mg/kg per day. There are no reports of Reye syndrome in patients on low dose aspirin typically used with CHD or with COVID-19. Because of that currently there is no need to stop aspirin in children or adults with CHD and COVID-19.

Effect of COVID-19 on cardiac team members[47]

Based on the COVID-19 pandemic trends it is expected that many of the cardiovascular care team members will be exposed to patients with COVID 19 in the coming weeks and months. In anticipation of the spread of COVID-19, many hospitals and cardiology practices have changed their care models and policies to accommodate the care of patients impacted by COVID-19 and prevent the spread of the disease.

What CHD (and other) patients must do/expect during the COVID-19 pandemic and beyond[49,50]

- Social distancing (all, until further notice).
- Shielding of high-risk patients (i.e., single ventricle physiology, pulmonary arterial hypertension, immunosuppressed/compromised patients, other specific patients).
- Regular updates/information sharing about COVID-19.
- Mental and psychosocial well-being, exercise, lifestyle modification.
- Patients with congenital heart disease should be vaccinated against influenza and pneumococcal pneumonia.

Conclusion

Children with CHD are more susceptible to COVID-19. At this point, data are insufficient to suggest specific preventive measures in patients with congenital heart disease and all patients with CHD, irrespective of which group they are in, follow routine public health guidelines with regard to social distancing, scrupulous handwashing and avoiding unnecessary contact.

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REVIEW ARTICLE

Subclinical Hypothyroidism in Children: A Review

Rabi Biswas

Abstract

Subclinical hypothyroidism is defined as serum levels of TSH above the upper limit of the reference range in the presence of normal concentrations of total T4 or free T4. This biochemical profile might be an indication of mild hypothyroidism, with a potential increased risk of metabolic abnormalities and cardiovascular disease among adults. Whether subclinical hypothyroidism results in adverse health outcomes among children is a matter of debate and so management of this condition remains challenging. Mild forms of untreated subclinical hypothyroidism do not seem to be associated with impairments in growth, bone health or neurocognitive outcome. However, ongoing scientific investigations have highlighted the presence of subtle proatherogenic abnormalities among children with modest elevations in their TSH levels. Although current findings are insufficient to recommend levothyroxine treatment for all children with mild asymptomatic forms of subclinical hypothyroidism, they highlight the potential need for assessment of cardiovascular risk among children with this condition. Increased understanding of the early metabolic risk factors associated with subclinical hypothyroidism in childhood will help to improve the management of affected individuals.

Keywords: *Subclinical hypothyroidism, children.*

Introduction

From the biochemical point of view, subclinical hypothyroidism (SCH) is characterized by mildly elevated serum TSH concentrations, with normal concentrations of serum free and total triiodothyronine (T3) and thyroxine (T4), without the typical symptoms of thyroid disease. SCH prevalence in adults ranges from 4 to 10%.[1] In the pediatric population, the prevalence of this thyroid disorder is estimated to be less than 10%.[2] According to Biondi et al[1], children with SCH can present some minimal or nonspecific signs and symptoms. There is a paucity of long-term prospective research studying the natural history of subclinical hypothyroidism and its consequences in childhood.[3,4] A preliminary SCH diagnosis is confirmed by laboratory tests when TSH concentration is above the statistically defined upper limit of the reference range.[5]

In the adult population with subclinical thyroid disease, SCH is associated with a risk of progression to overt thyroid disease, lipid disorders, increased risk of atherosclerosis, and mortality due to cardiovascular diseases.[6] The published data regarding the clinical manifestation of SCH in children and adolescents are inconsistent as most papers indicate SCH to be asymptomatic.[7] Accordingly, the aim of this paper is to analyze studies reporting signs and symptoms presented by children and adolescents diagnosed with subclinical hypothyroidism.

Natural progression of SCH and effects of intervention

There are very few prospective studies evaluating the natural progression of SCH in pediatric age group (Table I). In a study from India, a cohort of 32 children with SCH and autoimmune thyroiditis (AIT) and goiter were followed.[8] Development of overt hypothyroidism (12.5% in this cohort) was insidious and was not accompanied by symptoms and signs. In a larger study on 323 children with either Hashimoto or idiopathic SCH followed up for 3 years, 13.5% of SCH developed overt hypothyroidism.[9] The study could not detect predictive factors for

Correspondence to: Dr. Rabi Biswas, Associate Professor, Department of Paediatric Endocrinology and Metabolic Disorders, Bangladesh Institute of Child Health & Dhaka Shishu (Children) Hospital, Dhaka. Cell: 01715287817, E-mail: rabibiswasdr@gmail.com

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progression of SCH to overt hypothyroidism in idiopathic SCH. Wasniewska et al[10] followed up 92 patients with idiopathic SCH over 2 years, and none of them developed overt hypothyroidism. Lazar et al[11] studied 3510 patients with SCH over 5 years and showed that 73.6% of them normalized TSH. Elevated antibodies [thyroid peroxidise (TPOab) and thryoglobulin antibodies (TGab)] may predict future overt hypothyroidism and TPOab>TGab may predict impending thyroid failure in AIT.[12,13]

Leonardi et al[14] studied 44 Italian children "false positive" to neonatal screening for congenital hypothyroidism; 28 of them had SCH on retesting at 2 to 3 years of age. Twenty of these 28 children were treated with replacement therapy and then withdrawn from therapy 2 to 3 months prior to re-evaluation. Out of the 28 children with SCH, TSH was normal in 9 children (32%) and persistently elevated in the remaining 19 (62%) at 4.1 to 6.6 years of age. At 7.2 to 9.5 years of age, TSH remained normal in 9 children who previously normalized their thyroid function, returned to normal in 5 out of 19 of the children with previous elevated TSH and persisted above normal in remaining 14 children.

Table I
Natural history and progression of SCH in Paediatric case series

Authors	Number of patients	Level of evidence/ Type of study	Period of follow-up	Key results	Comments
Gopalakri-shanan et al[8]	98 of which 32 had SCH	Longitudinal study	24 months	4/32 patients with SCH developed OH	Important to monitor TFT. Development of OH is insidious and may not be accompanied by symptoms and clinical signs.
Radetti et al[9]	323	Retrospective cross-sectional	3 years	13.5% of SCH developed OH	There were no predictors in pts of SCH.
Wasniewska et al[10]	92 with SCH	Prospective observational	2 years	38 normalized TSH54 remained SCH11 had increase of TSH more than 10miu/mL	None developed OH. Natural progression in idiopathic SCH is a progressive decrease over time of TSH in majority.
Lazar et al[11]	121052 of which 2.9% had SCH	Prospective observational	5 years	In SCH group 73.6% normalized TSH, 2% increase >10miu/mL, and 0.03% had OH	Female patients with >7.5miu/mL of TSH are at greater risk of sustained raise.
Radetti et al[12]	160 of which 55 were SCH Rest euthyroid	Prospective observational	5 years	16/55 SCH normalized TFT. 16 remained SCH 23 had twofold rise above the normal limit	Presence of goitre and elevated TGAb, together with increase in TPOab and TSH may predict future OH. At 5 yrs 50% of all participants remained euthyroid.
Zois et al[13]	29 with AIT of which 7 had SCH	Prospective observational	5 years	All 7 continued to be in SCH None of the 29 developed OH	TPOab>TGab increase predicted impending thyroid failure in AIT. Thyroid hypoechogenicity seem to predict the same
Leonardi et al[14]	44	Prospective observational	8 years	14 had SCH at end of the study. None developed OH	Newborn false positive TSH have an increased risk of developing SCH

SCH- Subclinical Hypothyroidism, TFT- Thyroid function tests, TPOab- thyroid peroxidise antibodies, TGab- thyroglobulin antibodies, TSH- Thyroid stimulating hormone, OH- Overt hypothyroidism, AIT- autoimmune thyroiditis.

Table II
Studies reporting effect of replacement therapy in childhood SCH

Authors	Patients	Type of study	Follow-up	Results	Comments
Wasniewska et al[15]	69 treated SCH vs 92 untreated SCH	Case control	2 y	Significant difference was not found	TSH value changes between treated and untreated groups were similar. therapy is unable to prevent the risk of further TSH increase after treatment withdrawal
Cetinkaya et al[16]	2067 total, 39 SCH	Interventional	12 mo	Showed improvement in growth velocity; no hyperthyroidism noted after replacement.	Short stature can be associated with SCH. Thyroid hormone replacement improves the height in such patients
Chase et al[17]	25 diabetic children with SCH	Case control	2 y	Prepubertal diabetics showed increased growth velocity than postpubertal diabetics	Higher the initial TSH value showed increased growth velocity
Aijaz et al[18]	11 SCH children	Interventional	91 d	Short term thyroxine therapy showed no neuropsychological benefits as compared to normal population	Thyroxine therapy showed no positive effect on neuro-psychological function in children with SCH
Moore et al[19]	18 with SCH and AIT	Prospective observational	5.8 yrs	7/18 were euthyroid10 remained SCH1 became OH	Expectant management is recommended in majority of SCH with minimally elevated TSH

SCH- Subclinical hypothyroidism, TFT- Thyroid function tests, TSH- Thyroid stimulating hormone, OH- Overt hypothyroidism, AIT- autoimmune thyroiditis, TRH- thyrotrophin releasing hormone.

Effects of treating children with SCH

This aspect has been even less investigated, and a summary of the evidence is presented in Table II. Wasniewska et al[15] compared thyroxine treated and thyroxine untreated SCH over 2 years and found no significant changes in TSH values in both groups. Cetinkaya et al[16] treated 39 children with short stature and SCH; an improvement in height was significant in prepubertal as compared to pubertal age group, with no progression to overt hypothyroidism in any in the cohort. Chase et al[17] noted a similar significant height increase in the prepubertal age group as compared to the pubertal age group when children with SCH and type 1 diabetes were given thyroxine replacement therapy. Aijaz et al[18] studied short-term thyroxine replacement therapy and its effects in neuropsychological outcome and concluded no significant change. Moore et al[19] recommended expectant management is in majority of SCH with minimally elevated TSH. Chase et al[17] found that prepubertal diabetics had increased growth velocity than postpubertal diabetics.

Diagnosis and management

The management of subclinical hypothyroidism in childhood is a controversial issue. The first step in managing a child with a modest increase in TSH levels should be the differentiation between persistent and transient forms of subclinical hypothyroidism (Fig 1).[20] Persistent subclinical hypothyroidism should be confirmed by re-evaluation of the TSH levels at 4-12 weeks after the first test to rule out abnormal values caused by laboratory problems, diurnal variation in TSH concentration and transient causes of subclinical hypothyroidism (recovery phase from non-thyroidal illness or subacute thyroiditis).

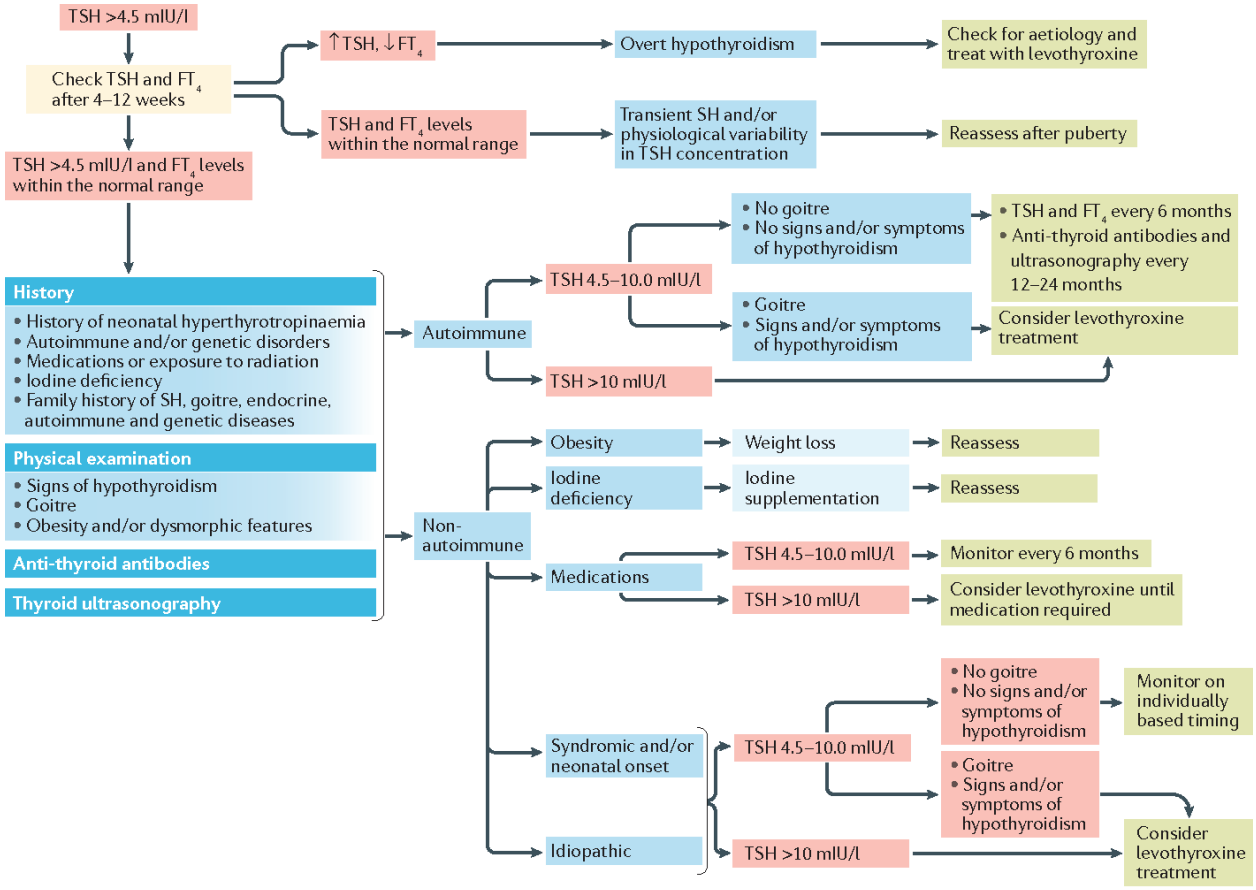

Fig 1 *Proposed management of children with subclinical hypothyroidism. The initial step in the management of a child with a mild increase in TSH concentration should be confirmation of hyperthyrotropinaemia by re-evaluation of TSH levels 4-12 weeks after the first test. If an elevated TSH concentration persists, the diagnostic process should first include careful assessment of the child's history and a clinical evaluation focused on the detection of signs and symptoms suggestive of thyroid dysfunction. Thereafter, evaluation of anti-thyroid antibodies and thyroid ultrasonography will enable differentiation between autoimmune and nonautoimmune forms of subclinical hypothyroidism (SCH). The subsequent management and follow-up will depend both on the aetiology and the degree of TSH elevation. The final decision on treatment should be based on the assessment of clinical symptoms or signs of mild thyroid impairment and on the risk of progression to overt hypothyroidism. FT4, free T4.*

If an elevated TSH level persists after retesting, a diagnostic evaluation is recommended. The child's history should focus on the presence of neonatal hyperthyrotropinaemia; autoimmune and/or genetic conditions, use of medications known to interfere with thyroid function; previous exposure to ionizing radiation; and endemic iodine deficiency. Attention should be given to the presence of subclinical hypothyroidism, goitre, endocrine diseases, autoimmune diseases or genetic conditions in other members of the patient's family. Physical examination should focus on signs of hypothyroidism, goitre, weight gain and clinical features suggestive of specific genetic conditions.[1]

Given that Hashimoto thyroiditis is the condition most often responsible for the onset of subclinical hypothyroidism in childhood, all patients with the persistent form should be screened for the presence of anti-thyroid antibodies and undergo ultrasonography of the thyroid gland. Moreover, based on the history and physical examination, further investigations can be considered for some children. These are *TSHR* genotype for cases arising in familial settings, urinary iodine excretion for those living in endemically deficient areas or screening for resistance to parathyroid hormone, follicle stimulating hormone or luteinizing hormone if pseudohypoparathyroidism type 1a is suspected.

The subsequent management and follow-up of persistent forms of subclinical hypothyroidism should depend both on the aetiology and degree of TSH elevation. The final decision on treatment should be made according to the assessment of clinical symptoms or signs of mild thyroid impairment and the risk of progression to overt hypothyroidism.[8]

In the most common clinical scenario of autoimmune subclinical hypothyroidism, treatment with levothyroxine should be considered for all children affected by severe forms (TSH level >10 mIU/l) or among those with mild subclinical hypothyroidism in the presence of goitre or the signs or symptoms of hypothyroidism.

Untreated children should be monitored every 6 months (thyroid function tests) and every 1-2 years (anti-thyroid antibodies and ultrasonography). Careful monitoring is particularly recommended in the presence of chromosomal abnormalities (Turner syndrome and Down syndrome)[21] or other autoimmune conditions to assess increased risk of progressive thyroid dysfunction.

Management of children with reversible causes of subclinical hypothyroidism should focus on modifiable factors. Diet and lifestyle changes are advisable for children who are overweight or obese; thyroid function should be checked after weight loss.[22] Iodine supplementation is recommended among children living in areas with endemic iodine deficiency and/or with documented reduced iodine excretion. Thyroid function in such cases should be re-evaluated after iodine normalization.[13]

The use of some medications, such as antiepileptic drugs and IFN-á, might interfere with thyroid function. Treatment with levothyroxine should be considered for children with a TSH level >10 mIU/l until medications are discontinued. Children with mild forms of subclinical hypothyroidism should be monitored every 6 months.[18]

The management of children with genetic conditions and neonatal hyperthyrotropinaemia should be evaluated on an individual basis.[15] Intervention should depend on the child's age, the degree of TSH elevation and the underlying genetic condition. However, as for other aetiologies, levothyroxine is recommended for severe forms of subclinical hypothyroidism and for symptomatic children, whereas careful monitoring is suggested for the mild and asymptomatic forms.

The management of idiopathic subclinical hypothyroidism is particularly challenging. Children with severe forms (TSH level >10 mIU/l), goitre or symptoms suggestive of hypothyroidism should receive treatment. For children with mild forms (TSH level <10 mIU/l), a trial of levothyroxine can be considered if there is a clinical suspicion of hypothyroidism. In the absence of signs and symptoms, regular clinical evaluation of TSH and free T4 levels, along with periodic re-evaluation of anti-thyroid antibodies, is advisable and should be tailored on the basis on the duration and degree of TSH elevation.[5]

Repeated TSH monitoring can be avoided for children with stable but mild increases of TSH concentration after 2 years of follow-up, unless indicated by the onset of goitre or signs and symptoms suggestive of hypothyroidism.

Finally, it must be highlighted that all forms of subclinical hypothyroidism that resolve at any point during follow-up should be considered for re-evaluation of thyroid function later in life, particularly during adolescence and pregnancy.

Conclusion

The decision about treatment of SCH in children and adolescents is still a matter of debate. None of the consensus statements published about the management of SCH addressed the issue of SCH in the pediatric population. However, according to the available limited evidence in children, SCH seems to be a self-limiting condition with a low rate of progression to overt hypothyroidism. Therefore, treatment of SCH in children should be considered only when TSH values are higher than 10 mIU/L, when clinical signs or symptoms of impaired thyroid function or goiter are detected, or when SCH is associated with other chronic diseases. On the other hand, in children with SCH having no goiter, negative anti-thyroid antibodies or a TSH level of 5-10 mIU/L, replacement therapy is not justified because of the low risk to develop overt hypothyroidism.

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CASE REPORT

Treatment Failure with IVIG in a Case of Multisystem Inflammatory Syndrome in Children Managed by Tocilizumab

Fahmida Zabeen[1], M Quamrul Hassan[2], Badrun Nessa[3], Sadia Khan[4], Jannatul Ferdouse[5]

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has rapidly spread around the world from the time when it was first identified in China in December 2019.[1,2] Among initial reports from China on corona virus disease 19 (COVID-19) in paediatric age group, very few have sporadically described critically ill children.[3] Most children with this disease are asymptomatic or exhibit a mild upper respiratory illness, and recover within 1 to 2 weeks.[4] However, reports have begun to emerge of multiple system involvement with circulatory shock and systemic inflammation that has presented predominantly in children with COVID-19. The first such report was from the United Kingdom involving a cohort of 8 children with evidence of severe inflammation and Kawasaki disease-like features.[5] Thereafter, similar reporting continued from Italy describing 10 children, and from France and Switzerland describing 35 children.[6,7] On 14 May, the US Centers for Disease Control and Prevention (CDC) formally termed this entity as multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19 and introduced a case definition.[8]

Epidemiologic evidence implicates SARS-CoV-2 as the likely cause of the newly recognized MIS-C, even though causation has not yet been established. The occurrence of clusters of MIS-C cases in places that have been heavily impacted by COVID-19 such as Italy, the UK, and New York City, is highly suggestive of an association to infection with SARS-CoV-2. While the incidence of MIS-C is uncertain, it appears to be an uncommon complication of COVID-19 in children. In one report, the estimated incidence of laboratory-confirmed SARS-CoV-2 infection in individuals less than 21 years old was 322 per 100,000 and the incidence of MIS-C was 2 per 100,000.[9]

CDC data on tracking reports of MIS-C cases shows strong evidence of its linkage with COVID-19. Almost all (98 %) cases were positive for antigen or antibody of SARS-Cov-2.[8] The majority of published cases with this syndrome were positive for serologic testing for SARS-CoV-2 (60/69, 87%) and less commonly positive for RT-PCR testing from nasopharyngeal swab (23/70, 32%), which suggests that this syndrome may be post-infectious rather than related to acute early infection.[10] The clinical presentation of MIS-C includes fever with severe illness, and the involvement of two or more organ systems, along with laboratory evidence of inflammation and laboratory or epidemiologic evidence of SARS-CoV-2 infection.[8] Laboratory findings include lymphopenia, hypoalbuminaemia, elevation in serum troponin, liver enzymes, D-dimer, and ferritin. C-reactive protein (CRP) and ESR are also elevated, along with cytokines elevation such as tumor necro-sis factor alpha, interleukin (IL)-4, IL-6, and IL-10.[11]

Specific immunomodulatory therapy depends on the clinical presentation of this severe illness. The goals of treatment for MIS-C are to reduce systemic inflammation and restore organ function, in order

1. Consultant, Department of Paediatrics, Evercare Hospital Dhaka.
2. Senior Consultant, Department of Paediatrics, Evercare Hospital Dhaka.
3. Specialist, Department of Paediatrics, Evercare Hospital Dhaka.
4. Senior Registrar, Department of Paediatrics, Evercare Hospital Dhaka.
4. Registrar, Department of Paediatrics, Evercare Hospital Dhaka.

Correspondence to: Fahmida Zabeen, Consultant, Department of Paediatrics, Evercare Hospital Dhaka. Cell: 01911302015, E-mail: fahmida.zabeen@hotmail.com

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to decrease mortality and reduce the risk of long-term sequelae, such as the development of coronary artery aneurysm (CAAs) or persistent cardiac dysfunction.[10] Overall, children will survive this hyperinflammatory condition with IVIG administration, steroids, a multidisciplinary team of relevant healthcare providers, and in few cases immunomodulatory agents.[12] In a very few reported cases where IVIG response was unsatisfactory, Interleukin-6 inhibitors, an immunomodulatory agent was found beneficial while given during the cytokine storm associated with COVID-19.[13] We are reporting a case of MIS-C from a tertiary care hospital (Evercare Hospital Dhaka), from Capital Dhaka, Bangladesh, who was successfully treated with IL-6 inhibitor (Tocilizumab), as a second line therapy after failed treatment with adequate dose of IVIG and steroid.

Case Report

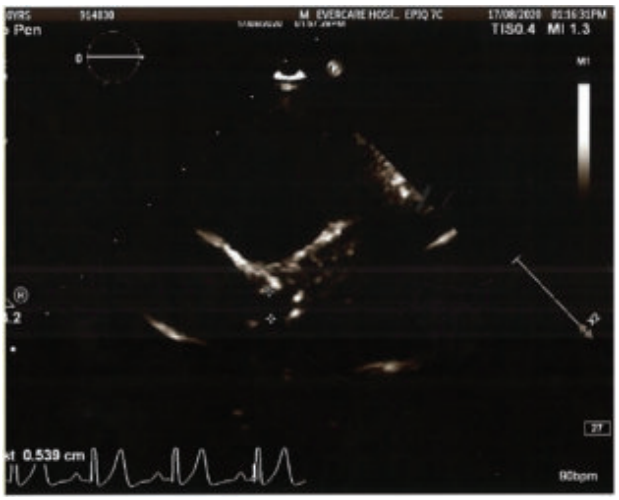
A 10 years 10 months old previously healthy boy was admitted through emergency room with the complaints of high-grade fever (maximum peak 106°F) for 2 days, repeated vomiting, severe abdominal pain and dry cough. Both his parents and the patient were positive for SARS-CoV-2 RT-PCR nasopharyngeal swab test three weeks prior to this illness. At that time, he had fever (102°F for about 2.5 days) with mild cough, which was managed conservatively at home.

On arrival, the boy was febrile with temperature 104°F, sick looking, mildly tachypneic with normal oxygen saturation. His heart rate was 128/min and he was normotensive with BP 90/60 mmHg. His chest was clear on auscultation, abdomen was soft with diffuse tenderness, and bowel sound was normal. Skin survey was normal and no signs of meningism were noted. Investigations on admission showed, neutrophilic leukocytosis with lymphopenia, slightly raised CRP and SGPT. His SARS-CoV-2 (RT-PCR) test came negative and chest radiograph was normal. Ultra-sonogram of whole abdomen showed trace free fluid. On suspicion of sepsis, Inj. Amoxycillin with Clavulanic acid was started empirically. On the following day, he also developed new symptom of intermittent delirium with irritability and complained of getting smell in everything around. After 36 hours of admission, on day 4 of illness, as there was no change of clinical condition, repeat investigations were done, which revealed thrombocytopenia and markedly raised inflammatory markers including S. ferritin, D-Dimer, LDH and ESR. He also had low S. albumin, proteinuria and normal troponin-I (1.9 ng/ml). Multisystem inflammatory syndrome in children (MIS-C) has been suspected and inj. Methyl-prednisolone (2 mg/kg/day) 12 hourly IV was added in treatment.

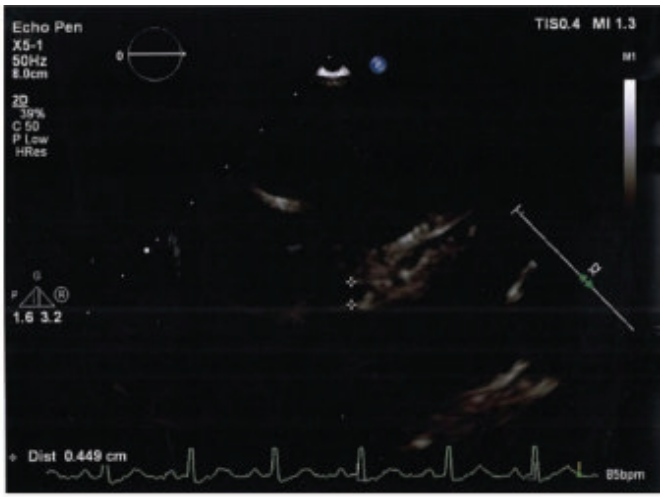
Next day, his general condition further deteriorated with continued high fever along with cough induced vomiting and persisting abdominal pain. Repeat investigations revealed persisting lymphopenia, markedly raised C-reactive protein (127 mg/L), raised procalcitonin, normal Widal titre, further increasing D-Dimer and high fibrinogen level (717.2 mg/dl) with negative septic screen. 2D colour doppler echocardiography (Fig. 1) revealed medium aneurysmal dilation of coronary arteries [LMCA (Z-score +5.95) and LAD (Z -score +5.26)] with irregular and distorted vascular wall and electrocardiogram (EKG) showed sinus tachycardia. Our patient fulfilled the CDC case definition of MIS-C.[8] We have started IVIG (1.5 g/kg) continuous infusion over 24 hours. Antibiotic was switched to Meropenem. Inj. Enoxaparin S/C and low dose Aspirin were also started. He became afebrile day after IVIG infusion and started showing general wellbeing. His cough as well as vomiting and abdominal pain also subsided.

However, 72 hours after IVIG infusion (on Day 9 of illness), his fever recurred with increasing peak along with excessive dry cough, anorexia and repeated vomiting. His ESR further raised along with raised inflammatory markers, and he also developed hyponatraemia. On day 11 of illness, 48 hours after new onset fever, he also developed macular rash on both palms, bilateral conjunctival injection (Fig. 2) and erythematous throat with mildly tender left cervical lymphadenopathy. His blood pressure and oxygen saturation remained within normal range. Antifungal Tab. Fluconazole was added. His subsequent lab test showed very low S. albumin, further rising inflammatory markers with markedly high CRP, D-dimer as well as ESR. His 2nd set of septic screen also came negative and repeat chest radiograph also revealed normal. On day 12 of illness, Inj. Tocilizumab (8 mg/kg) single dose was infused. Shortly after the infusion, 2 hours later, his fever subsided and there was significant improvement of wellbeing along with

resolution of cough and vomiting. Four days after Tocilizumab infusion, investigations were repeated and yielded normal lymphocyte count, improving CRP and ESR, near normal procalcitonin and normal D-dimer (Fig. 3). He developed thrombocytosis (455 10^9/L), further rising S. ferritin & SGPT (422 IU/L). 2-D echo (Fig. 1) before discharge revealed reduction in aneurysmal dilation of LMCA (Z- score +3.13) and LAD (Z- score +3.38) with irregular vascular wall. He was discharged in vitally stable state after 15 days of hospital stay with advice of tapering oral steroid and low dose aspirin. All his relevant laboratory tests during admission and subsequent follow up are shown in the Table I and trend of inflammatory markers during hospital stay in (Fig. 3). He attended follow-up visits in outpatient clinic after 1, 3 and 6 weeks of discharge, where he was found vitally stable with normalization of his inflammatory markers, but he had persisting small aneurysmal dilatation of LMCA and LAD with irregular vascular wall in 2-D echocardiogram even at 3 weeks after discharge. On further follow up, at 7 weeks, all coronary arteries became normal.



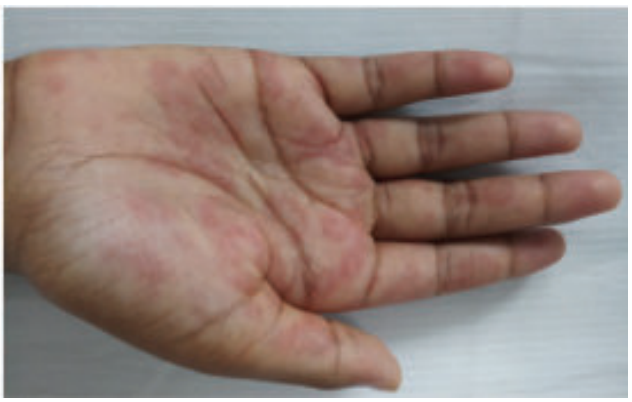
1st 2D-Echocardiogram showing medium aneurysmal LMCA dilation on day 5 of illness



2nd 2D-Echocardiogram showing small aneurysmal LMCA dilation on day 15 of illness

Fig 1 *1st and 2nd echocardiogram images showing aneurysmal dilation of coronary arteries with irregular and distorted vascular wall*

Conjunctival injection



Palmer rash

Fig 2 *Changes in eyes and hands on day 11 of illness*

Table I
Laboratory findings during hospital stay and follow-up

Laboratory test	During Hospitalization								1st F-up	2nd F-up
	Day of illness of specific treatment									
	1	4	5	7	10	12	14	17	24	56
			IVIG			Tocilizumab				
TLC 10^9/L (normal: 5-13)	13.93	7.71	6.42	4.65	9.67	14.82		15.59	12.97	6.13
Absolute Neutrophil count 10^9/L (normal: 2-7)	12.79	6.37	5.74	3.18	8.23	12.96		11.3	9	3.71
Absolute Lymphocyte count 10^9/L (normal: 1-3)	0.87	1.13	0.61	0.97	0.85	1.34		3.31	3.68	1.83
Platelets 10^9/L (normal 150-400)	161	139	165	244	292	284		4.55	319	257
CRP mg/L (normal <3.3)	5.2		127	70.9	53.7	178		162	28.6	<2.9
Procalcitonin ng/mL (normal <0.05)	0.75		2.97	0.7	0.38			0.14		
ESR mm in 1st hour	80			121	134			110	41	11
Ferritin ng/ml (12-140)	148	239		349		454		796	259	86
D-Dimer µg/L (<500)	462	2314	2646	1618	1422	1917		923	305	184
Fibrinogen mg/dL (180-350)			717	358						
LDH U/L (normal <250)		264					194			
Troponin ng/mL, (normal 3-17)		1.9								
SGPT IU/L (normal 14-63)	73		50		75	44		422	140	64
S. Albumin g/dL (normal 3.5-5)		3.3			2.9	2.2		2.6	3.3	
S. Sodium mmol/L (normal 135-145)	135	136			130	134				136
Urine Protein		Trace			Trace			NIL		
Aerobic C/S blood		No growth				No growth				
Aerobic C/S urine		No growth				No growth				

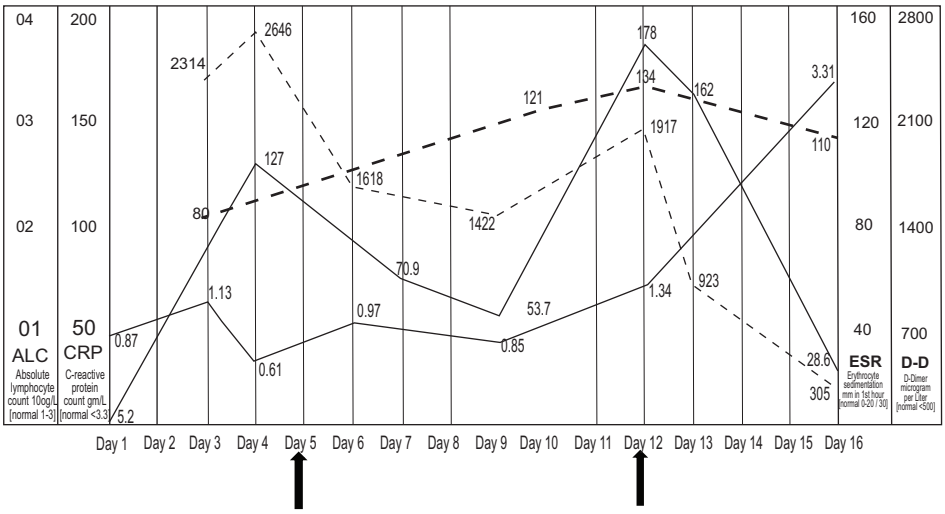


Fig 3 *Trend of inflammatory markers with effect of IVIG and tocilizumab during hospital stay*

Discussion

Multisystem inflammatory syndrome in children (MIS-C) is a rare but severe inflammatory condition that has been reported in previously healthy pediatric patients having SARS-CoV-2 exposure.[14] Evidence supporting an underlying link with SARS CoV- 2 includes a strong historical association with COVID-19 activity, diagnosis of SARS-CoV-2 infection through RT-PCR or antibody testing in most patients, and hyper inflammatory manifestations like COVID-19 infected adults.[15-17] We report a previously healthy boy, who fulfilled the CDC case definition[8] of MIS-C and was positive for SARS-CoV-2 RT PCR nasopharyngeal swab test three weeks prior to his illness. MIS-C is speculated to be a delayed immunological phenomenon associated with

inflammation (stage III hyperinflammation phase) following either symptomatic or asymptomatic COVID infection.[10]

There is resemblance between MIS-C and atypical Kawasaki disease (KD); however, there are some noticeable clinical differences, such as presentation at older age, a higher frequency of gastrointestinal symptoms on presentation, and a higher rate of cardiac involvement in MIS-C.[6-8,18]

Our reported case had several systemic involvements including cardiac, gastrointestinal, hematological, hepatic and nervous system. He presented very early within 2 days of illness, and we could record the evolution of clinical and laboratory features. His brief mucocutaneous manifestations with cervical lymphadenitis resembling features of incomplete KD developed late in the disease course on 11th day of illness during second peak of febrile episode.

Current management of MIS-C emphasizes on supportive care and treatment of the underlying inflammatory process to reverse organ dysfunction and prevent further complications. Although there are no specific therapies approved by the U.S. Food and Drug Administration (FDA) for this condition, several agents are being used in different clinical trials and under institutional protocols based on their clinical benefit in similar conditions.[8,18] Stepwise immunomodulatory treatment in MIS-C is recommended with intravenous immunoglobulin (IVIG) and/or glucocorticoids as first line agents. This immunomodulatory approach is the most commonly used treatment reported to date in patients with MIS-C.[5-7,19-24] We have seen brief positive clinical response in our patient after treatment with IVIG and steroid. But after 3 days of IVIG infusion, his fever recurred along with clinical deterioration and rapidly rising inflammatory markers. Verdoni et al[6], reported that, the KD cases who presented during the COVID-19 pandemic showed high rate of IVIG resistance, as compared to that in a past cohort of KD patients, suggesting a role for glucocorticoids in MIS-C.

In case of patients not responding or partially responding to IVIG and/or steroid, alternative agents have been used in different centers. Considering the cytokine release syndrome as the important contributor to severe inflammation in some patients with MIS-C.[25] American College of Rheumatology guidance recommended anakinra (Interleukin-1 antagonist) in patients with MIS-C who are refractory to IVIG and/or glucocorticoids.[26]

This recommendation is based on the relative safety of anakinra in pediatric patients with hyperinflammatory syndromes even with active infection, and the outcomes mentioned in the literature in some of MIS-C patients.[13,14,24,27-30] IL-6 is an important cytokine in this inflammatory process and a few studies suggest that CS is certainly correlated with disease severity.[31] IL-6 is a proinflammatory cytokine that is involved in T-cell activation, immunoglobulin secretion induction, acute-phase protein synthesis initiation in liver, and stimulation of hematopoietic precursor cell proliferation and differentiation.[32] Assuming the relationship between increased IL-6 levels and negative outcomes in COVID-19, IL-6 neutralization with tocilizumab can be a potential treatment option.[16,33,34] This monoclonal antibody blocks IL-6-mediated signaling by competitively binding to both soluble and membrane-bound IL-6 receptors, and it is approved by the US FDA for treating cytokine release syndrome (CRS). [6]

Our reported patient was declared as treatment failure with IVIG and was labeled as an IVIG refractory case of MIS-C. We chose tocilizumab (IL-6 inhibitor) empirically as the second line treatment considering role of IL-6 in cytokine storm, as anakinra (IL-1 inhibitor) is not available in commercial market, and we lack laboratory facility for doing IL-6 assay. He demonstrated quick and significant as well as sustained clinical remission and improvement in laboratory parameters after treatment with inj. tocilizumab.

Children's Hospital of the King's Daughters (CHKD) protocolized tocilizumab for patients with continued fever for 24 hours after IVIG and/or steroids or moderate to severe presentation. They recommended a single dose of tocilizumab 12 mg/kg IV in patients less than 30 kg and 8 mg/kg IV (Max: 800 mg) in patients 30 kg or more and mentioned the typical response time within 48 to 72 hours.[35] We have used 8 mg/kg single dose in our patient. In 3 New York City tertiary care children's hospitals, (n = 33; age 2 months to 20 years), Kaushik et al[28] treated 12 (36%) patients with tocilizumab along with IVIG or methylprednisolone. Tocilizumab was given to patients with high IL-6 concentrations.[36] In another 3 systematic reviews of MIS-C patients (n =

662 to 783), interleukin-6 inhibitors were administered to 6% to 6.5% of patients. Sixty eight to seventy one percent of patients were in the intensive care unit and there was 1.5% to 1.7% mortality rate.[37-39] In an observational study (n=27; median age 6 years) tocilizumab was administered to 2 patients with suspected cytokine storm syndrome with no mortality.[40]

Fourteen percent of patients among 186 MIS-C cases reported to receive tocilizumab or siltuximab in addition to IVIG and other therapies. Eighty percent of patients were in the critical care unit and 20% received mechanical ventilation.[14] Gruber et al[40] reported in a case series of 8 patients with median age 11.5 years, all patients received 1 to 3 doses of tocilizumab within 1 day of admission. Seven of the 8 patients also received IVIG. Markers of inflammation, coagulopathy and cardiac injury normalized rapidly in all patients.

For tocilizumab use, there is risk of GI perforation, hepatotoxicity and infusion-related reactions.[32] In our experience while managing the case, tocilizumab was well tolerated. Tocilizumab is much cost effective than that of IVIG. Our reported case showed rapid drop in his later raised CRP and D-dimer, and lymphopenia as well as thrombocytosis soon corrected within 4 days following intravenous tocilizumab. We have seen, ferritin, ESR and later raised SGPT took time to normalize, which we are not considering markers for immediate treatment success. Nozawa et al[41], reported coronary-artery aneurysm in tocilizumab-treated children with kawasaki's disease. In our case, on further follow up upto 6 weeks, there was no significant adverse effects like worsening of coronary artery aneurysm or flare of infection associated with tocilizumab use. Rather, we have seen normalization of coronary arteries at 6 weeks follow up visit.

MIS-C patients who require treatment with steroids, irrespective of the dose, frequently require a gradual tapering over 2-3 weeks to avoid rebound inflammation.[26] For our patient, we continued oral steroid with gradual taper over 3 weeks after discharge, and we also did not experience any such rebound inflammation.

Conclusion

Though IVIG and steroid are so far widely used effective first line agents to treat severe MIS-C, failure to treatment can happen which may take about 72 hours to be evident. Predictors for treatment failure of MIS-C with IVIG need to be studied further. In this case report, tocilizumab, the IL-6 inhibitor, has been safely and successfully used in an adolescent as second line therapy. Considering this experience of safety, quick recovery response and relatively cheaper option, use of tocilizumab as a second line agent instead of repeat use of costly IVIG may be considered. If it is proved safe in larger study, it can be considered as even a first line therapeutic agent in treating MIS-C.

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CASE REPORT

A Boy with COVID-19 Associated Severe AKI

Sawrav Deb Bappy[1], Mohammed Maruf-ul-Quader[2], Dhiman Chowdhury[3], Tanvir Mahmud[4], Syed Mahtab ul Islam[5]

Introduction

COVID-19 is a newly discovered acute infectious disease caused by the SARS-CoV-2 virus, which is mainly manifested as acute respiratory disease characterized by acute interstitial and alveolar pneumonia and can affect multiple organs such as kidneys, heart, digestive tract and blood.[1] The reported incidence of acute kidney injury (AKI) in COVID-19 is found variable from 0.5-23% country to country in adults. Paediatric AKI is less common than adult, accounted for 1% in <10 years and 1.2-4.8% among total pediatric population. Amongst those who develop severe infection and require hospitalization, AKI was reported.[2] This case report presenting a paediatric case of COVID-19 associated AKI.

Case Report

Manik, 12 years old boy hailing from Cox's Bazar, got admitted in the Department of Paediatrics, Chittagong Medical College Hospital on 27 July, 2020 with the complaints of oedema, anuria for last 48 hrs and vomiting for several times for 1 day. Prior to the admission mother gave history of high grade fever for 1 day, not associated with chills and rigor, sweating, cough, respiratory distress, burning micturition, loose motion, altered consciousness and convulsions. No history of fever was found among the family members and close contacts and no history of travelling was found.

On examination, patient was found conscious, oriented, afebrile, having facial puffiness and pitting oedema of both extremities, pulse - 100/min, BP - 100/60 mmHg, RR - 28/min, SpO_2 - 100% in room air. No organomegaly and non-palpable bladder but ascites was present. Respiratory system and other systemic examinations revealed normal findings. Investigation revealed Hb - 11.4 gm/dL, ESR-28 mm, total leucocyte count 14,600/ mm^3, neutrophil - 83%, lymphocyte - 07%, platelet count - 1,50,000/mm^3, PBF - neutrophilic leukocytosis, S. creatinine 5.50 mg/dL, S. electrolytes (Na-130, K - 4.6, Cl-99 mmol/L), CRP - 6 mg/L, S. ALT - 187 U/L, S. albumin - 1.96 gm/dL, S. cholesterol-198 mg/dL, PT - 14.3 sec with INR-1.1, S. PTH - 516.8 pg/mL, CXR-normal, USG of whole abdomen showed acute renal parenchymal disease, moderate ascites, minimal bilateral pleural effusion. Sample for blood C/S was sent and as the patient was anuric, urine sample for routine, microscopic examination and culture could not been sent. Patient was provisionally diagnosed as Rapidly progressive glomerulo-nephritis (RPGN) and treatment was initiated with IV Methylprednisolon and injectable antibiotics (Ceftriaxone and Teicoplanin). Parents were counselled for kidney replacement therapy (KRT).

After 24 hrs, further investigation reports revealed low Hb (9.1 g/dL), neutrophilic leucocytosis with lymphopenia (10%), normal platelet count; raised blood urea (319 mg/dL) and creatinine (9.46 mg/dL), further drop of Na, hyperkalemia, metabolic acidosis. CRP raised to 20.5 mg/L. Raised ferritin - 824 ng/mL,D-dimer >10 mg/L with normal troponin-I, C3, C4, ANA, P-ANCA, C-ANCA and negative HBsAg, Anti-HCV, Anti-HIV were found. Sample for RT-PCR for COVID-19 was sent. Vitals remained

1. Assistant Registrar, Department of Paediatrics, Chittagong Medical College Hospital.
2. Associate Professor, Department of Paediatric Nephrology, Chittagong Medical College Hospital.
3. Junior Consultant, Department of Paediatrics, Chittagong Medical College Hospital.
4. MD Phase B Resident (Nephrology), Chittagong Medical College Hospital.
5. Assistant Professor, Department of Nephrology, Chittagong Medical College Hospital.

Correspondence to: Dr. Mohammed Maruf-ul-Quader, Associate Professor, Department of Paediatric Nephrology, Chittagong Medical College Hospital, Chattogram, Bangladesh. Cell no: +8801911223237, E-mail: marufulquader@yahoo.com

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stable with normal saturation at room air.

Intermittent peritoneal dialysis (IPD) was initiated. IPD was continued for 72 hrs but condition didn't improve rather rising trend of creatinine to12.72 mg/dL. Meanwhile, blood culture report revealed growth of *Acinetobacter baumannii* and RT-PCR for COVID-19 was found positive. Patient was then diagnosed as multisystem Iinflammatory syndrome in childern (MIS-C). Hemodialysis was initiated. Antibiotic was changed to Tygecycline according to culture-sensitivity report, subcutaneous LMWH was initiated. Oral prednisolone was initiated after 5 doses of I/V methylprednisolon. Patient got 3 sessions of hemodialysis by femoral catheter. On 9 August, 2020, patient developed blood vomiting and expired.

Discussion

According to KDIGO severe AKI (Stage 3) defined as when serum creatinine 3 times baseline or increase in S. Cr to ≥4 mg/dl (≥353.6 μmol/l) or initiation of RRT or in patients <18 years, decrease in eGFR to <35ml/min/1.73m^2.[3] So this is a case of severe AKI. Confirmed case of COVID-19 is defined as a person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.[4]

Case definition of MIS-C by CDC[5] is defined as an individual aged <21 years presenting with fever (i), laboratory evidence of inflammation (ii) and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2 organs) involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological) and no alternative plausible diagnoses and positive for current or recent SARS-CoV-2 infection by RT-PCR serology, or antigen test; or COVID-19 exposure within 4 weeks prior to the onset of symptoms.

In this case scenario, patient was 12 years old having history of fever for 24 hrs, laboratory evidence of infection (elevated CRP, d-dimer, ferritin, elevated neutrophils, lymphopenia and low albumin) and clinically severe illness with renal and hematologic involvement are consistent with MIS-C.

According to Morbidity and Mortality Weekly Report (MMWR)[6] 570 MIS-C patients were reported from March to July 2020, 565 patients were positive for SARS-CoV-2 by RT-PCR. Among them, 18.4% had AKI. In Great Ormond Street Hospital for Children NHS Foundation Trust (London, UK), most cases of AKI were found in those admitted to PICU (93%) and those with pediatric multisystem inflammatory syndrome temporarily associated with SIRS-CoV-2 (PIMS-TS, 73%).[7]

Several mechanisms are possible for AKI in COVID-19 patients, including multi-organ dysfunction syndrome, SARS-CoV-2 direct proximal tubular and podocyte injury, imbalanced renin-angiotensin aldosterone system (RAAS), hypovolaemia, hypoxia, acute respiratory distress syndrome (ARDS), infection-related generalized mitochondrial failure, and cytokine storm syndrome.[8]

Renal biopsy was not done. Diffuse proximal tubule injury with the loss of brush border, clusters of coronavirus like particles with distinctive spikes in the tubular epithelium and podocyte could not be demonstrated in this case.[9]

Cytokine storm syndrome (CSS) and MIS-C share some features but CSS typically present later in the course of acute infection (often during the 2nd week of the respiratory illness) with clinical decline, whereas the time frame of the development of MIS-C following COVID-19 exposure is 2-6 weeks, and affected patients are generally well prior to onset of symptoms. GI symptoms (diarrhea) and evidence of myocardial dysfunction tend to be more prominent in MIS-C than in CSS.[10] This patient had no respiratory symptoms and there was no fall of SpO_2. So remdesivir was not given. [8,11]

Continuous kidney replacement therapy (CKRT) specifically continuous venovenous hemo-diafiltration (CVVHDF) was the best choice for this patient for better clearance of cytokines by convection and diffusion. But in resource limited settings, intermittent hemodialysis by right internal jugular vein with increased blood flow than non COVID patient, even PD is a feasible alternative to CKRT.[12] There is sufficient evidence to prove that PD is equally effective as other forms of KRT.[13] As per the best expertise of our institution, peritoneal dialysis followed by hemodialysis was given to this patient.

Conclusion

This is the first paediatric COVID-19 positive severe AKI in our department. Paediatric studies are warranted to determine the cause-effect relationship between COVID-19 and AKI and effective management strategy in resource poor setting.

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CASE REPORT

COVID-19 Infection in a 8 Day Old Neonate: Report of the 1st Case in a Term Neonate in Special Care Baby Unit (SCABU) at Dhaka Shishu (Children) Hospital

Israt Jahan Zerin[1], M Monir Hossain[2], Md. Mahbubul Hoque[3]

Introduction

The human coronavirus MARS-COV, SARS-COV & SARS-COV-2, have been the causes of serious infections, in which the coronavirus infection disease 2019 (COVID 19) was responsible for an outbreak in Wuhan city, China and gradually became pandemic in early 2020.[1,2] Most reported cases of the disease were in adults, but the disease has also been reported in children, including neonates.[3,4] The important findings in neonate were fever and respiratory distress.[5,6] There is limited data regarding the clinical features, morbidity and mortality of neonates suffering from COVID-19 and also about vertical transmission to fetus.[7] A research conducted on PubMed database from December 2019 to April 27, 2020 revealed that, 25 neonates were affected by SARS-CoV-2.[8]

Our aim is to present the non specific clinical presentation of COVID-19 in neonates that should be picked up at earliest possible time to decrease the morbidity and mortality in neonates.

Case Report

A 4 day old neonate, 1st issue of her non consanguineous parents, got admitted in special care baby unit of Dhaka Shishu (Children) Hospital on 5 May 2020 with the complaints of respiratory distress since birth. She was admitted previously in a general hospital where she was delivered at 38 weeks of gestation by LUCS due to breech presentation and oligohydramnios. Mother, a 21 year old normotensive and non diabetic lady was on regular antenatal check up. She had no history of fever, cough, sore throat, respiratory distress, GI symptoms or exposure to any suspected or confirm case of COVID-19 during her pregnancy period. Birth weight was 2600 gm with an APGAR score of 6/10 at 1 minute and 7/10 at 5 minute. The newborn received resuscitation with tactile stimulation, oropharyngeal and nasopharyngeal suction followed by oxygen inhalation. She was admitted in neonatal ward of Dhaka Shishu (Children) Hospital on her 1st day of life, supportive treatment was started with oxygen inhalation through facemask, infusion 10% dextrose in aqua and emperical antibiotics (Inj Ampicillin and inj Gentamicin). Initially she maintained SpO_2 98% with 5L/min O_2. But at her 3rd day of age baby developed respiratory distress along with occasional grunting respiration. As the condition was not improving there, the neonate was transferred to special care baby unit for further evaluation and better management at her 4th day of life. On admission in SCABU, the neonate was lethargic, dyspnoeic, respiratory rate was 76/min, mild subcostal recession was present, temperature was 39^0C, heart rate 184/min, blood pressure 65/30 mmHg, SpO_2 78% while breathing in room air. There was multiple maculopapular rash all over the body specially in chest and abdomen. Baby was given oxygen through headbox immediately and SpO_2 gradually increased up to 97% with 8 L/min oxygen. Tepid sponging with other supportive care started along with 10% dextrose in 0.225% NaCl solution (120mL/kg/day), injectable antibiotics (Ceftazidime

1. MD Neonatology Phase B Resident, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Dhaka.
2. Professor, Critical Care in Paediatrics, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Dhaka.
3. Professor, Department of Neonatal Medicine, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Dhaka.

Correspondence to: Dr. Israt Jahan Zerin, MD Neonatology Phase B Resident, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital, Dhaka. Cell: 01723415633, E-mail: jerin.mgcc@gmail.com
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and Amikacin). After sponging, temperature decreased to 37^0C and rash disappeared after few hours. The neonate showed constant temperature spikes and these febrile spikes were often associated with maculopapular rash. The rash lasted for several hours after defervescence. Initial investigation sent on admission revealed Hb% - 18.6gm/dl, Hct- 54%, MCV - 94.3fl, WBC 11,500/cumm (N - 54%, L - 36%, M - 08%, E - 02%), CRP - 2.3 mg/L, Serum Na - 148 mmol/L, K - 5.1 mmol/L, Cl - 108 mmol/L, Serum Calcium - 2.6 mmol/L, Serum creatinine - 30 μmol/L, Serum albumin 28.5 g/dl. Arterial blood gas showed pH - 7.26, pCO_2 - 22.1 mmHg, PO_2 - 56 mmHg, HCO_3 - 10.6 mmol/L, B/E - 13.2 mmol/L. Her INR was 0.75, APTT - Control was -28 sec and test 38 sec. Chest X-ray revealed normal findings.

The neonate's condition was static even after 2 days of admission. Fever spikes with evanescent rash continued to appear. The temperature never touched the baseline since admission. At 3rd day of admission, her oxygen demand increased up to 10L/min with increasing respiratory distress with moderate retraction. Repeat CXR was done and revealed nonspecific streaky infiltrates on whole of the right lung field (Fig. 1). Blood Culture sent on admission revealed no growth.

At 4th day of admission, neonate's condition deteriorated. She developed profuse bleeding through nasogastric tube along with mottled skin (CRT 3 sec). Infusion normal saline 20mL/kg bolus given. Inj. Vitamin K, Inj Omeprazole and Inj. Dopamine (7.5ug/kg/min) were added. Fever and rash continued to appear. CRP was increased to 8.5 mg/L (normal <5 mg/L). Nasal swab was obtained from the neonate for the detection of SARS-COV-2 and the test was positive for COVID-19 on his 8th day of age. All the supportive care were continued. The neonate developed sudden desaturation and cardiac arrest at 9th day of life. CPR and bolus adrenaline were given but we failed to resuscitate the neonate. She was declared dead after 20 minutes of resuscitation according to protocol.

As both of the parents and caregivers were asymptomatic, so none of them were tested. As well as breast milk sample, cord blood nucleic acid test were not done due to unavailability in our country.

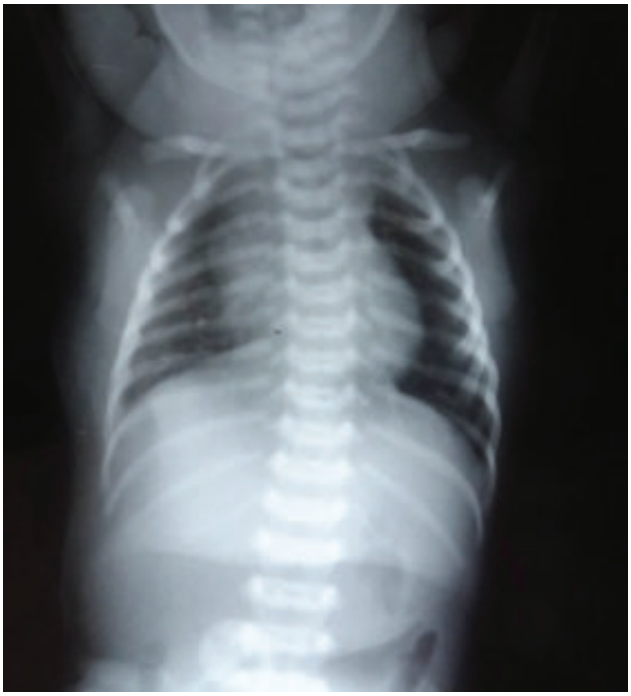

Fig 1 *Chest x ray revealed nonspecific streaky infiltrates on whole of the right lung field.*

Discussion

The important findings in our neonate consistent with the other studies, were the presence of fever & respiratory distress.[5,6] But our case had no cough, rhinorrhea or any GI symptoms. Mottling was reported in a previous study but evanescent rash was not reported in any other neonatal case.[6] We suspect this is a case of nosocomial transmission as both of the parents and caregivers were asymptomatic and absence of skin to skin contact at birth. Throughout her admission in hospital, it seems that, the neonate was infected by nosocomial spread of aerosolized virus or by infected health workers. Although the caregivers used surgical mask at the bedside and personal protective equipment were used by all the heath care workers presented in SCABU. Breastfeeding was excluded as a route of transmission as the neonate was on IV crystalloid solution throughout the course of admission. But still vertical transmission cannot be excluded due to lack of antenatal and perinatal evaluation.

This case strongly influenced the need for collaboration between the obstetricians and neonatologists along with establishment of COVID dedicated maternal and neonatal ward as well as NICU for a secure and isolated environment. Proper guideline and clear protocol should be developed

for not only the pregnant women and neonates but also for the screening and management for all parents, caregivers and staff entering the SCABU and NICU.

This case suggests that, the neonates infected with SARS-COV-2 might be susceptible to severe disease with clinically significant morbidity and mortality. Although all the reported cases throughout the world had stable vitals and no serious complication were reported. So, proper recognition of illness in this population in earliest possible time and clear protocol is essential to reduce the morbidity and mortality in severe SARS-COV-2 infected neonates with or without associated morbidity.

Conclusion

Although there are several hypothesis explaining the reasons for neonates being at lower risk for severe COVID-19, our case appeared to be an exceptional one. Therefore larger cohorts are required for more insight in neonatal COVID-19. As fever is one of the main presenting symptoms, testing should be considered in a febrile neonate for prompt recognition of this illness and for better prognosis.

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CASE REPORT

Acute Promyelocytic Leukemia (APML) in A Four Year Old Child: A Case Report

Sheikh Farjana Sonia[1], Ahmed Murtaza Choudhury[2]

Introduction

Leukemia is the most common malignancy of childhood representing about 30 % of oncohematological diseases diagnosed in children less than 15 years of age. Acute myeloid leukemia (AML) in paediatric field represents the 15-20% of oncohematological disease and the related mortality is approximately 30%. Among paediatric AML the incidence of acute promyelocytic leukemia (APML) is <10%.[1]

The genetic hallmark of APML is the balanced reciprocal translocation of (15:17) (q24:q21), leading to the fusion of promyelocyte (PML) gene with the retinoic acid receptor alpha (RARA) gene. The resulting PML-RARA hybrid oncoprotein is responsible for the block of differentiation of leukaemic promyelocytes and is able to induce leukaemia.[2,3]

The disease is frequently accompanied by a consumptive coagulopathy with life threatening haemorrhages (most severe one occurring in brain and lungs) and more rarely thrombosis. A rapid diagnosis of APML and the initiation of adequate anti leukaemic and supportive therapy are of paramount importance to prevent early death, which is currently considered the most important obstacle to the final cure of this disease. With the introduction of differentiation therapy with ATRA combined with conventional chemotherapy and the subsequent advent of ATO, APML has been transformed from the most rapidly fatal to the most frequently curable form of acute leukemia with long time survival rates up to 90%.[4]

Case Report

A four-year old girl presented at Dr. M R Khan Shishu Hospital and Institute of Child Health with history of gradual pallor and high grade continued fever for two weeks. On examination she was anaemic, febrile and her O2 saturation was 98%. She had bony tenderness, bilateral cervical lymphadenopathy, hepatomegaly and gum hypertrophy (Fig 1) with significant bleeding gums with extensive bruising and petechiae located in the lower limbs.

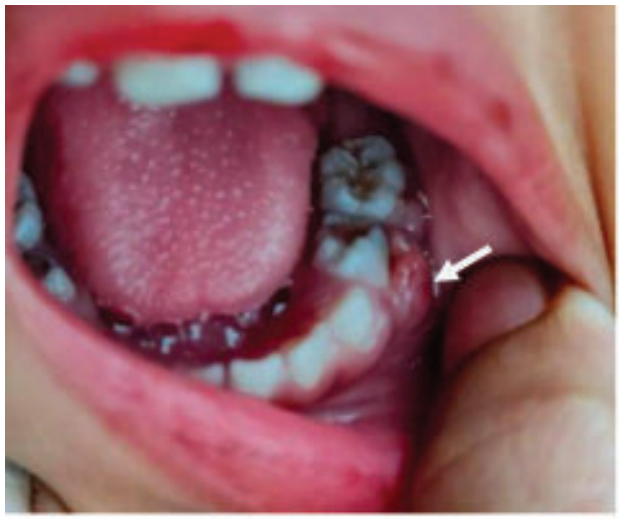

Fig 1 *Gum hypertrophy of the child*

The complete blood count (CBC) showed severe normocytic normochromic anemia (Hb - 4.9 g/dl), severe thrombocytopenia (PLT - $15x10^3$ /il) and leukocytosis (WBC - $37x10^3$/il) with neutropenia (Neutrophils - $0.41x10^3$/il). The peripheral blood film (PBF) showed several blasts (43%) with small and stubby cytoplasmatic auer roads, bilobbed nucleus with atypical appearance of internuclear bridge (Fig 2). Prothrombin time was 15 s (control 14 s), activated partial thromboplastin time (APTT) was 38 s (control 34 s) and fibrinogen was 1.5 g/L (2-4 g/L).

1. Assistant Professor, Department of Paediatrics, Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka, Bangladesh.
2. Professor, Department of Paediatrics, Dr. MR Khan Shishu Hospital and Institute of Child Health, Dhaka, Bangladesh.

Correspondence to: Dr. Sheikh Farjana Sonia**,** Assistant Professor, Department of Paediatrics**,** Dr. MR Khan Shishu Hospital and Institute of Child Health**,** Dhaka, Bangladesh. Cell: +8801752038848, E-mail: soniafarzana7@gmail.com
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Bone marrow was hypercellular with >90% atypical cell. The blasts have enough cytoplasm with granules and occasional faggots, loose chromatin with 1-3 nucleoli resembling atypical promyelocytes which give evidence for APML-M3. Flowcytometry (Fig 3) revealed a predominant CD 45 (98.7%) population which are positive for myeloid cell markers CD 13 (76.7%), CD 33 (96.5%), CD 117 (44.2%), MPO (64.7%) and precursor marker Cd 34. PML-RARá was detected in the bone marrow aspirate by RT-PCR.

So the child was diagnosed as a case of APML (PML-RARA positive). Treatment was started immediately with conventional ATRA and ATO protocol and prophylaxis with dexamethasone for differentiation syndrome. Supportive management including blood transfusion was given accordingly.

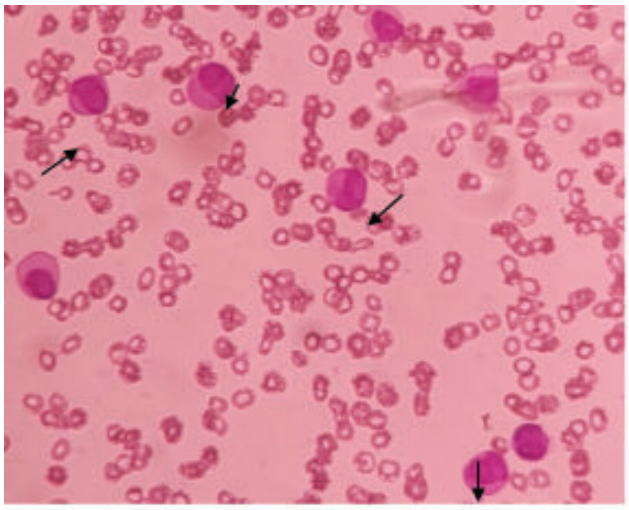

Fig 2 *PBF of the child with APML showing blast with bilobbed neucleoli*

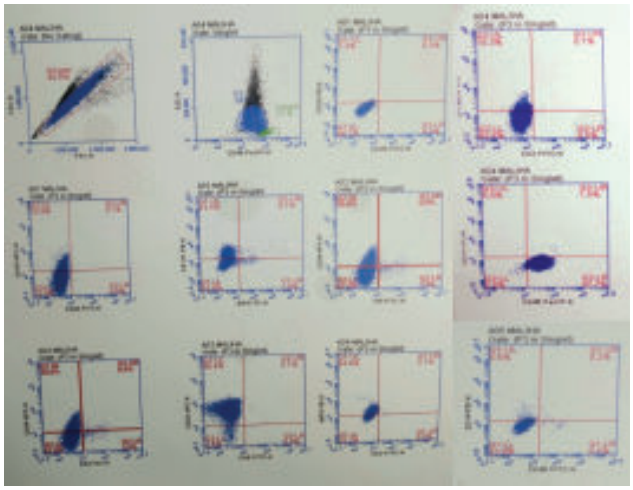

Fig 3 *Flowcytometry of the child with APML*

Discussion

APML was first described in late 1950s in Norway and France as a hyperacute fatal illness associated with hemorrhagic syndrome.[5] Over the last few decades, APML has been transformed from a highly fatal disease to a highly curable one.[6] APML, the French-American-British (FAB) M3 subtype of AML, results from clonal proliferation of myeloid lineage cells that are arrested at the promyelocyte stage. So the defect is in normal granulocyte cell maturation and apoptosis. A gene translocation occurs in an abnormal cell between chromosome 15 and 17 in between the retinoic acid receptor, or RARA (RARá) and the promyelocytic gene, or PML gene, which is active in cell death and tumor suppression.[7] This unique break point allows for three isoforms of the gene, the most typical of which is t(15;17) (q22; q21).[8,9]

Children with APML usually present with the signs and symptoms of cytopenias common to other leukemias. Fatigue, pallor, shortness of breath, fever and bleeding manifestation like bruising, and peticheia of the mouth and other parts of the body are frequent presentation.[10] Our patient presented with the fever, pallor and bleeding manifestations. Extramedullary diseases such as hepatomegaly, splenomegaly, and lymphadenopathy are seen less commonly in APML compared with other subtypes of AML, and CNS leukemia is rare.[11] Gum hypertrophy is a common finding.[12] Our patient also presented with gum hypertrophy.

The central distinguishing feature of APML, as compared to other forms of leukemia, is its propensity to cause disseminated intravascular coagulopathy (DIC). 80-90% of patients with APML will have evidence of bleeding diathesis as well as intracranial haemorrhage on initial presentation.[13,14] Secondary infections like *Candida albicans* in the oropharyngeal area and Varicella zoster virus can appear in pediatric APML patients as well as localized soft tissue infections of herpes simplex virus can also occur.[12,15]

CBC typically reveals a lowered hemoglobin, hematocrit and leukocytosis or pancytopenia. PBF indicates a significant population (at least 20%) of large promyelocytes of hypergranular or microgranular bilobed form.[16,17] Our patient had leukocytosis with thrombocytopenia and also bilobed form of blast in blood film. The presence of Auer rods is also a significant clue. Severe coagulopathy and DIC are evidenced by lowered fibrinogen, overproduction of plasmin, elevated FDP and Ddimer

and increased prothrombin or thromboplastin times.[18] Bacterial and fungal cultures may be necessary to identify infections. CSF studies may also be recommended for high white blood cell counts to evaluate cellular movement in the body.[18]

In suspected APML with t(15;17), a bone marrow biopsy and aspirate should be quickly obtained for cellular differentials, histology studies, myeloperoxidase activity, and cell antigen marker testing.[19] Morphologically over 25 % of paediatric APML appear as microgranular variant.[19] In flow cytometry studies, a single major cluster population with a wide range of side scatter on a scatter dot plot suggests an APML profile.[20] Cellular antigen CD33, co-expression of CD13, lack of or weak HLA-DR, and CD34 are also further evidence of the atypical population.[20] For molecular confirmation, samples should be send for investigation with FISH probing to search for the typical translocation and also for cytogenetic studies to look for an abnormal chromosomal karyotype.[16] Quantitative PCR results of the gene transcript ratio also serves as a positive confirmatory procedure. Because the classic t(15;17) translocation creates two fusion genes from one splice, 70% of cases with translocation, harbor a RARA/PML gene, and 100% show the reciprocal PML/RARA gene.[20] This makes qPCR a useful assay for disease screening.

Treatment of APML with t(15;17) is different from other variations of AML in that it is the only one with a target specific therapy.[16] The use of all-*trans* retinoic acid (ATRA) initiates differentiation of the immature myeloid cells and helps manage coagulopathy.[7] This vitamin A derivative releases repressor complexes from the RARA receptor fusion gene, thus help to get rid the blood of promyelocytes and their destructive granular material which contributes to DIC.[16] Patients undergoing ATRA treatment are at risk for differentiation/retinoic acid syndrome.[12,15] This syndrome is thought to arise from inflammatory cytokines released from inducing maturation of promyelocytes with ATRA from treated cells.[21] Symptoms are fever, respiratory distress, weight gain, pleural and pericardial efusions, hypotension, and/or renal failure.[15,21] Pediatric patients are particularly at risk for pulmonary edema.[15] Treatment of this entity consists of discontinuation of ATRA, administering dexamethasone and providing cardiorespiratory support.[22] In our patient we started Dexamethasone for prophylaxis of differentiation syndrome.

In addition to ATRA, use of arsenic trioxide (ATO) has also shown effectiveness in improving prognosis. It has become an additional standard of care since 2000, especially in patients with ATRA resistance and relapsing cases.[23] Arsenic trioxide is a destructive therapy for the abnormal fusion protein, and aids in marking the oncoprotein for degradation.[7] It functions similarly in advocating cell differentiation and apoptosis. APML with high risk patient should be treated with additional chemotherapy because cell differentiation and remission is not long-lasting.[16,20] Possible chemotherapeutic drugs to support ATRA and ATO therapy include anthracycline and cytarabine.[20, 24] In conjunction with chemotherapy, aggressive therapy of DIC should be undertaken. Fresh frozen plasma and/or cryoprecipitate should be transfused to maintain fbrinogen levels over 150 g/dL and platelets should be transfused to maintain platelet counts over 50 x109 /liter. Heparin has not been demonstrated to have a clear beneft and is not recommended for DIC related to APML.[25]

The overall prognosis of APML is excellent, with more than 90% of patients achieving complete remission and 5- year overall survival rates in excess of 80%.[26]

Conclusion

Acute promyelocytic leukemia (APML) is one of the few hematologic diseases that can be diagnosed with certainty by morphological examination of blood film and bone marrow aspirate by the practicing hematologist. However, whenever APML is suspected based on clinical presentation and/or peripheral blood smear, disease-targeted therapy should be initiated as soon as possible to reduce the mortality from APML.

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DS (Child) H J 2020; 36(2) : 170-173

ABSTRACTS FROM CURRENT LITERATURE

Determining the optimal strategy for reopening schools, the impact of test and trace interventions, and the risk of occurrence of a second COVID-19 epidemic wave in the UK: a modelling study

Jasmina Panovska-Griffiths, Cliff C Kerr, Robyn M Stuart, Dina Mistry, Daniel J Klein, Russell M Viner, Chris Bonell

Lancet Child Adolesc Health 2020;4:817-27.

Background: As lockdown measures to slow the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection begin to ease in the UK, it is important to assess the impact of any changes in policy, including school reopening and broader relaxation of physical distancing measures. We aimed to use an individual-based model to predict the impact of two possible strategies for reopening schools to all students in the UK from September, 2020, in combination with different assumptions about relaxation of physical distancing measures and the scale-up of testing.

Methods: In this modelling study, we used Covasim, a stochastic individual-based model for transmission of SARS-CoV-2, calibrated to the UK epidemic. The model describes individuals' contact networks stratified into household, school, workplace, and community layers, and uses demographic and epidemiological data from the UK. We simulated six different scenarios, representing the combination of two school reopening strategies (full time and a part-time rota system with 50% of students attending school on alternate weeks) and three testing scenarios (68% contact tracing with no scale-up in testing, 68% contact tracing with sufficient testing to avoid a second COVID-19 wave, and 40% contact tracing with sufficient testing to avoid a second COVID-19 wave). We estimated the number of new infections, cases, and deaths, as well as the effective reproduction number (R) under different strategies. In a sensitivity analysis to account for uncertainties within the stochastic simulation, we also simulated infectiousness of children and young adults aged younger than 20 years at 50% relative to older ages (20 years and older).

Findings: With increased levels of testing (between 59% and 87% of symptomatic people tested at some point during an active SARS-CoV-2 infection, depending on the scenario), and effective contact tracing and isolation, an epidemic rebound might be prevented. Assuming 68% of contacts could be traced, we estimate that 75% of individuals with symptomatic infection would need to be tested and positive cases isolated if schools return full-time in September, or 65% if a part-time rota system were used. If only 40% of contacts could be traced, these figures would increase to 87% and 75%, respectively. However, without these levels of testing and contact tracing, reopening of schools together with gradual relaxing of the lockdown measures are likely to induce a second wave that would peak in December, 2020, if schools open full-time in September, and in February, 2021, if a part-time rota system were adopted. In either case, the second wave would result in R rising above 1 and a resulting second wave of infections 2·0–2·3 times the size of the original COVID-19 wave. When infectiousness of children and young adults was varied from 100% to 50% of that of older ages, we still found that a comprehensive and effective test–trace–isolate strategy would be required to avoid a second COVID-19 wave.

Interpretation: To prevent a second COVID-19 wave, relaxation of physical distancing, including reopening of schools, in the UK must be accompanied by large-scale, population-wide testing of symptomatic individuals and effective tracing of their contacts, followed by isolation of diagnosed individuals.

Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study

Christine M Salvatore, Jin-Young Han, Karen P Acker, Priyanka Tiwari, Jenny Jin, Michael Brandler, Carla Cangemi, Laurie Gordon, Aimee Parow, Jennifer DiPace, Patricia DeLaMora

Lancet Child Adolesc Health 2020;4:721-27.

Background: The risk of vertical and perinatal transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, which causes COVID-

19), the most appropriate management, and the neonate's risk of developing COVID-19 during the perinatal period are unknown. Therefore, we aimed to elucidate best practices regarding infection control in mother–newborn dyads, and identify potential risk factors associated with transmission.

Methods: In this observational cohort study, we identified all neonates born between March 22 and May 17, 2020, at three New York Presbyterian Hospitals in New York City (NY, USA) to mothers positive for SARS-CoV-2 at delivery. Mothers could practice skin-to-skin care and breastfeed in the delivery room, but had to wear a surgical mask when near their neonate and practice proper hand hygiene before skin-to-skin contact, breastfeeding, and routine care. Unless medically required, neonates were kept in a closed Giraffe isolette in the same room as their mothers, and were held by mothers for feeding after appropriate hand hygiene, breast cleansing, and placement of a surgical mask. Neonates were tested for SARS-CoV-2 by use of real-time PCR on nasopharyngeal swabs taken at 24 h, 5–7 days, and 14 days of life, and were clinically evaluated by telemedicine at 1 month of age. We recorded demographics, neonatal, and maternal clinical presentation, as well as infection control practices in the hospital and at home.

Findings: Of 1481 deliveries, 116 (8%) mothers tested positive for SARS-CoV-2; 120 neonates were identified. All neonates were tested at 24 h of life and none were positive for SARS-CoV-2. 82 (68%) neonates completed follow-up at day 5–7 of life. Of the 82 neonates, 68 (83%) roomed in with the mothers. All mothers were allowed to breastfeed; at 5–7 days of life, 64 (78%) were still breastfeeding. 79 (96%) of 82 neonates had a repeat PCR at 5–7 days of life, which was negative in all; 72 (88%) neonates were also tested at 14 days of life and none were positive. None of the neonates had symptoms of COVID-19.

Interpretation: Our data suggest that perinatal transmission of COVID-19 is unlikely to occur if correct hygiene precautions are undertaken, and that allowing neonates to room in with their mothers and direct breastfeeding are safe procedures when paired with effective parental education of infant protective strategies.

Intensive care admissions of children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the UK: a multicentre observational study

Patrick Davies, Claire Evans, Hari Krishnan Kanthimathinathan, Jon Lillie, Joseph Brierley, Gareth Waters, Mae Johnson, Benedict Griffiths, Pascale du Pré, Zoha Mohammad, Akash Deep, Stephen Playfor, Davinder Singh, David Inwald, Michelle Jardine, Oliver Ross, Nayan Shetty, Mark Worrall, Ruchi Sinha, Ashwani Koul, Elizabeth Whittaker, Harish Vyas, Barnaby R Scholefield, Padmanabhan Ramnarayan

Lancet Child Adolesc Health 2020;4:669-77.

Background: In April, 2020, clinicians in the UK observed a cluster of children with unexplained inflammation requiring admission to paediatric intensive care units (PICUs). We aimed to describe the clinical characteristics, course, management, and outcomes of patients admitted to PICUs with this condition, which is now known as paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS).

Methods: We did a multicentre observational study of children (aged <18 years), admitted to PICUs in the UK between April 1 and May 10, 2020, fulfilling the case definition of PIMS-TS published by the Royal College of Paediatrics and Child Health. We analysed routinely collected, de-identified data, including demographic details, presenting clinical features, underlying comorbidities, laboratory markers, echocardiographic findings, interventions, treatments, and outcomes; serology information was collected if available. PICU admission rates of PIMS-TS were compared with historical trends of PICU admissions for four similar inflammatory conditions (Kawasaki disease, toxic shock syndrome, haemophagocytic lymphohistiocytosis, and macrophage activation syndrome).

Findings: 78 cases of PIMS-TS were reported by 21 of 23 PICUs in the UK. Historical data for similar inflammatory conditions showed a mean of one (95% CI 0·85–1·22) admission per week, compared to an average of 14 admissions per week for PIMS-TS and a peak of 32 admissions per week during the study

period. The median age of patients was 11 years (IQR 8–14). Male patients (52 [67%] of 78) and those from ethnic minority backgrounds (61 [78%] of 78) were over-represented. Fever (78 [100%] patients), shock (68 [87%]), abdominal pain (48 [62%]), vomiting (49 [63%]), and diarrhoea (50 [64%]) were common presenting features. Longitudinal data over the first 4 days of admission showed a serial reduction in C-reactive protein (from a median of 264 mg/L on day 1 to 96 mg/L on day 4), D-dimer (4030 ìg/L to 1659 ìg/L), and ferritin (1042 ìg/L to 757 ìg/L), whereas the lymphocyte count increased to more than $1{\cdot}0 \times 10^9$ cells per L by day 3 and troponin increased over the 4 days (from a median of 157 ng/mL to 358 ng/mL). 36 (46%) of 78 patients were invasively ventilated and 65 (83%) needed vasoactive infusions; 57 (73%) received steroids, 59 (76%) received intravenous immunoglobulin, and 17 (22%) received biologic therapies. 28 (36%) had evidence of coronary artery abnormalities (18 aneurysms and ten echogenicity). Three children needed extracorporeal membrane oxygenation, and two children died.

Interpretation: During the study period, the rate of PICU admissions for PIMS-TS was at least 11-fold higher than historical trends for similar inflammatory conditions. Clinical presentations and treatments varied. Coronary artery aneurysms appear to be an important complication. Although immediate survival is high, the long-term outcomes of children with PIMS-TS are unknown.

Emergence of Kawasaki disease related to SARS-CoV-2 infection in an epicentre of the French COVID-19 epidemic: a time-series analysis

Naim Ouldali, Marie Pouletty, Patricia Mariani, Constance Beyler, Audrey Blachier, Stephane Bonacorsi, Kostas Danis, Maryline Chomton, Laure Maurice, Fleur Le Bourgeois, Marion Caseris, Jean Gaschignard, Julie Poline, Robert Cohen, Luigi Titomanlio, Albert Faye, Isabelle Melki, Ulrich Meinzer

Lancet Child Adolesc Health 2020;4:662-68.

Background: Kawasaki disease is an acute febrile systemic childhood vasculitis, which is suspected to be triggered by respiratory viral infections. We aimed to examine whether the ongoing COVID-19 epidemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is associated with an increase in the incidence of Kawasaki disease.

Methods: We did a quasi-experimental interrupted time series analysis over the past 15 years in a tertiary paediatric centre in the Paris region, a French epicentre of the COVID-19 outbreak. The main outcome was the number of Kawasaki disease cases over time, estimated by quasi-Poisson regression. In the same centre, we recorded the number of hospital admissions from the emergency department (2005–2020) and the results of nasopharyngeal multiplex PCR to identify respiratory pathogens (2017–2020). These data were compared with daily hospital admissions due to confirmed COVID-19 in the same region, recorded by Public Health France.

Findings: Between Dec 1, 2005, and May 20, 2020, we included 230 patients with Kawasaki disease. The median number of Kawasaki disease hospitalisations estimated by the quasi-Poisson model was 1·2 per month (IQR 1·1–1·3). In April, 2020, we identified a rapid increase of Kawasaki disease that was related to SARS-CoV-2 (six cases per month; 497% increase [95% CI 72–1082]; p=0·0011), starting 2 weeks after the peak of the COVID-19 epidemic. SARS-CoV-2 was the only virus circulating intensely during this period, and was found in eight (80%) of ten patients with Kawasaki disease since April 15 (SARS-CoV-2-positive PCR or serology). A second peak of hospital admissions due to Kawasaki disease was observed in December, 2009 (six cases per month; 365% increase ([31–719]; p=0.0053), concomitant with the influenza A H1N1 pandemic.

Interpretation: Our study further suggests that viral respiratory infections, including SAR-CoV-2, could be triggers for Kawasaki disease and indicates the potential timing of an increase in incidence of the disease in COVID-19 epidemics. Health-care providers should be prepared to manage an influx of patients with severe Kawasaki disease, particularly in countries where the peak of COVID-19 has recently been reached.

Epidemiological and Clinical Profile of Pediatric Inflammatory Multisystem Syndrome - Temporally Associated with SARS-CoV-2 (PIMS-TS) in Indian Children

K Dhanalakshmi, Aishwarya Venkataraman, S Balasubramanian, Manoj Madhusudan, Sumanth Amperayani, Sulochana Putilibai, Kalaimaran Sadasivam, Bala Ramachandran and AV Ramanan

Indian Pediatr 2020;57:1010-14.

Background: We describe the demographic, clinical and labo-ratory findings along with the treatment and outcomes among children meeting the case definition of Pediatric Inflammatory Multisystem Syndrome - Temporally associated with SARS-CoV-2 (PIMS-TS).

Methods: We analyzed the clinical and laboratory findings of children who presented with PIMS-TS during an 8-week period from May 4, 2020 to July 8, 2020.

Results: We report 19 children with a median age of 6 year (IQR: 13 months-16 years), who met the case definition of PIMS-TS. All of them presented with fever. Multi organ involvement (79%), mucocutaneous involvement (74%), cardiovascular symptoms (63%) and gastrointestinal symptoms (42%) were the other features. Elevated levels of C-reactive protein was found in all of them and the majority of them had evidence of coagulopathy; intensive care admissions were needed in 12 (63%) and vasoactive medications were given to 6 (31.5%) children. There were no deaths.

Conclusion: Children with PIMS-TS present with a wide range of signs and symptoms. Fewer children in this series had coronary artery abnormalities, and there was a low incidence of RT-PCR positivity with high presence of SARS-CoV-2 antibodies.

Multisystem Inflammatory Syndrome in Children With COVID-19 in Mumbai, India

Shreepal Jain, Supratim Sen, Srinivas Lakshmivenkateshiah, Prashant Bobhate, Sumitra Venkatesh, Soonu Udani, Laxmi Shobhavat, Parmanand Andankar, Tanuja Karande and Snehal Kulkarni

Indian Pediatr 2020;57:1015-19

Objective: We describe the presentation, treatment and outcome of children with multisystem inflammatory syndrome with COVID-19 (MIS-C) in Mumbai metropolitan area in India.

Methods: This is an observational study conducted at four tertiary hospitals in Mumbai. Parameters including demographics, symptomatology, laboratory markers, medications and outcome were obtained from patient hospital records and analyzed in patients treated for MIS-C (as per WHO criteria) from 1 May, 2020 to 15 July, 2020.

Results: 23 patients (11 males) with median (range) age of 7.2 (0.8-14) years were included. COVID-19 RT-PCR or antibody was positive in 39.1% and 30.4%, respectively; 34.8% had a positive contact. 65% patients presented in shock; these children had a higher age (P=0.05), and significantly higher incidence of myocarditis with elevated troponin, NT pro BNP and left ventri-cular dysfunction, along with significant neutrophilia and lympho-penia, as compared to those without shock. Coronary artery dilation was seen in 26% patients overall. Steroids were used most commonly for treatment (96%), usually along with intra-venous immunoglobulin (IVIg) (65%). Outcome was good with only one death.

Conclusion: Initial data on MIS-C from India is presented. Further studies and longer surveillance of patients with MIS-C are required to improve our diagnostic, treatment and surveillance criteria.

BICH NEWS

BICH is the academic wing of Dhaka Shishu Hospital. It was established in 30 January 1983. It is affiliated with Dhaka University, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Bangladesh College of Physicians and Surgeons (BCPS). It has established Basic Science Department in the year 2006. It has been conducting different courses e.g. FCPS (in General Paediatrics and also subspeciality like FCPS Neonatology, Paediatric Nephrology, Paediatric Haemato-oncology, Paediatric Neurology and Development, Paediatric Pulmonology, Paediatric Cardiology under BCPS), MD Residency Course in General Paediatrics and Neonatology and Nephrology under BSMMU. MD Non residency courses under Dhaka University and BSMMU, MS (Paediatric Surgery) Residency Course under BSMMU, MS (Paediatric surgery) non residency course under Dhaka University, DCH course under BSMMU. BICH is also conducting Diploma in Paediatric Nursing course under Bangladesh Nursing Council, BSc in Health Technology course under Dhaka University. It conducts 3 months certificate course in Paediatrics and 15 days Intensive course for MCPS examinee. It organizes different programme, seminars and symposium on Paediatrics. Apart from these the Institute also runs its regular academic activities. During COVID-19 Pandamic BICH is conducting online classes and other academic activities and seminars since April 2020.

Library facilities

The library of BICH has a rich collection of updated medical texts and reference books and reputed Medical Journals form home and abroad. BICH has introduced Broad Band facilities which are open to all students, teachers/ consultants of hospital for 24 hours. Facilities of library are also improved by HINARI. Students can download 2230 Medical Journals & more than 50 Paediatric Journals.

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Postgraduate Courses and Training in Paediatrics in BICH

1. BICH has course for FCPS in General Paediatrics (2nd part): Student can be registrared twice in a year, in the months of January and July.
2. BICH and Dhaka Shishu (Children) Hospital is a recognized center by BCPS for training in FCPS (Paeditric Medicine and Surgery).
3. It is a recognized centre for course and training in different subspeciality of Paediatrics like Neonatology, Paediatric Nephrology, Paediatric Haematology and Oncology, Paediatric Pulmonology, Paediatric Neuroscience and Paeditric Cardiology.
4. There is MD Residency program in General Paediatrics, Neonatology, Paediatric Nephrology and MS Paediatric Surgery. Phase A commences in the month of March every year. There is also MD Paediatrics and Paediatric Surgery Non Residency Courses which commences in the month of January and July.
5. DCH course: Once in a year in the month of July.
6. Other courses conducted by BICH are
   - Paediatric Nursing.
   - BSc in Health Technology.
   - Three months certificate course: Every year the institute conducts 3 months certificate course on Paediatrics for general practitioners & other post graduate candidates e.g. MCPS.
   - Training programme on Essential Newborn Care for doctors and nurses, KMC (Kangaroo Mother Care) training, ETAT (Emergency Triage, Assessment and Treatment) training, IMCI (Integrated management of childhood illness), newborn and paediatric standards and use of oxygen therapy for hypoxemia management etc. are conducted by BICH.

Contact Person : Academic Director
Bangladesh Institute of Child Health
Sher-e-Bangla Nagar, Dhaka - 1207.

Contact : Phone No. 55059063, 55059064, 55059051-60 Ext. 411.
E-mail: infodshjournal@gmail.com, info.bich@gmail.com

Students Qualified from Bangladesh Institute of Child Health

Student qualified from BICH till December 2020

Course	Number
DCH	370
MD Paediatrics	104
MS Paediatrics	99
FCPS Paediatrics	16
MD Neonatology	11
MD Pediatrics Nephrology	05
Total	605

Foreign student qualified from BICH till December 2020

Course of origin	Course	Number
Nepal	DCH	23
	MS (Paediatric Surgery)	02
	MD (Paediatrics)	01
India	MD (Paediatrics)	01
Iran	DCH	01
Iraq	DCH	01
Somalia	DCH	01
Sudan	DCH	01
Total		31

Present Students (December 2020)

Name of Courses	Number of Students
MD (General Paediatrics) Phase - A	26
MD (Neonatology) Phase - A	4
MD (Paediatric Nephrology) Phase - A	3
MS (Paediatric Surgery) Phase - A	4
FCPS (Paediatric) Part - II	2
MD (Paediatrics) Part - III	8
FCPS (Paediatric Cardiology)	1
FCPS (Paediatric Nephrology)	1
MS (Paediatrics Surgery) Part - III	2
DCH	22
MD (General Paediatrics) Phase - B	17
MD (Neonatology) Phase - B	4
MD (Nephrology) Phase - B	3
MS (Paediatric Surgery) Phase - B	6
Total	103

INSTRUCTIONS FOR AUTHORS

Dhaka Shishu (Children) Hospital Journal is the official organ of Bangladesh Institute of Child Health (BICH) which is the academic wing of Dhaka Shishu (Children) Hospital. It is a peer reviewed, open access journal published twice a year since 1984. This journal is recognized by Bangladesh Medical and Dental Council (BMDC) which is the highest body for the recognition of medical journals in Bangladesh. All parts of the journal are indexed/tracked/covered by DOI/CrossRef and BanglaJOL. The present Editorial board has decided that the cover design will be in accordance with the subjects of editorial in each issue. The editor welcomes articles to be published to the journal as leading article, original article, review article, case report, current issues of child health, short report and junior's page where trainee doctors are encouraged to publish their topic of interest.

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- Manuscript should be typed in English and on one side of A4 (220) x 210 cm) size 12, with single space.
- There should be one original and two paper copies and one IBM compatible electronic copy. (CD or Pen drive)
- There should be a margin of 2.5 cm at top and bottom, and 1.2 cm left and right.
- Pages should be numbered in English numerical at the upper right hand, consecutively, beginning with the title page.
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- Name of authors, e.g. 1. Prof. Saiful Islam, 2. Dr. Nurun Nahar, these two author's name will be written like this; Saiful Islam1, Nurun Nahar2, etc. (Font size 12). Author's designation and name of place of study will be written after the end of the abstract (Font size 10).
- Abstract with a structured format with five sections (about 250 words maximum): Background, Objective, Methods, Results and Conclusion. All these sections will be in Times New Roman, Font size 12, italic and bold. Text will not be bold and after the text there will be Key words (not more than 10). No references are allowed in the abstract.

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DHAKA SHISHU (CHILDREN) HOSPITAL

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Dhaka Shishu (Children) Hospital has been modernized with sophisticated equipments for the following investigations

Pathology

1. Mythic18 Automated Haematology Analyser having 18 parameters: WBC count with 3 parts differential - RBC count, Haemoglobin percentage, HCT, MCV, MCH, MCHC, RDW, Platelet count, MPV, PDW
2. Haemoglobin Electrophoresis
3. BT, CT, PT, APTT
4. Routine urine exam, including pH, urobilinogen, bilirubin, haemoglobin and morphology of RBC in urine.
5. Routine stool exam, including reducing substances and occult blood test
6. Osmotic Fragility test
7. NESTROFT for screeing of beta thalassaemia
8. LE cell Phenomenon
9. Sputum for Eosinophils

Microbiology

1. All types of cultures and sensitivity test of aerobic and anaerobic organisms
2. Serological Test - Widal test, Febrile Antigen, ASO titre, RA Test, VDRL, HbsAg, ICT for Kala-Azar, Malaria, Filaria and Dengue
3. Cytology-
   CSF analysis with Latex agglutination test for bacterial antigens
4. Staining - gram stain, AFB stain, KLB stain
5. Skin scrapping for fungus

Biochemistry

1. Full auto biochemistry analyzer (Dade Behring)- Dimension RxL Max with random acesss test- Bilirubin, SGPT, SGOT, Alkaline Phosphatase, Urea, Creatinine, Calcium, Phosphate, Uric Acids, Protein, Albumin, Glucose, CPK, Serum Electrolytes, Serum Ferritin, CRP, ammonia, lactate
2. Semi Auto Biochemistry analyzer - Routine biochemical tests
3. Electrolyte analyzer - Na, K, Cl, TCO_2
4. Gas analyzer - Blood pH, PCO_2, PO_2, HCO_3, O_2 saturation, Base excess, Oxyhemoglobin, Carboxy hemoglobin, Methemoglobin, Deoxyhemoglobin, Oxygen binding capacity

Blood Bank

1. Blood grouping and cross matching
2. Screening test - HbsAg, HCV, HIV, VDRL, MP
3. Coomb's test - direct and indirect
4. Collection of platelet & concentrate

Histopathology : Histopathology of all surgical specimens

Cytology: FNAB of all superficial and deep masses. Cytology of all effusions

Radiology and Imaging

1. All types of plain x-ray - 24 hours service, contrast radiographic examination-Barium swallow, enema, IVU and MCU both neonates and children
2. Conventional Ultrasonography by SIEMENS Sonoline Prima Having Multi frequency, multi probe facilities. USG are performed like- brain, abdomen, eye, hipjoint and musculoskeletal system
3. Color Doppler study by SIEMENS Color Doppler Machine (Sonoline - G40), study of abdominal vessels, portal vein, renal artery, cerebral arteries, vascular malformation of neck- upper/lower limbs
4. Portable USG for very sick indoor patients
5. Colour Doppler Echocardiogram

Director
Dhaka Shishu (Children) Hospital

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