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Address of correspondence :
Editor
Journal of Dhaka Medical College
Dhaka Medical College and Hospital, Dhaka

Telephone :
Office : +880-2-8613252 (Direct)
+880-2-8626812-23 / 2305 (PABX)
E-mail : jdmceditor@gmail.com

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The **title page** should carry 1) the title of the article, which should be concise but informative; 2) authors' name, with highest academic degree and institutional affiliation.

The abstract of original article should be structured and of no more than 250 words. The specimen of a structured abstract follows :

Title

Multiorgan failure in a cardiac surgical intensive care unit.

Abstract

Background/Context : To find out incidence and various risk factors associated with multiorgans failure in patient after cardiac surgery.

Materials and Methods : A prospective study of 935 consecutive admissions to cardiac surgical intensive care unit over a period of one year, April 1994 to March 1995. Cardiac surgical intensive care unit, National Institute of Cardiovascular Diseases, Dhaka. Nine hundred thirty five patients admitted to cardiac surgical intensive care unit after cardiac surgery.

Results : Mean age of patients was 29.6 years; males were 66.8%. As regards preoperative risk factors, 24.3% had systemic disease, 19.5% had cardiac dysfunction, 7.5% and 3.4% had hepatic and renal dysfunction respectively, 7.3% underwent emergency surgery, seventy percent of patients underwent surgery on cardiopulmonary bypass. Postoperatively 18.3% patients developed low cardiac output syndrome. Respiratory, acute renal and hepatic failure was seen in 7.5%, 4.6% and 2.9% respectively. 2.8% patients developed septicaemia and 2.2% developed multiorgan failure. Mean duration of intensive care unit stay was 1.9 days.

Conclusion : Cardiac surgical patients form a separate subset of multiorgan failure with different predisposing factors, pathophysiology and outcome. Pre-existing organ dysfunction, clinical status, surgery on cardio-pulmonary bypass, post-operative low cardiac output syndrome and septicaemia play significant role in causing multiorgan failure.

Three to six **key words** should be added to the bottom of the abstract.

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Abood S. Quality improvement initiative in nursing homes: the ANA acts in an advisory role. Am J Nurs I

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Haq MM, Barman A, Majumder MAA, Mashreky SMSR, editors. Training health professionals through unity of education and practice for quality health care. Proceedings of 3rd National Conference on Medical Education of National Association for Medical Education (NAME) 2000 February 19-20. Bangladesh : Dhaka;2000.

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Avoid **abbreviations** in the title and abstract. The full term for which an abbreviation stands should precede its first use in the text, unless it is a standard unit of measurement.

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EDITORIAL

Advancing Medical Education in Bangladesh through Integration and Group Discussion

Bangladesh has made great progress in recent years in modernizing its medical school system to meet international standards and generate skilled and kind medical professionals. The implementation of integrated medical education and the use of group discussions as a teaching technique are crucial components of this change. These strategies have enormous potential to support medical students' clinical competency, teamwork, and critical thinking while meeting Bangladesh's changing healthcare delivery needs. This editorial examines the value of group discussions and integrated medical education in Bangladesh, emphasizing their contributions to the development of qualified medical professionals.

The Case for Integrated Medical Education

Integrated medical education moves away from traditional, discipline-based teaching, where subjects like anatomy dieses, physiology, and pharmacology are taught in isolation. Instead, it emphasizes a holistic curriculum that interweaves basic sciences with clinical practice from the early years of medical training. In Bangladesh, studies have shown that students and faculty view integrated teaching favorably, with a 2021 cross-sectional study reporting a mean score of 3.47 (out of 4) for adopting integrated curricula in MBBS programs, compared to 1.2 for the existing curriculum.[1] This shift is crucial for preparing students to address complex clinical scenarios that require synthesizing knowledge across disciplines.

The benefits of integration are manifold. It promotes contextual learning, enhances retention of knowledge, and prepares students for real-world challenges where patients present with multifaceted conditions. For instance, pharmacology, a core preclinical science, can be integrated across all phases of medical education to improve prescribing competency, a critical skill for future physicians.[2] In Bangladesh, where the healthcare system faces challenges such as resource constraints and a high patient load, an integrated curriculum ensures that graduates are better equipped to make informed, logical decisions in clinical practice.

However, implementing integrated curricula is not without challenges. Faculty training, curriculum redesign, and resource allocation are significant hurdles, particularly in private medical colleges where infrastructure may lag. The government's initiatives, such as the Further Improvement of Medical Colleges (FIMC) Project and the establishment of the Centre for Medical Education (CME), have laid a foundation for reform, but sustained investment and stakeholder collaboration are essential to scale these efforts.[3]

The Role of Group Discussion in Medical Education

Complementing integrated education, **group discussion** is a powerful active learning strategy that fosters critical thinking, communication skills, and teamwork—essential for modern medical practice. In Bangladesh, where medical students often rely on rote memorization due to large class sizes and exam-oriented teaching, group discussions offer a dynamic platform for peer-to-peer learning and problem-solving. A 2019 survey revealed that 90% of medical students preferred using social media platforms like Facebook and WhatsApp for collaborative study, indicating a natural inclination toward group-based learning.[4] Formalizing group discussions within the curriculum can harness this enthusiasm while addressing gaps in critical academic skills.

Group discussions, particularly in the form of problem-based learning (PBL) or case-based discussions, encourage students to engage with clinical scenarios, question assumptions, and develop evidence-based reasoning. For example, discussing a patient case involving diabetes can integrate knowledge of biochemistry, pathology, and clinical management while promoting teamwork and communication. These skills are vital in Bangladesh's healthcare context, where physicians often work in multidisciplinary teams under time and resource constraints.

Moreover, group discussions can address the lack of adequate clinical exposure, a concern highlighted in a study of Bangladeshi medical colleges, where private institutions reported fewer functioning clinical units than required.[5] By simulating clinical scenarios in a classroom setting, group discussions can bridge this gap, ensuring students develop practical skills even when hands-on opportunities are limited.

Challenges and Opportunities

Despite their promise, integrating these approaches faces logistical and cultural barriers. Faculty resistance to change, limited training in active learning methodologies, and a lack of standardized assessment tools for group-based learning are significant obstacles. Additionally, the integration of Information and Communication Technology (ICT), which could enhance group discussions through virtual platforms, remains inadequate in many medical colleges. The 2019 survey noted that 74% of students felt the current syllabus lacked sufficient ICT integration, hindering their professional skills development.[4]

Yet, opportunities abound. The growing recognition among stakeholders of the need for curriculum reform, coupled with a "critical mass" of trained medical educators, provides a strong foundation for change. The Association for Medical Education (AME) and the Bangladesh Medical and Dental Council (BM&DC) can play pivotal roles in standardizing integrated curricula and promoting active learning strategies. Additionally, leveraging digital platforms, as demonstrated by students' preference for social media collaboration, can make group discussions more accessible and scalable, even in resource-constrained settings.

A Path Forward

To realize the full potential of integrated medical education and group discussion in Bangladesh, a multifaceted approach is needed:

1. **Curriculum Reform**: Develop a national framework for integrated curricula, drawing on successful models from institutions like King Edward Medical University or Kathmandu Valley medical colleges.[6] Pilot programs in selected medical colleges can test and refine these curricula before nationwide implementation.
2. **Faculty Development**: Invest in training programs to equip educators with skills in integrated teaching and facilitation of group discussions. Workshops by organizations like the CME can build capacity among faculty.
3. **Technology Integration**: Incorporate ICT into the curriculum to support virtual group discussions and access to digital resources like PubMed and Medscape, addressing students' call for a basic ICT learning program.[4]
4. **Assessment Innovation**: Develop robust assessment methods to evaluate competencies gained through integrated learning and group discussions, such as peer assessments, reflective essays, and case-based evaluations.
5. **Stakeholder Collaboration**: Foster partnerships between the government, AME, BM&DC, and international organizations to secure funding and expertise for sustained reform.

Conclusion

The transformation of medical education in Bangladesh through integrated curricula and group discussion is not merely an academic exercise but a necessity to produce physicians who can navigate the complexities of modern healthcare. By fostering a learning environment that emphasizes integration, collaboration, and critical thinking, Bangladesh can ensure that its medical graduates are not only competent but also compassionate and adaptable. As the nation continues its journey toward a robust healthcare system, these educational reforms will serve as a cornerstone for building a healthier future.

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Dr. Nadim Ahmed
Associate Professor, Department of Surgery
Dhaka Medical College, Mobile: 01711155052
E-mail: nadimdrdmc@gmail.com

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Association of Serum Zinc Level with Febrile Seizure in Children

Karim W[1], Banerjee M[2], Yeasmin S[3], Shamsad IA[4], Sarmin ZU[5], Jahan N[6], Glory P[7]

Abstract

Background: *Febrile seizure is a common pediatric emergency. This is the most common type of seizure in children aged 6 months to 6 years constituting 30% of all seizure types. Despite the high clinical burden of febrile seizure, little advance has been made in understanding its etiology. This study was undertaken to find out whether low serum zinc level is a risk factor of febrile seizure in children.*

Methodology: *This case-control study was conducted in department of Pediatrics, Dhaka Medical College Hospital, Dhaka from March, 2021 to February, 2022. Sixty-nine children presenting with febrile seizure, fulfilling inclusion criteria were enrolled as cases, along with similar number (sixty-nine) of age and sex matched healthy controls. Venous blood samples were obtained and analyses of serum zinc levels were done.*

Results: *The results of cases and controls were compared. Data were analyzed through SPSS (version 26) software. Significance for the statistical tests (Chi Square test & unpaired t-test) were determined at a probability value of less than 0.05 ($p<0.05$). Mean age of the respondents was 21.53±11.52 months in case group and 24.33±16.80 months in control group. Majority (59 to 62%) patients were male in both groups and majority (95.65%) of cases were simple febrile seizure and mean duration of seizure was 10.46±5.60 minutes. The mean serum zinc was found 76.84±14.16 µg/dl in case group and 81.59±13.28 µg/dl in control group. The difference between the case and control group was significant (P value = 0.044). ROC curve showed OR= 2.21, cut off value =84.5 (<65 µg/dl), p = 0.045, 95% CI, sensitivity = 71.0%, Specificity = 50.0%.*

Conclusion: *Serum zinc was found to be significantly low in children with febrile seizure than that of febrile children without seizure. However further large-scale studies are needed to generalized the result of this study.*

Keywords: *Febrile seizure, children, serum zinc level.*

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Introduction

Febrile seizure is a very common emergency in paediatric ward and happens to be the most common type of seizure in the age group of 6 months to 60 months. It constitutes 30% of all seizure types.[1,2] Current definition is, Febrile seizures are seizures that occur between the ages of 6 and 60 months (peak 12-18 months) with a temperature of 38°C (100.4°F) or higher, that are not the result of CNS infection or any metabolic imbalance, and that occur in the absence of a history of prior afebrile seizures.[3]

Febrile seizure may present in different form. A simple febrile seizure is a primary generalized, usually tonic-clonic, attack associated with

1. Dr. Wahidul Karim, MD Resident Student, DMCH, Dhaka
2. Dr. Manisha Banerjee, Professor and Head of department of Neonatology, Dhaka
3. Dr. Shamima Yeasmin, Assistant Professor of Pediatrics, DMCH), Dhaka.
4. Dr. Iffat Ara Shamsad, Professor and Head of Department of pediatrics, DMCH), Dhaka.
5. Dr. Zannat-ul-Sarmin, Junior consultant Pediatrics, DMCH, Dhaka
6. Dr. Nusrat Jahan, Junior Consultant, Pediatrics, DMCH, Dhaka
7. Dr. Pandora Glory, Registrar, Department of Neonatology, Dhaka

Correspondence: Wahidul Karim, MD Resident Student, DMCH, Dhaka. Mobile No-01701841851, E-mail: abir4069@gmail.com

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fever, lasting for a maximum of 15 minutes, and not recurrent within a 24 hours period. A complex febrile seizure is more prolonged (>15 minutes), and/or is focal, and/or recurs within 24 hours. Febrile status epilepticus is a febrile seizure that lasts longer than 30 minutes.[3] Various risk factors involved in development of febrile seizures like infections (Bacterial and viral), temperature susceptibility of immature brain, interleukins, circulating toxins association, micronutrient deficiency and iron deficiency.[4,5,6] Role of various micronutrients like copper, zinc, magnesium and selenium have been described in association with febrile seizures.[7,8]

Zinc is necessary for the activity of over 300 enzymes.[9,10,11,12,13] Zinc homeostasis in glutaminergic neuron-rich areas (such as, the hippocampus and amygdala) may be associated with the etiology and manifestation of epileptic seizures.[14]

Zinc homeostasis in the brain plays vital role for prevention of seizure development because it can act either as proconvulsan or anticonvulsant.[15,16] As Zinc stimulates the activity of pyridoxal kinase thereby it modulates the activity of glutamic acid decarboxylase and the synthesis of GABA.[17] After being formed within GABAergic axon terminals, GABA is released into the synapse, where it acts at one of two types of receptors: $GABA_A$, which controls chloride entry into the cell, and $GABA_B$, which increases potassium conductance, decreases calcium entry, and inhibits the presynaptic release of other transmitters.[18] Zinc deficiency is quite common among febrile seizure patients compared to other patients with febrile illness but without seizur.[20]

As zinc deficiency is fairly common, this study was undertaken to find out the serum zinc levels and its association with febrile seizures.

Methodology

This case-control study was conducted in department of Pediatrics, Dhaka Medical College Hospital, Dhaka from March, 2021 to February.Children from 6 to 60 months of age with febrile seizure admitted to Paediatric department of Dhaka Medical College Hospital, Dhaka who met the inclusion criteria were enrolled as cases and similar number of febrile children without seizure were taken as controls. Children who have history of afebrile seizure, history of neonatal seizures, suspected CNS infections, suspected neurometabolic disorders, severe acute malnutrition, receiving zinc supplementation were excluded. Sixty nine children with febrile seizure were enrolled as cases and sixty nine febrile children without seizure were enrolled as controls. Data was collected through predesigned questionnaire. After selection of the patients; aims, objectives and procedures of the study was explained with understandable language to the parents. Risks and benefits were also made clear to the parents of the patients. Then they were encouraged for voluntary participation and were allowed being free to withdraw themselves from the study. Then, informed written consent was taken for each patient. With all aseptic precaution Two (2) ml of blood sample was collected in plain (Red) tube and sent to Department of Biochemistry, BSMMU for serum zinc level estimation. After centrifuging serum zinc level estimation was done by Thermo scientific Indiko Plus automated, random access benchtop analyzer by colorimetric method. Complete blood count (CBC) was done in SYSMEX XE-5000 analyzer. With all aseptic precaution 3 ml of blood was collected in an EDTA tube and was sent to Haematology department of DMCH for CBC estimation. Serum electrolytes, serum calcium and RBS estimation was done by Dimension EXL-200 analyzer. With all aseptic precaution 3 ml of blood was collected in a plain (Red) tube and was sent to Laboratory medicine department of DMCH for estimation. Data were processed, compiled and analysis was done with Statistical Package for Social Science (SPSS) version 26.0 for Windows.

Results

Patient selection:

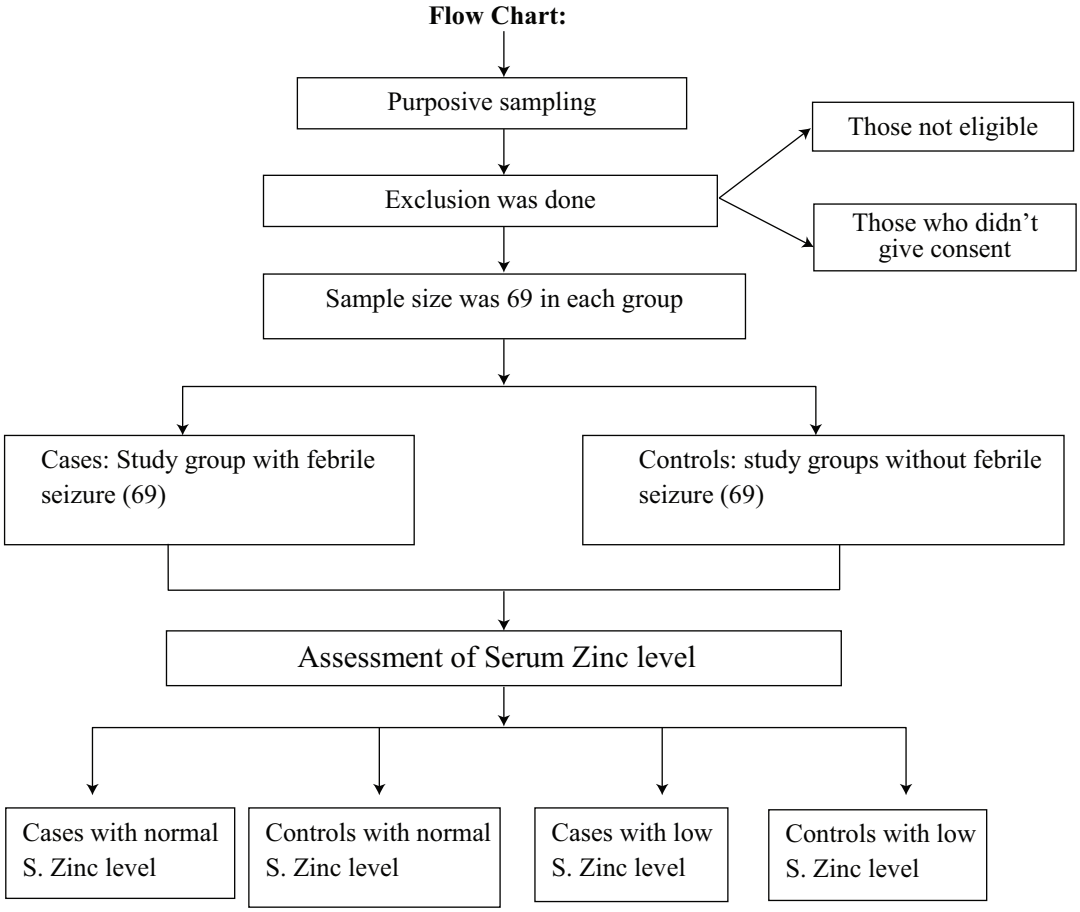

Table I- shows that almost 50% patients belonged to age 12 to <24 months in case group and 29% in control group. In age group <12 months and 12 to <24 months, P value between case and control group was statistically significant. The mean age was found 21.53±11.52 months in case group and 24.33±16.80 months in control group. The difference was not statistically significant (P>0.05) between two groups. Majority (59 to 62%) patients were male in both groups. Male and female ratio was 1.6:1 in case and 1.4:1 in control group. The difference was not statistically significant (P>0.05) between two groups.

Table I

Distribution of the study population by age and sex (n=138)

Age (months)	Case (n=69)		Control (n=69)		P value
	n	%	n	%	
<12	8	11.59	18	26.08	0.029
12 to <24	35	50.72	20	28.98	0.009
24 to <36	15	21.73	15	21.73	1.000
36 to <48	6	8.69	4	5.79	0.511
48 to 60	5	7.24	12	17.39	0.069
Mean±SD	21.53±11.52		24.33±16.80		0.25^{ns}
Male	43	62.32	41	59.42	0.727^{ns}
Female	26	37.68	28	40.58	

Table II shows in majority (95.65%) of cases are simple febrile seizure. Mean duration of seizure was 10.46±5.60 minutes and range was 5 to 30 minutes. Most of the cases suffered from respiratory tract infection (42.03%). Others were gastroenteritis (11.59%) and urinary tract infection (7.24%). A vast portion of cases were suspected viral infections (39.13%).

Table II

Characteristics and etiology of seizure in cases (n=69)

Duration of seizure (Minutes)	No. of Cases (n=69)	Percentage %
≤15	66	95.65
≥30	3	4.35
Types of febrile seizure		
Simple febrile seizure	66	95.65
Febrile status epilepticus	3	4.35
Etiology of fever		
Respiratory Tract Infection	29	42.03
Gastroenteritis	08	11.59
Urinary Tract Infection	05	07.24
Suspected viral infection	27	39.13

Table III- shows that the mean blood glucose was found 5.90±1.23 mmol/L in case group and 6.03±1.06 mmol/L in control group. The difference was statistically not significant (P>0.05) between two groups. The mean serum sodium was found 136.71±3.30 mmol/L in case group and 137.63±3.13 mmol/L in control group. The difference of mean was statistically not significant (P>0.05) between two groups. The mean serum calcium was found 9.25±0.63 in case group and 9.44±0.63 in control group. The difference of mean was statistically not significant (P>0.05) between two groups.

Table IV- shows that 19 (27.54%) patients were found with hypozincaemia (<65 µg/dl) in case group and 10 (14.49%) in control group. The mean serum zinc was found 76.84±14.16 µg/dl in case group and 81.59±13.28 µg/dl in control group. The difference between means was significant (P= 0.045, OR= 2.24) between two groups.

Table III

Blood glucose, Serum sodium and Serum calcium level of the study population (n=138)

Blood glucose (mmol/dl)	Case (n=69)	Control (n=69)	P value
Mean±SD (mmol/L)	5.90±1.23	6.03±1.06	0.505^{ns}
Range (min-max)	3.40-8.35	4.10-8.60	
Serum sodium (mmol/L)	Case(n=69)	Control(n=69)	P value
Mean±SD (mmol/L)	136.71±3.30	137.63±3.13	0.093^{ns}
Range (min-max)	131-145	130-143	
Serum calcium (mg/dl)	Case (n=69)	Control (n=69)	P value
Mean±SD (mg/dl)	9.25±0.63	9.44±0.63	0.087^{ns}
Range (min-max)	7.90-10.90	8.20-11.20	

Table IV

Serum zinc level of the study population (n=138)

Serum zinc (mg/dl)	Case(n=69)		Control(n=69)		Odds ratio	P value
	n	%	n	%	(OR)	
Hypozincaemia (<65 µg/dl)	19	27.54	10	14.49	2.24	0.045^{s}
Normal	50	72.46	59	85.51		
Mean±SD (µg/dl)	76.84±14.16		81.59±13.28			
Median	78.0		84.0			
Range (min-max)	54-102		54-105			

p value obtained by Mann Whitney U test,

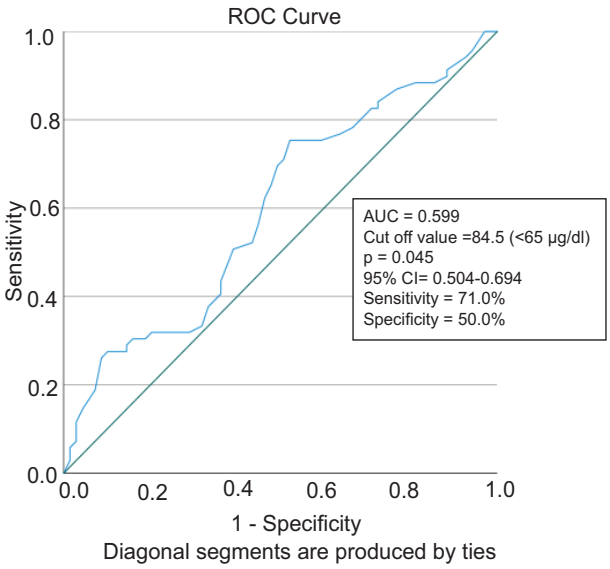

Fig.-1: *ROC analysis was performed to evaluate the predictive ability of serum zinc levels for febrile seizures.*

Figure-1 showed that statistically significant association between serum zinc levels and febrile seizures in children (p=0.045). The area under the curve (AUC) analysis showed a moderate predictive ability (AUC = 0.599), suggesting that serum zinc levels may have some potential as a predictor for febrile seizures. The sensitivity of the test was 71.0%, indicating a relatively high probability of a positive result in children with febrile seizures, while the specificity was 50.0%, indicating a 50% chance of obtaining a negative result in children without febrile seizures.

Discussion:

This study was conducted to determine the role of serum zinc level in children with febrile seizure which was compared to febrile children without convulsion. These two groups of children were compared with respect to their age, sex, characteristics of seizure, serum zinc etc.

In this study, majority of cases were between 12 to 24 months of age which corresponds to the age of peak incidence (12-18 months) of febrile seizure.[3] This is almost similar to a study by Allam et al.[26] The mean age in cases is similar to another study (Mollah et al. 2008) conducted in Bangladesh.[21] In this study, the mean age of febrile seizure was above the peak incidence age (18 months) due to inclusion of some recurrent febrile seizure cases. Some studies showed that mean age of febrile seizure happen in children between 24 and 30 months of age.[22,23] Though febrile seizure occurs in both male and female children without any significant gender predominance but in this study majority of the cases were male but the difference was not statistically significant. Mollah et al. (2008) in Bangladesh also revealed that male children were more prone to develop febrile seizure than female children.[21] Another study in Bangladesh by Begum et al. (2019) also found male predominance in febrile seizure.[28] Other studies also showed male predominance.[1,26] This may be due to the fact that, males are found to be more susceptible to temporal lobe like seizures because of higher levels of testosterone than female.[34]

In this study, duration of seizure was d”15 minutes in most of cases. This is similar to some studies where majority of cases had <15 minutes seizure duration.[24,28,29]

In this study, respiratory tract infection was the most common cause of fever in children with febrile seizure followed by gastroenteritis and urinary tract infection. In some cases cause of fever was undetermined. Study done by Absar et al. (2020) with 100 febrile seizure cases revealed majority of children presented with acute respiratory tract infection as the cause of fever followed by acute gastroenteritis and urinary tract infection.[24] In some other studies conducted in Bangladesh also showed majority cases presented with respiratory tract infection which is similar to present study.[28,29]

In present study, hyponatraemia was seen in 17.39% cases. This is similar to the study done by Baek et al. (2018) where 21.1% cases had hyponatremia[27]. In this study mean serum sodium was 136±3.30 mmol/L which is similar to the study done by Namakin et al. (216) where it was 136.2±3.3 mmol/L.[22]

Current study shows 14.49% cases had hypocalcaemia. This is similar to a study by Al-Hakeim, Al-Hillawi & Al-Kindi (2015) which revealed that 21.7% cases were hypocalcaemic[25]. In this study mean serum calcium level in cases were 9.25±0.63 mg/dl

which is similar to mean 9.45±0.57 mg/dl found by Amouian et al. (2011)[35]. In this study no statistically significant difference was found between case and control group. Although Al-Hakeim, Al-Hillawi & Al-Kindi (2015) found no significant difference, but Namakin et al. (2016) found that calcium level was significantly low in children with febrile seizure.[25,22]

All (100%) patients were normoglycemic in both case and control group. The mean blood glucose was found 5.90±1.23 mmol/L in case group and 6.03±1.06 mmol/L in control group. Higher mean blood glucose may be related to the fact that there is stress hyperglycaemia.[33] CSF study was done in 11 cases (8 cases below 12 months of age and 3 cases of febrile status epilepticus), which revealed no abnormality.

In the current study, serum zinc level was found significantly low in cases than the controls. Hypozincaemia was noticed in 27.54% children with febrile seizure. On the other hand, 14.49% of the controls were with low serum zinc level. Vidyasagar, Venugopal and Darshan (2015) found higher percentage of cases (60%) and controls (33.8%) were affected with hypozincaemia, which is contradictory to present study.[20] In the present study mean serum zinc level difference between two groups is statistically significant (P value <0.05). In Pakistan Qudrat et al. (2020) found the frequency of hypozincemia in febrile seizures among children presenting at tertiary care hospitals was 54.48% and mean serum zinc levels were calculated as 64.28±12.13 µg/dl.[36] Whereas Reddy and Solomon (2019) found the mean serum zinc levels were 64.92 µg/dl, 81.03 µg/dl respectively in febrile seizure and febrile children without seizure[37]. Several studies showed that serum zinc level was significantly lower in febrile seizure patients compared to febrile children without seizure.[8,20,21,22] Rahman et al. (2016) conducted a cross sectional nationwide survey, which showed about 44.6% of pre-school age children (6-59 months) had zinc deficiency.[19] That doesn't match with the current study.

Reddy and Solomon (2019) found in a study that decreased serum zinc level is a significant predisposing factor for febrile convulsions[37]. Same conclusion was done by Allam et al. (2018)[26]. This study showed no correlation of serum zinc with age and sex in febrile seizure.

Conclusion:

It can be concluded that serum zinc is significantly low among the children with febrile seizure compared to febrile children without seizure. So, hypozincaemia might be regarded as a risk factor of febrile seizure in children.

Recommendations:

Routine assessment of serum zinc level can be recommended in children with febrile seizure but further large-scale studies are needed to generalize the result of this study. Other studies can be carried out whether zinc supplementation could prevent the recurrence of febrile seizure in children.

Limitations of the study:

This study has been conducted in a single centre with small sample size. This study was conducted in a single tertiary care hospital; therefore, the findings may not represent the whole population of our country. Other risk factors of febrile seizure were not assessed in this study.

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Clinical Profile, Risk Factors and Outcome of the Patient with Cerebral Venous Sinus Thrombosis at 3 Months: Prospective Cohort Study in a Tertiary Care Hospital

Jewel MH,[1] Ahmed KGU[2], Mahmud R[3], Chowdhury AH[4], Islam MM[5]

Abstract:

Background: *Cerebral venous sinus thrombosis (CVST) one of the important type of venous stroke. With the advent of the newer imaging technique, it is now increasingly diagnosed in our country. There are limited studies regarding venous stroke specially about its outcome in Bangladesh. So, we conducted the study to observe the clinical profile, risk factors and outcome of the patient with cerebral venous sinus thrombosis at 3-month in a tertiary care hospital.*

Methods: *This Prospective cohort study was carried out in the Department of Neurology, Dhaka Medical College Hospital during January 2022 to December 2023. The patients suffering from cerebral venous sinus thrombosis confirmed by imaging were included in this study. The outcome was assessed with mRS score.*

Results: *We included 58 patients with venous stroke, among them about 2/3rd were female. The mean age (SD) of the was 36.46(13.56). Most of the patients were between 20 and 40 years.*

The most common clinical presentations were headache 54(93%), vomiting 36(62%) and seizure 21 (36.2%). The focal neurologic deficit was present in 17(29%) and papilledema in 33(56.89%) of the patients. The risk factors for CVST identified in the study included CNS infections 22 (41%), then pregnancy and puerperium 8(62%), intake of OCP and other hormonal preparation 6(90%), COVID -19 infection and post vaccination (6.90%), and idiopathic 34(48%). D-dimer was elevated in half of the patients. The commonest sinuses involve were transverse sinus 31(65.51%), and superior sagittal sinus 13 (43.10%). Multiple sinuses involvement was present in more than 2/3rd cases. The mean (SD)hospital stay was 12.4 (3.8) days. At 3-month 44(76%) had mRS 2 score and only 10% patient died. Mortality was higher among males, who had multiple sinus involvement and multiple comorbid conditions.

Conclusion: *CVST largely affect the young female, mostly present with headache vomiting and seizure. Generally, the outcome is good with conventional treatment.*

Keywords: *Cerebral venous sinus thrombosis; Headache; Puerperium; MR Venogram; OCP; Seizure.*

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Introduction

Thrombosis of the cerebral venous sinus (CVST) is a form of venous stroke, usually affecting young individuals.[1] Despite advances in the recognition of CVST in recent years, diagnosis and management can be difficult because of the diversity of clinical profile, underlying risk factors and the absence of a uniform treatment approach. CVST represents 0.5% to 3% of all strokes.[2,3]

In recent years, cerebral venous sinus thrombosis (CVST) has been diagnosed substantially more frequently than in the past

1. Dr. Meahedi Hasan Jewel, Resident, Department of Neurology, Dhaka Medical College Hospital.
2. Prof Dr. Kazi Gias Uddin Ahmed, Professor, Department of Neurology, Dhaka Medical College hospital.
3. Dr. Reaz Mahmud, Assistant Professor Department of Neurology, Dhaka Medical College Hospital.
4. Prof Dr. Ahmed Hossain Chowdhury, Professor, Department of Neurology, Dhaka Medical College Hospital.
5. Dr. Mohammad Munirul Islam, MD Neurology, Department of Neurology, Dhaka Medical College Hospital.

Correspondence : Dr. Reaz Mahmud, Assistant Professor, Department of Neurology, Dhaka Medical College. Dhaka, Bangladesh. Phone-+8801912270803. E-mail-reazdmc22@yahoo.com. rmahmudneuro@dmc.gov.bd. Orchid ID-0000-0002-9427-1746

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due to the expanded use of noninvasive brain imaging methods. However, the actual incidence of CVST is most likely even higher. Many cases remain unrecognized due to the high variability of their clinical presentation and the possible absence of any symptoms.

CVST can be caused by prothrombotic states (congenital or acquired) such as deficiencies in anticoagulation-promoting protein, use of oral contraceptives, pregnancy, dehydration, trauma, inflammatory diseases, infections and haematological conditions. The presenting clinical profiles of CVST quite puzzling. CVST may be encountered not only by neurologists and neurosurgeons but also by emergency physicians, oncologists, ophthalmologists, hematologist's, obstetricians, family practitioners due to diversity of causes and presenting scenarios.[4]

Clinical findings in CVST usually fall into two major categories, depending on the mechanism of neurological dysfunction: Those that are related to increased intracranial pressure attributable to impaired drainage and those related to focal brain injury from venous ischemia/infarction or hemorrhage. The clinical presentation of CVST can be with focal neurological deficits and/or seizures, headache, papilledema, and intracranial hypertension and coma and may lead to death.[5] Headache is one of the common presenting symptoms in around 70%-90% of patients. Still others can present with diffuse encephalopathy, painful ophthalmoplegia, or status epilepticus.[5] Acute symptomatic seizures are reported in about 35%-50% and around 76% in peripartum period in 29% of the patients, seizure is the presenting sign, and 59% of them had a generalized seizure.[6]

The diagnosis of CVST is typically based on clinical suspicion and imaging confirmation. Various laboratory studies along with MRI and MRV are necessary for stablishing a diagnosis. Recently, CVST is diagnosed early and with increased frequency due to easier access to magnetic resonance imaging (MRI). MRI with magnetic resonance venogram (MRV) has very high sensitivity and specificity and has become the modality of choice.[7]

CVST treatment options include treatment of the identified risk factors; (antithrombotic therapy; and symptomatic treatment of intracranial hypertension, seizures, and other complications including secondary infections, physiotherapy, and supportive measures. Antithrombotic therapy are anticoagulation with unfractionated heparin or low molecular weight heparin, even the patient have intracranial hemorrhage.[8]

CVST may cause serious neurological syndromes and the mortality rate ranges 5.5-30%.[9]

The prognosis of CVST patients has improved over the last decades due to increase in diagnosis of CVST and improved care and early treatment. Mortality in the West is now below 5%. About 80% of the patients make a full independent recovery. Mortality is mainly related to fatal brain herniation, caused by large hemispheric hemorrhagic infarcts.[10] Other deaths are related to metabolic derangements, status epilepticus, infections, aspiration pneumonia, and rarely to pulmonary embolism.[11]

The optimal duration of oral anticoagulation after the acute phase is unclear. Oral anticoagulation may be given for 3 months if CVST was secondary to a transient risk factor; for 6–12 months in patients with idiopathic CVST and in those with mild hereditary thrombophilia, and indefinite anticoagulation should be considered in patients with chronic major risk factors for thrombosis or recurrent venous thromboembolism of CVST.[12,13,14]

Overall, the patient with CVST have a favorable outcome. Most of the patient with CVST survive without physical disability, but some symptoms negatively affect quality of life. The outcome of CVST depends upon various factors. Women with younger age, having no comorbidity and mRS < 3 with better outcome compared with male patients with CVST.[15] Poor prognostic factors are advance age, active cancer, decrease

level of consciousness, and intracerebellar hemorrhage.[16] The were limited studies about CVST in Bangladesh. So, the base line information about its presentation, risk factors and outcome is largely unknown among Bangladeshi population.

So, present study has been designed to identify the clinical presentations, risk factors, and outcome of patients with CVST.

Materials and Methods

It was a prospective cohort study conducted in the department of Neurology, Dhaka Medical College Hospital. Ethical approval was obtained from the Dhaka Medical College ethical review board prior to the study. Informed written consent was obtained from all the study participants.

Study participants:

The study included patients aged more than 18 years, both sexes and confirmed cerebral venous sinus thrombosis by MRV or DSA. Patients with previous venous stroke, concomitant ischemic stroke, and prior disability due to other causes were excluded from the study. We included every consecutive patient, fulfilling the inclusion and exclusion criteria.

Study procedure:

We collected the data by interviewing the patients or their attendant and recorded the data in the case record form. The history of previous disease and personal habits as well as demographic, vascular risk factor, biochemical data and CT or MRI findings was recorded. In all patients, neurological assessment was conducted by the consultant Neurologist. Cerebral venous sinus thrombosis was diagnosed on the basis of positive lesions on CT head, MRI of brain, MRV or DSA of brain. The patient was treated by the respective Department according to standard guideline. Th-e outcome determinants was mortality and morbidity, recurrence, as measured using the modified Rankin Scale (mRS) at discharge, at end of 1 month and at the end of 3 months. A mRS of 3-6 will be considered as poor outcome and mRS of 0-2 as good outcome. In cases where the patient was failed to visit the hospital, a telephonic mRS was recorded. The telephone guideline was validated.

Statistical analysis

The data was analyzed with Statistical Package for Social Scientists-26 (IBM SPSS-26). The qualitative data was expressed with n (%). The quantitative data were test for the normality. The data were found normally distributed and were expressed with mean (SD). The groups were compared with chi-square test if qualitative variable and unpaired t-test in case of quantitative variable. The predictors for mortality were determined with logistic regression test and OR was expressed with 95% CI. The p value <0.05 was considered as significant.

Results

During the study period, total 100 patients was admitted to this institute with CVST. Among the 58 included in this study as per inclusion criteria. the majority of our patients (67.24%) were female. The mean (SD) age of the participants was 36.46(13.56). The most common symptoms were headache in 54 patients (93.10%) and most common clinical sign was papilledema (33 patients,56.89%; Table 1). Disease onset was acute in 46 patients (79%), but was subacute or chronic in in 8 (13.8%) and four (6.9%) respectively. Clinical presentations of CVST were variable. Most of the patient with CVST presented with headache 54 (93.10%). Headache was variable in characteristics ranges from mild to moderate, dull or throbbing in nature. A few patients presented with sudden severe thunderclap like headache (10%). Other presentation included were vomiting (62.07%), seizure (36.21%), focal neurological deficit (29.32%). (Table II).

The most common risk factors for CVST in this study were infection (22.41%), pregnancy and puerperium (8.62%), post vaccination (6.90%), OCP and other hormonal preparation (6.90%), malignancy (5.17%) and idiopathic (39.66%). The most common clinical sign in this study was papilledema (56.8%). (Table III).

Table I

Demographic characteristics of patient with cerebral venous sinus thrombosis:

Variable	Results	Percentage
Age(mean±SD)	36.46±13.56	
Sex		
Female	39	67.24
Male	19	32.76
Hospital stay (mean±SD)	14.46±4.05	
Educational status		
Primary	22	37.93
Secondary	21	36.21
Graduate	15	25.86
Occupation		
Homemaker	33	56.90
Students	8	13.80
Others	17	29.31
Comorbidity		
No	46	79.31
DM	8	13.79
HTN	4	6.90

Table II

Clinical presentation of patients with cerebral venous sinus thrombosis:

Symptoms and signs	Number	Percentage
Headache	54	93.10
Vomiting	36	62.07
Seizure	21	36.21
Focal neurological deficit	17	29.32
Papilledema	33	56.89

Table III

Risk factors of patients with cerebral venous sinus thrombosis:

Name	Frequency	Percentage
Infection	13	22.41
Pregnancy and puerperium	5	8.62
Post vaccination	4	6.90
Drugs	4	6.90
Malignancy	3	5.17
Idiopathic	23	39.66
Others	6	10.34

In MRV most commonly involved sinuses are transverse sinus 31 (65.51%), superior sagittal sinus 13(43.10%), sigmoid sinus 7 (12%) and multiple sinus involvement was present in 46 cases (79.31%), and single sinus involvement in only 12 cases (20.69%) (Table IV)

Table IV

Sinus involvement in patient with cerebral venous sinus thrombosis:

Name of sinus	Number	Percentage
Transverse sinus	38	65.51
Superior sagittal sinus	25	43.10
Sigmoid sinus	7	12
Deep venous sinus	2	3.40
cavernous sinus	1	1.70
Multiple sinus involvement	46	79.31
Single sinus involvement	12	20.69

Table V

causes of CVST by different infection

Infection	
Abdominal TB	01
CSOM	02
Brain abscess	02
Bacterial meningitis	03
Encephalitis	01
Septicemia	01
Dengue encephalitis	01
Acute pancreatitis	01
Puerperal sepsis	01

Bacterial meningitis and CSOM were important cause of infection causing CVST.

Average hospital stay was 12.46+3.81 days. There was significant improvement (mRS<3) of symptoms at discharge. Multiple logistic regression analysis revealed female sex, those who are married, OCP users, event during puerperium and post vaccination had poor outcome. Those who had involvement of superior sagittal sinus and transverse sinus had poor outcome. The mortality rate in the current study was 6(10.34%) (Figure 1).

Table V

Predictors of outcome among cerebral venous sinus thrombosis:

Variable	OR (95%CI)	P-value
Age	1.184(1.007-1.391)	0.041
Sex	1.635(0.046-58.705)	0.788
Headache	0.248(0.005-20823.95)	0.810
Vomiting	0.027(0.001-0.844)	0.040
Altered consciousness	18.5(1.81-188.38)	0.009
Hemiparesis	57.283(1.580-2077.369)	0.027
Papilledema	0.241(0.054-2.938)	0.043
6th nerve palsy	1.14(0.134 – 10.54)	0.588
DM	0.89(0.81-0.98)	0.724
OCP	1.19(1.00-1.41)	0.352
Infection	0.87(0.778-0.984)	0.311
TST	1.15(1.01-1.303)	0.237
SSST	1.12(1.01-1.25)	0.513
Sigmoid sinus	1.02(0.152-6.59)	0.690
Deep venous	0.896(0.813-0.981)	0.808
Cavernous sinus	0.898(0.817-0.987)	0.900

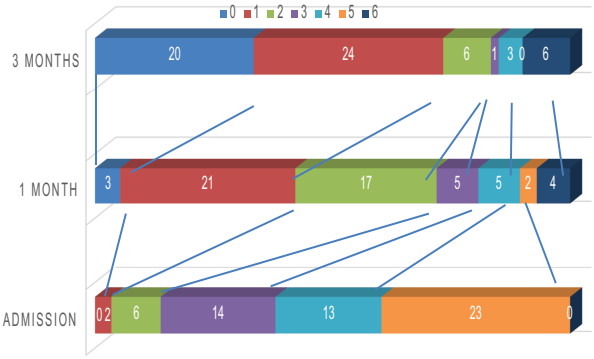

Figure 1: *Score on the modified Ranking scale at admission, end of one month and at three months:*

Discussion

In this study the majority of our patients were young female, mostly presented with headache, vomiting and seizure. Most of the patient had multiple venous sinus involvement. Transverse sinus thrombosis was the most common site of thrombosis followed by superior sagittal sinus and sigmoid sinus. Overall outcome at 3 month was good and the mortality was low.

We cannot generalize the study findings for whole Bangladesh, as population was selected from one selected hospital in Dhaka city, Outcome may differ in different treatment facilities.

Most of the patients were between 20 and 40 years. In a study by Saposnik G al 2011 most of the patients were between 25-35 years with a maximum 72 years.[2] The study by Patil et al in 2014 found that 78% of patients were younger than 50 years.[17] As in our study female preponderance was also noted in the study by Saposnik G al 2011.[2] Gender specific factors like use of OCP, pregnancy, puerperium, HRT might be responsible for such preponderance.[12]

The clinical presentation like headache, seizure, vomiting and focal signs found in this study is similar to other studies.[12,17,18]

The nature of the Headache in about one fourth of the patients was as thunderclap, was similar in De Bruijn et al.[4] Seizures were focal in one quarter of patients, in another quarter they begin as focal then generalized, and remaining half are generalized which is similar to other studies.[19]

Focal neurological deficit such as paresis, dysarthria and aphasia are due to localized damage in cerebral cortex.

In our study Papilledema was the commonest clinical finding which was present more than half of patients that matched with other studies.[20, 21] It due to raised ICP due to venous stasis.[22]

CVST has multifactorial etiology. The risk factors for developing cerebral venous sinus thrombosis are infection, pregnancy and puerperium, post vaccination, OCP and other hormonal preparation, malignancy and idiopathic.[23]

A local infection i.e. CSOM, meningitis become a strong risk factor in our study(table 5). Septic venous sinus thrombosis is rare in the anti-biotic era[24], but after the COVID pandemic we get increasing evidence of septic venous thrombosis.[25]

D-dimer was found to be raised in half of total patients in this study which is almost similar to the study. But has low sensitivity and specificity in diagnosis CVST.[26] In our study it is also not a predictor of bad outcome as well.

Neuro-imaging is the cornerstone in the diagnosis of cerebral venous sinus thrombosis. Imaging modalities of choice in CVST are CT scan and MRI of brain with MR Angiogram. CT scan may be normal in 1/3rd cases but MRI with MRV is almost 100% diagnostic.[18] In this study only more than half of patients have CT brain abnormality and 100% of patients had MRV abnormality.

All patients were treated with low molecular weight heparin (LMWH) followed by DOAC. Fifty patients (86%) stabilized and later improved. Heparin was then switched to oral anticoagulants. Average hospital stay was 12.46+3.81 days. There was significant improvement (mRS<3) of symptoms at discharge. Hemiplegia was persistent at discharge in less than 1/3rd cases.

The patients who presented with headache, vomiting, double vision, blurring of vision, had better outcome (mRS<3) whereas those who presented with seizure, altered level of consciousness and focal neurological deficit papilledema, had poor outcome (mRS>2). Multiple logistic regression analysis revealed female sex, those who are married, OCP users, event during puerperium and post vaccination had poor outcome.

The mortality rate in the current study was 6(10.34%) which was similar to that in other studies.[18] The patients who died are female and of younger age <30 years and presented with headache, repeated seizures and altered level of Consciousness and hemiparesis.

Conclusion:

CVST largely affect the young female, mostly present with headache vomiting and seizure. Generally, the outcome is good with conventional treatment.

Acknowledgement

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Conflict of interest

The authors have no conflicts of interest

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Outcome of Anterior Cervical Discectomy and Fusion in Symptomatic Cervical Disc Herniation with Autologous Iliac Bone Graft and Metallic Implant

Akon MSI[1], Mahmud AA[2], Rashed HH[3], Islam KMA[4], Parvej M[5], Saikat NM[6], Hasan MZ[7], Mollah MRA[8], Hossain SZ[9]

Abstract

Background: *Anterior cervical discectomy and fusion (ACDF) is a challenging surgical procedure where appropriate patient selection is very important for operation outcome and choice of surgical procedure. The first-line treatment strategy for managing cervical disc herniation is conservative. In some cases, surgery is indicated either due to signs and symptoms of severe and progressive neurological deficits, or failure of proper conservative treatment. Treatment of cervical disc herniation using ACDF has been successfully reported in the literature.*

Objectives: *The aim of this study is to determine the outcome of ACDF in the treatment of symptomatic cervical disc herniation.*

Methods: *It is a retrospective study conducted in Dhaka Medical College Hospital (DMCH) and other private hospitals from January 2013 to December 2022. We evaluated 28 patients who had undergone ACDF for cervical disc herniation in 35 levels. Fusion was attained with autologous iliac bone graft with additional anterior plating or cages. Radicular pain, neck pain and patient satisfaction with the treatment were scored using the visual analogue scale (VAS), ODI and Odom's criteria.*

Results: A total of 28 patients fulfilled the inclusion criteria. Out of these, 21(75%) patients were male. The age range was from 21 to 65 with a mean age of 47.45 years. 10 patients (35.71%) had disc herniation at C5/6 level and 7(25%) patients had at C6/7 level. Regarding clinical assessment, the ODI percentage has decreased and VAS for neck and radicular pain also showed a significant reduction. Odom's criteria was applied to determine the outcome of the procedure. Excellent results were noted in 20 (71.42%) patients. 5 (17.85%) patients had good results. 3 patients (10.71%) had fair and no patient had a poor outcome.

Conclusion: *ACDF is a successful surgical technique for the management of cervical disc herniation among Bangladeshi people.*

Key word: *ACDF, Cervical disc herniation, Cervical plating, Stand alone cage.*

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1. Dr. Md. Shahidul Islam Akon, Associate Professor (Spine Surgery), Department of Orthopaedic Surgery, Dhaka Medical College, Dhaka
2. Dr. Abdullah Al Mahmud, Associate Professor, Department of Orthopaedic Surgery, Ibn Sina Medical College, Dhaka
3. Dr. Hamidul Haque Rashed, Assistant Professor, Department of Orthopaedic Surgery, Ibn Sina Medical College, Dhaka
4. Dr. K M Atiqul Islam, Assistant Professor, Department of Neurosurgery, National Institute of Neurosciences & Hospital, Dhaka.
5. Dr. Masud Parvej, Junior Consultant (Orthopaedic Surgery), Kuwait Bangladesh Friendship Govt. Hospital, Uttara, Dhaka
6. Dr. Nurul Mahmud Saikat, Junior Consultant (Orthopaedic Surgery), Upazila Health Complex, Daulatpur, Manikganj
7. Dr. Md. Ziaul Hasan, Indoor Medical Officer, National Institute of Traumatology and Orthopaedic Rehabilitation (NITOR), Dhaka
8. Dr. Md. Rayhan Ali Mollah, Assistant Professor, Department of Orthopaedic Surgery, International Medical College, Gazipur
9. Dr. Syed Zakir Hossain, Associate Professor, Department of Orthopaedic Surgery, Dhaka Medical College, Dhaka

Correspondence: Dr. Md. Shahidul Islam Akon, Associate Professor (Spine Surgery), Department of Orthopaedic Surgery, Dhaka Medical College, Dhaka. Mobile: +8801745663585, Email: shahid.akon@yahoo.com

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Introduction

Cervical radiculopathy may be caused by disc herniation, spondylosis, instability, trauma and on rare occasions by tumors.[1] Cervical disc herniation mostly affects individuals aged between 30 and 50 years.[2] Cervical radiculopathy is a painful and relatively common condition with a reported prevalence of about 30%.[3] Patients presenting with cervical radiculopathy usually complain of pain in the neck and one arm, with a combination of sensory loss, motor function

loss, or reflex changes in the affected nerve-root distribution.[4] C5-C6 level is the most commonly involved level of herniation.[5] The vast majority of patients with symptomatic cervical disc degeneration (CDD) respond well to conservative treatment.[6] First-line treatment in management of CDH is conservative measures. Approximately 83% of patients with cervical radiculopathy respond to conservative treatment methods[3], while an approximate one-third of patients will suffer from persistent symptoms.[7] Surgery is indicated for cases that have signs/symptoms of severe/progressive neurological deficits and persistence of radicular pain despite proper conservative treatment. The gold standard for ACDF has been fusion with an Autogenous Iliac Crest Graft - AICG.[8,9,10] This is a relatively safe procedure with few complications.[11,12,13] Surgery is mostly performed via an anterior approach with or without fusion[14], although traditionally posterior approach is another method.[15] Anterior cervical decompression and fusion (ACDF) is usually considered as a better procedure.[16] We present our study and share our experience of surgical outcome of ACDF with autologous bone graft from iliac bone along with plate-screw or metallic cage application in terms of efficacy, symptom relief, graft fusion and complications.

Materials and Methods

Study Design and Setting

We conducted a prospective cohort study of patients undergoing anterior cervical discectomy and fusion (ACDF) between January 2013 and December 2022 at a tertiary care center and affiliated private hospitals in Dhaka, Bangladesh. The Institutional Review Board approved the study protocol and all participants provided written informed consent.

Participants

Inclusion Criteria:

1. Age 20-70 years
2. Persistent cervical radiculopathy or myelopathy refractory to e”6 weeks of conservative management
3. MRI-confirmed single or two-level disc herniation with corresponding neural compression

Exclusion Criteria:

1. Ossification of posterior longitudinal ligament (OPLL)
2. Cervical deformity (Cobb angle >10°)
3. Previous cervical spine surgery
4. Active infection or malignancy
5. Incomplete medical records

Preoperative Evaluation

All patients underwent:

1. Comprehensive neurological examination
2. Standard cervical spine radiographs (AP, lateral, flexion-extension)
3. 1.5T MRI with T1/T2-weighted sequences
4. CT scans for cases with suspected calcific disc pathology

Surgical Procedure

The standardized ACDF technique included:

1. **Positioning:** Supine with cervical traction (5-10 lbs)
2. **Approach:** Right-sided Smith-Robinson anteromedial approach
3. **Discectomy:** Complete removal of pathological disc material
4. **Decompression:** Uncovertebral joint osteophytectomy as needed
5. **Fusion:**

- Autologous tricortical iliac crest graft (n=22)
- PEEK cages with local bone graft (n=6)

6. **Fixation:** Titanium anterior cervical plate system
7. **Confirmation:** Intraoperative fluoroscopic verification

Postoperative Protocol

1. Rigid cervical collar immobilization for 6 weeks
2. Progressive range-of-motion exercises post-collar removal
3. Scheduled follow-ups at 6 weeks, 3 months, 6 months, and annually

Outcome Measures

Primary Endpoints:

1. Clinical improvement:

- Visual Analog Scale (VAS) for neck/arm pain
- Modified Japanese Orthopaedic Association (mJOA) score

2. Radiographic fusion:

- Bridging trabecular bone on CT scan
- <2° motion on dynamic radiographs

Secondary Endpoints:

1. Operative time and blood loss
2. Complication rates (dysphagia, hardware failure, etc.)
3. Reoperation rate

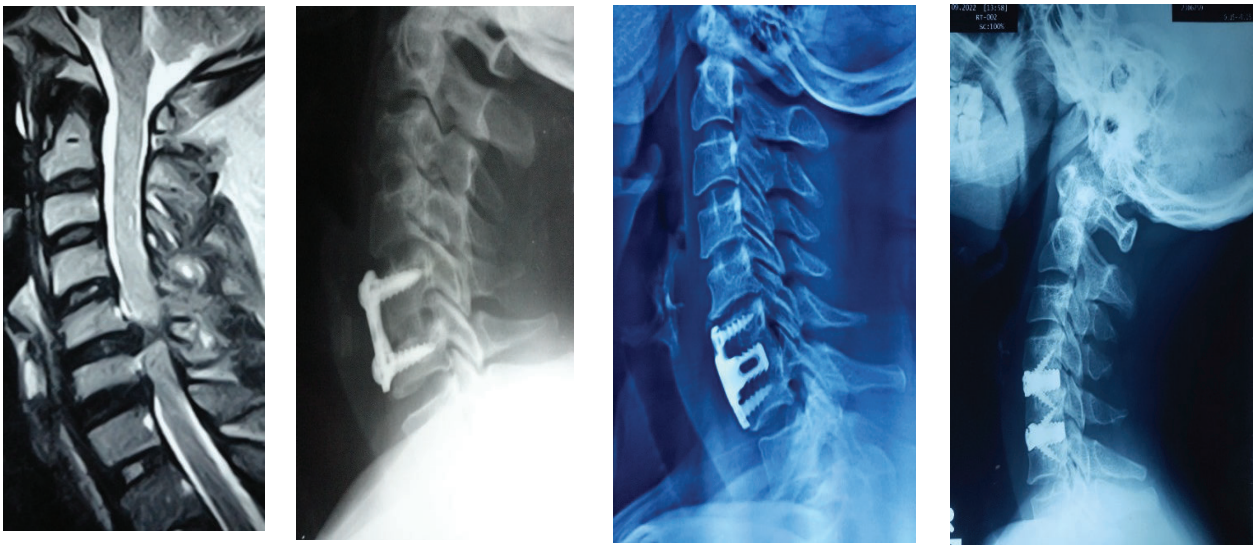
Results

Our mean follow-up time was 56.64 months (range: 06–120 months. 28 cases (35 levels) were studied. 21 cases had one level disc herniation and 7 cases had two level involvement (Table 1). 21 cases were male and 7 were female. Mean age was 47.45 years. The majority (18, 64.28%) of cases were sedentary worker. Mean preoperative VAS for neck pain and radicular pain were 8.92 and 9.57, respectively. Mean postoperative VAS (at the time of follow-up) for neck and radicular pain were 1.64 and 1.32 respectively. Most (10, 35.71%) of our cases had disc herniation at the level of C5-C6. Two-level disc herniation was mostly (4, 14.29%) encountered at C5-C6 and C6-C7 levels. Vertebral levels involvement presented in figure 1.

Table I

Different level of Disc herniation

Involved Disc	No. of Patients	Percentage
Single Level	21	14.29%
Double Level	7	35.71%



Preoperative MRI | Postoperative X-ray with Plate | Postoperative X-ray with cage and plate | Postoperative X-ray with Stand alone cage (Two levels)

Figure 2: *Different implant used.*

Autologous iliac crest graft was used for all (28) cases. Out of 28, plate and screw used was for 12 (42.86%), cage with plate system was used for 13 (46.43%) and stand alone cage was used for 3 (10.71%) presented in figure 2.

Fusion was confirmed with imaging studies in all 28 cases that came for follow-up imaging study (100% fusion rate). We had no intraoperative complications. Early postoperative complications were hoarseness (2 cases, 7.14%). During the follow-up time, none of the patients complained of symptoms recurrence. 3(10.71%) patients complained of negligible neck pain and 1 patient developed adjacent segment disease.

Odom's criteria were utilized to determine the results of the procedure. Excellent results were noted in 20 (71.42%). 5 (17.85%) patients had good results. 3(10.71%) patients had fair and no patient had a poor outcome.

Outcomes were not related to age, gender, job, duration of pain, level of disc herniation, number of levels treated, and implant used.

Discussion

The objective of putting graft into disc space is to have solid bone fusion and achieve alignment. Addition of plate prevent graft dislodgement and graft collapse, decrease the need for external orthosis and hence early mobilization.[17,18,19]

Regarding residual complaints, we observed that 3(10.71%) cases complained of minor residual symptoms at the final follow-up. Peolsson[20] reported that 70% of their study population suffered from persistent pain and disability at 6-year follow-up.

ACDF has been advocated as a safe procedure, but complications could still arise. Among its complications are nonunion, postoperative dysphagia[21], recurrent laryngeal nerve palsy, esophageal tear, carotid artery injury, vertebral artery injury, neurologic deficit, postoperative respiratory embarrassment, and disc space infection[22]. Injury to RLN was found by Flynn to be the most frequently encountered neurologic complication[23]. Two studies[24,25] reported dysphagia as the most common ACDF-related complication. We had no case of dysphagia, but the incidence of dysphagia reported in other studies that ranged between 2.5 and 21.3%.[26,27,28]

In a study conducted by Chen et al.[30] incidence of 0.16% was reported for hoarseness, while this rate was reported higher (4.9%) by Baron et al.[31] We observed 7.14% among our study population, which is even higher. An average rate of 4.3% (range: 1.6%–12.1%) has been documented in literature for the incidence of C5 root palsy after anterior decompression and fusion[32]. In our series, we had no case of C5 root palsy. We had no case of graft extrusion but, incidence of graft extrusion has ranged between 0 and 0.88%[32,25,34]. With an average follow-up duration of 18 months, Kulkarni et al.[35] reported that none of their study population had cage extrusion or migration. Cabraja et al.[36] demonstrated no cage extrusion on average follow-up period of 28.4 months. In a study conducted by Nanda et al.[25], cases with graft extrusion had persistent neurological symptoms after the operation, but we had no graft extrusion in our patients in minimum 6 months follow- up.

Incidence of adjacent segment degeneration (ASdeg) after ACDF has been reported to range from 16 to 51[37,38]. Herkowitz et al.[39] showed that 41% of their series developed ASdeg. The reported incidence for ASdeg ranges between 2%[37] and 41%[39]. One case (3.57%) with symptomatic ASdeg were observed in our series. With an average follow-up period of 6 years, Bohlman et al.[40] stated that 9% of their patients required additional surgery for ASdeg. In another series[41], 17% of the study population required additional surgery for ASdeg at an average of 4.5 years of follow-up.

Kulkarni et al.[35] reported a fusion rate of 93.33% for PEEK cage at 6 months. At a mean follow-up of 10 months, 100% fusion rate was observed by Cho et al.[42] With an average of 18 months follow-up, Kulkarni et al.'s[35] study population fusion was maintained at their last follow-up. At mean follow-up of 28.4 months, Cabraja et al.[36] achieved a fusion rate of 88.1% for PEEK cage. At mean follow-up of 25.6 months, Liu et al.[33] observed fusion rate of 72%. Song et al.[43] had 78.9% fusion. In a prospective study by Niu et al.[44] fusion rate at 12-month

follow-up was 100% for PEEK cage group. With mean follow-up period of 18.9 months, Ha et al.[45] achieved 94.5% fusion. We achieved 100% fusion rate at mean follow-up period of 56.64 months.

Conclusion

ACDF is a successful surgical technique for the management of symptomatic cervical disc herniation. ACDF with autologous iliac bone graft and metallic implant is the choice of treatment in appropriately selected patients. It increases chances of fusion and helps in early mobilization.

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BCL-2 Expression and Histopathological Staging of Renal Cell Carcinoma in a Tertiary Care Setting Hospital

***Anjum M[1], Snigdha SS[2], Nasrin M[3], Hasan M[4] , Akther S[5], Hossain MF[6]**

Abstract

Background: *Renal cell carcinoma (RCC) represents the commonest form of kidney cancer, constituting approximately 90% of all diagnosed kidney cancer. Patients with over expression of BCL-2 in renal cell carcinoma have a poorer prognosis. BCL-2 expression in RCC may assist in the targeted therapies and improve patient management.*

Aim: *To evaluate the expression of BCL-2 in histomorphologically diagnosed renal cell carcinoma and its association with histopathological stage (pT).*

Methods: *This cross-sectional study was conducted in the Department of Pathology, Dhaka Medical College, Dhaka, from March 2021 to February 2023 among purposively included 60 histomorphologically diagnosed RCC patients. Immunostaining with BCL-2 antibody was also done and findings were recorded. Statistical analysis was carried out using the SPSS software version 25.*

Results: *A total of 26 (43.3%) patients were in pT2 stage, 24 (40.0%) patients belonged to pT1 stage and the remaining 10 (16.7%) patients were in pT3 stage. Positive expression of BCL-2 was detected in 37 (61.7%) cases while 23 (38.3%) patients had negative BCL-2 expression. BCL-2 expression was significantly associated with pT stage (p=0.035).*

Conclusion: *BCL-2 immunomarker, combined with histopathological staging can identify individuals at high risk for kidney cancer. BCL-2 expression is crucial for patients with cancer that does not respond to chemotherapy.*

Keywords: *Renal Cell Carcinoma, BCL-2 Expression, Histopathological Staging.*

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Introduction

Renal cell carcinoma accounts for 1-3% of all cancers in humans and represents 75-80% of kidney cancer cases in adults.[1] RCC originates from renal stem cells primarily found in the proximal nephron and tubular epithelium.[2]

Risk factors for renal cell cancer include tobacco smoking, prolong use or misuse of certain pain medications, obesity, hypertension, family history of renal cell cancer, genetic history or hereditary papillary renal cancer.[3]

BCL-2 is significant for comprehending the progression and prognosis of renal cell carcinoma (RCC). The B cell leukemia/ lymphoma 2 gene (BCL-2) is classified as a proto-oncogene. It is found on chromosome 18q21.33. This gene was initially identified by cloning the breakpoint region of the t (14;18) translocation, a chromosomal abnormality typically associated with follicular lymphomas.[4] Unlike many oncogenes, BCL-2 does not induce cell division but instead promotes cell survival by inhibiting apoptosis.[5]

Several studies show that elevated BCL-2 expression correlate with various clinical factors, such as the tumor stage, size, and its

1. Dr. Munira Anjum, Assistant Professor, Department of Pathology, Marks Medical College, Mirpur -14, Dhaka.
2. Dr. Shyla Sharmin Snigdha, Assistant Professor, Department of Pathology, Zainul Haque Sikder Women's Medical College & Hospital, Dhaka.
3. Dr. Mehnaj Nasrin, Medical officer, Department of Pathology, Mugda Medical College, Dhaka.
4. Dr. Marufa Hasan, Lecturer, Department of Pathology, Mugda Medical College, Dhaka.
5. Dr. Shahina Akther, Clinical Pathologist, Dhaka Medical College Hospital.
6. Dr. Mohammad Farid Hossain, Assistant Professor, Department of Glaucoma, National Institute of Opthalmology & Hospital, Sher- E- Bangla Nagar, Dhaka.

Correspondence : Dr Munira Anjum , MD (Pathology), Assistant Professor, Department of Pathology, Marks Medical College, Mirpur -14, Dhaka, Bangladesh. Contact: 01742191226, E-mail: munirarmc87@gmail.com

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metastatic spread. This implies that BCL-2 could aid in forecasting patient outcomes. Increased BCL-2 expression are associated with more advanced stages of renal cell carcinoma (RCC), indicating a potentially more aggressive cancer. The BCL-2 expression is linked to tumor progression.[6] Sometimes, BCL-2 expression correlates with poorer survival outcomes.[7]

Elevated BCL-2 expression, in conjunction with larger tumor size are significant risk factors for recurrence of the disease and mortality in patients.[8] Typically, BCL-2 expression are more pronounced in aneuploid tumors, which might suggest a more aggressive cancer type; however, its precise role in prognosis remains uncertain.[9]

Though BCL-2 expression is frequently observed in RCC, its effectiveness as predictor is limited. This indicates a need for further investigation to enhance the understanding of its significance in clinical environments.[7] This study was conducted to assess the expression of BCL-2 in histomorphologically diagnosed renal cell carcinoma and its association with histopathological stage (pT).

Materials and Methods

This was a part of large cross-sectional study carried out from the period March 2021 to February 2023 in the Department of Pathology, Dhaka Medical College, Dhaka. The objective was to assess BCL-2 expression and its association with staging in renal cell carcinoma. By purposive sampling technique total 60 histomorphologically diagnosed renal cell carcinoma patients of any age and sex were included in this study. Informed written consent was taken from each participant after describing the purpose and procedure of the study. Data was collected by face-to-face interviewing and reviewing medical records. Immunostaining for BCL-2 were done on all the 60 cases at Department of Pathology, Bangabandhu Sheikh Mujib Medical University, Dhaka. Histopathological stage was categorized in two groups: 1) Low stage: pT1 and pT2, 2) High Stage: pT3 and pT4. After thorough checking and coding statistical analyses were carried out using Statistical Package for the Social Science (SPSS) version 25. Categorical variables were presented as frequencies and percentages, numerical variables were presented as mean and standard deviation. Chi-square and Fisher Exact tests were used to analyze association between categorical variables. Statistical significance was set as 95% confidence level. Results having p-values <0.05 were considered as statistically significant. Ethics was maintained strictly at every point of this study. Ethical clearance was obtained from Ethical Review Committee (ERC) of DMC.

Results

This study was carried out among 60 histopathologically diagnosed cases of renal cell carcinoma to assess expression of BCL-2 and its association with staging in renal cell carcinoma.

Table-I described that mean (±SD) age was 57.2 (±11.7) years. Smoking was found in majority 66.7% of the patients as risk factors. Maximum 83.3% patient (n=50) underwent radical nephrectomy. A total of 58.3% cases (n=35) RCC were located in upper pole of kidney.

Table-I

Distribution of patients according to baseline characteristics (n=60)

Attributes	Frequency (n)	Percentage (%)
Age (Years)		
24-44	06	10
45-64	35	58.3
65-75	19	31.7
Mean (±SD) =57.2 (±11.7)		
Risk factors (multiple response)		
Smoking	40	66.7
Hypertension	37	61.7
Obesity	34	56.7
Type of specimen		
Partial	10	16.7
Radical	50	83.3
Location of RCC		
Upper	35	58.3
Lower	25	41.7

Table-II

Distribution of patients according to histopathological staging (pT) of renal cell carcinoma and BCL-2 expression (n=60).

Attributes	Frequency (n)	Percentage (%)
Staging		
pT1	24	40
pT2	26	43.3
pT3	10	16.7
BCL-2 expression		
Positive	37	61.7
Negative	23	38.3

Majority 43.3% of patients (n=26) belonged to pT2 stage followed by 40% (n=24) in pT1 stage and remaining 16.7% patients (n=10) were in pT3 stage of RCC. BCL-2 expression was detected positive in 61.7% patients (n=37) while 38.3% patients (n=23) showed negative BCL-2 expression (Table-II).

Table-III

Association between histopathological staging and BCL-2 expression (n=60)

Staging (pT)	BCL-2 expression		p-value
	Positive	Negative	
pT1 & pT2	34 (68%)	16 (32%)	0.035
pT3	3 (30%)	7 (70%)	

Among the patients who were in pT1 & pT2 stage, 68% patients (n=34) were detected as positive expression of BCL-2 and 32% cases (n=16) showed negative expression. About 70% patients (n=7) were detected as negative expression and 30% cases (n=3) showed positivity of pT3 stage. Staging of RCC was statistically associated with BCL-2 expression ($p<0.05$) stated in Table-III.

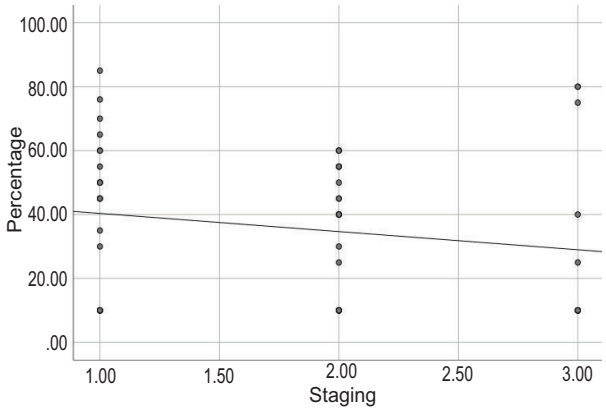

Fig 1 : *Scatter diagram showing association between histopathological staging and percentages of BCL-2 expression (n=60)*

Figure 1 showed that there was significant negative correlation between histopathological staging and percentages of BCL-2 expression.

Discussion

The current study revealed 58.3% RCC patients were in age range of 45-64 years. Smoking was found in majority 66.7% of the patients followed by hypertension in 61.7% and obesity in 56.7% of patients as risk factors for RCC. Tobacco smoking has been linked to many common cancers including RCC. A variety of carcinogens associated with the pathogenesis of RCC are present in tobacco smoke. There is epidemiological evidence supporting a causal association with tobacco, including a dose-response relationship between risk and daily cigarette consumption and a decline in risk with more years of smoking cessation.[10] Similarly another study confirmed that obesity was significantly associated with RCC risk (BMI e" 35 vs. < 25 kg/m2).[11] Another study also found strong smoking history (71%) and (58%) RCC patients were hypertensive.[12]

There are different types of surgery like partial nephrectomy, radical nephrectomy which involves taking out the kidney, the adrenal gland, nearby tissue, and usually the nearby lymph nodes as well.[3] The present study stated that maximum 83.3% patients (n=50) underwent radical nephrectomy and remaining 16.7% patients (n=10) went for partial nephrectomy. Regarding location of renal cell

carcinoma (RCC) in majority 58.3% cases (n=35) RCC were located in upper pole of kidney and in remaining 41.7% cases (n=25) RCC were located in lower pole.

In the present study, it was detected that 43.3% patients were in pT2 stage, 40.0% patients belonged to pT1 stage and the remaining 16.7% patients were in pT3 stage. A similar study reported 34.2% cases were in pT1 stage, 28.5% patients in pT2 stage and 34.2% cases in pT3 stage.[13] Moreover Girgin et al. (2022) also found 44 cases in pT1 stage, 27.4% cases in pT3 stage followed by 27.4% patients in pT4 stage.[14]

High expression of BCL-2 prevents cell proliferation, suppresses tumor growth and thereby is associated with a lower pT stage in RCCs, as previously stated.[7] It was additionally detected in the current study that BCL-2 expression was significantly associated with stage in a statistically significant level ($p<0.05$). Therefore, BCL-2 expression might be applied as a novel predictor of better prognosis in RCC patients.[7]

In this study, BCL-2 expression was inversely associated with pT stage. In pT1 and pT2 stage, 34 (68.0%) were detected with positive expression and 16 (32.0%) showed negative expression. Again, in pT3 stage, 3 (30.0%) cases showed positive expression and 7 (70.0%) showed negative expression. A study found a significant inverse relationship between BCL-2 expression and pT stage of RCCs.[15] A possible explanation to this might be based on the suggested anti proliferative role of BCL-2 protein.[7,16]

Studies showed that BCL-2 was more frequently detected in tumors with pT stage.[17] Contrary to inferential belief that BCL-2 as anti-apoptotic gene would promote cell cycle, Pierce et al. (2002) found that the expression of the protein interferes with the cell cycle progression.[16] It has also been proposed that by increasing cell survival, BCL-2 may facilitate differentiation and that loss of expression is related to loss of differentiation and neoplastic progression.[18]

According to the present study, RCC with low stage (pT1 and pT2) demonstrates higher expression of BCL-2. But it does not reveal any significant association with histopathological types of RCC. Therefore, it could be hypothesized that high expression of BCL-2 prevents cell proliferation, suppresses tumor growth and thereby is associated with a lower pT stage in RCCs. This study might open a new avenue for the clinical evaluation of BCL-2 to provide a therapeutic benefit for the treatment of RCC patients.

There were some limitations. Firstly, specimens were gathered exclusively from DMCH. Collecting specimens from various centers across the country would provide more comprehensive information. Secondly, patient follow-up was not conducted. Finally, it was not feasible to make remarks on the patients' outcomes.

Conclusion

BCL-2 immunomarker along with histopathological staging can help to diagnose individuals at high risk for kidney cancer. BCL-2 may also have therapeutic uses. It may help to determine cancers especially those are chemotherapy resistant.

Declarations

Ethics approval and consent to participate

Before data collection, both verbal and written informed consent was taken from patients.

Consent for publication

All authors have approved this manuscript for publication.

Availability of data and materials

The datasets supporting the conclusions of this article are included within the article generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

MA, MN, and MH participated in the design of the study, data interpretation and drafted the manuscript. MA, MN, MFH, and MH contributed to the data design, data interpretation and data analysis. SSS, SA, and MFH did the critical review of the manuscript.

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Frequencies of Different Risk Factors for Functional Constipation in Pediatric Population: Experience from Tertiary Care Center of Bangladesh

Reza R[1], Poly FH[2], Akram L[3], Haque MM[4], Mariom ML[5], Mazumder MW[6]

Abstract

Background: *Functional constipation is a common pediatric dilemma. It causes psychological stress, behavioural abnormality and growth impairment. In our country constipation in children is frequently overlooked and desired evaluation is often ignored. Factual knowledge viewing risk factors of constipation will lead to proper evaluation and early diagnosis which will ensure timely management of constipation.*

Methods: *This was cross-sectional study, carried out in Paediatric Gastroenterology & Nutrition Department, BSMMU from January to December 2022. Total 75 children aged 2-16 years were enrolled here. Samples were collected purposively from outpatient department with consent of parents. Diagnosis of functional constipation was made by Rome IV criteria. Children who fulfilled ROME IV criteria were evaluated for risk factors of constipation.*

Result: *We included 75 children in our study where 56% were male and 44% were female. Constipation was more prevalent in 6 to 10 years (42.7 %). Most common risk factors were unhygienic (69.3%), inadequate toilets (61.7 %) in academic area and during school hours child's embarrassment (65.1%) to use toilet. We observed long duration academic activity (48 %), reading in madrasa (46.6 %), screen time more than two hours (60 %), preference of indoor games (56 %) and child maltreatment (physical abuse 10.6 %; emotional abuse 25.3 %; familial disharmony 18.6 %) as potential risk factors. Inadequate fibre (53.3%) & fluid intake (50.6%), regular junk food consumption (48%) and cow's milk ingestion (34.7 %) were diet related influence of FC.*

Conclusion: *Infrequent number and unclean toilet in academic premises, child's embarrassment to use toilet during school hours, long duration educational activity, use of screen time daily two hours or more, preference of indoor games & lack of physical activity, child maltreatment and familial disharmony were found as frequent risk factors. Regular cow's milk ingestion, junk food consumption, inadequate Fiber and fluid intake and regular were frequent dietary risk factors.*

Key words: *Functional constipation (FC), Risk factors, Children.*

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Introduction:

Constipation is a common disorder of pediatric population. Its prevalence continues to remain high, affecting 1% to 30% of children worldwide.[1,2] It accounts 3% of all primary pediatric care visits and 10–25% of pediatric gastroenterologist visit.[3]

Functional constipation is defined as persistently difficult and infrequent defecation without evidence of a primary cause (neurologic, anatomic, metabolic). According to Rome IV criteria to diagnose FC, for children e"4 years at least two of following ROME IV criteria must be present with duration of minimum one

1. Dr. Renesa Reza, Consultant (Pediatrics) National center for control of Rheumatic fever and heart disease, Sher e Bangla Nagar, Dhaka. Phone no: 01713000884; E-mail: rezarenesa78@gmail.com
2. Dr. Ferdousi Hossain Poly, Shaheed Suhrawardy Medical College and Hospital, Dhaka.
3. Dr. Lubana Akram, Pediatric Gastroenterologist, MO, Dhaka Dental College Hospital, Dhaka.
4. Dr. Mohammad Mominul Haque, Consultant, Department of Anesthesia, Analgesia & Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka.
5. Dr. Most Lubna Mariom, Consultant, Department of Anesthesia, Analgesia & Intensive Care Medicine Bangabandhu Sheikh Mujib Medical University, Dhaka.
6. Dr. Md. Wahiduzzaman Mazumder, Associate Professor, Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University, Dhaka,

Correspondence : Dr. Renesa Reza, Consultant (Pediatrics) National center for control of Rheumatic fever and heart disease, Sher e Bangla Nagar, Dhaka. Phone no: 01713000884; E-mail: rezarenesa78@gmail.com

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month: 1) Two or fewer defecations in the toilet per week. 2) History of painful bowel movement 3) History of retentive posturing or excessive straining 4) One episode of fecal incontinence at least per week 5) History of large diameter stool that obstruct toilet 6) Presence of large fecal mass in rectum. And these symptoms cannot be fully explained by another medical condition and symptoms are insufficient to fulfill the diagnostic criteria of irritable bowel syndrome.[4]

Recent systematic reviews and meta-analyses revealed global prevalence of childhood constipation around 9.5% (0.5–32%).[5] General perception is constipation is limited in South Asian nations such as Bangladesh, India as their diets are high in fiber. But FC in our children is not less and its prevalence in Bangladeshi children is about 11%.[6] And it is more frequent above 5 years age group.[7]

Constipation has remarkable physical and mental impact on a child.[8] It may even cause decelerated physical growth (underweight, short stature).[9] Due to lack of knowledge and understanding of impact, most parents do not pay much attention to identify its risk factors. Limited research works have done to find out prevalence, risk factors and effect of functional constipation in our children. As functional constipation has significant influence on physical growth and quality of life, this study was undertaken to ascertain frequencies of different risk factors for functional constipation in Bangladeshi children.

Methodology:

It was a cross-sectional study, conducted at the department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University (BSMMU) from January 2022 to December 2022 (12 months). A total of 75 children aged 2 to 16 years, having functional constipation were enrolled in this study. Children were recruited from outdoor visit. Proper history, clinical examination, relevant investigation, Rome IV criteria were done and samples were selected purposeively. Children having constipation but did not fulfill Rome IV criteria, having organic or chronic disease and already on treatment for constipation were excluded from study. Details clinical history, examination findings and investigation reports were recorded in a predesigned structured data sheet.

Results:

A total of 75 subjects were included in final analysis. Among them 56% (n = 42) were male and 44% (n = 33) were female. Constipation was found to be higher in 6-10 years age group (42.7%).

Table I

Demographic variables of study participants (n= 75)

Age group (years)	Children with FC, n=75, n (%)
1-5	16 (21.3)
6-10	32 (42.7)
11-15	26 (34.7)
>15	1 (1.3)
Male	42 (56)
Female	33 (44)

Table II noted long duration academic activity of 6 hours or more, reading in madrasa, unhygienic and inadequate number of toilets in school premises, feel embarrassed to use toilet during school hours as probable association of functional constipation.

Table II

School related factors in children with functional constipation

Risk Factors	Children with FC, n=75 n (%)
Long time academic activity (≥6 hours)	36 (48)
School (Bengali & English)	33(44)
Madrasa	35(46.6)
No School	7 (9.3)
Adequate Number of toilets	26 (38.2)
Inadequate Number of toilets	42 (61.7)
Hygienic toilet	16 (23.5)
Unhygienic toilet	52 (69.3)
Embarrass to use toilet at school	49(65.1)

Table III analyzed children with functional constipation had **screen time** more than two hours (60%) and had habit of playing indoor games (56%).

Table-III

Analysis of Screen time and Physical activity in children with functional constipation

Risk Factors	Children with FC n=75 n (%)
Screen time <2 hours	30 (40)
Screen time> 2 hours	45 (60)
Physical activity-Outdoor games	33(44.0)
Physical activity-Indoor games	42 (56.0)

Table IV revealed Child maltreatment (physical & emotional abuse) and familial disharmony were higher among children with functional constipation.

Table-IV

Analysis of Psychological factors in children with functional constipation

Risk Factors	Children with FC n=75 n (%)
Child maltreatment	
Physical abuse	8 (10.6)
Emotional abuse	19 (25.3)
Familial disharmony	4 (18.6)

Children with functional constipation had history of less fiber and inadequate fluid intake. They had habit of dietary intake of cow's milk and regular junk food consumption (table V).

Table V

Analysis of Dietary factors in children with functional constipation

Risk Factors	Children with FC n=75 n (%)
cow's milk intake	26 (34.7)
Inadequate fiber consumption	40(53.3)
Inadequate fluid intake	38 (50.6)
Junk food consumption	
Occasional	17 (22.6)
Regular	36(48)

History of constipation in parents (46.6%) & siblings (42.6%), low maternal education (45.3%) and lower economic background (57.3%) were associated risk factors in children with functional constipation (table VI).

Table-VI

Family related risk factors of children with functional constipation

Risk Factors	Children with FC n=75 n (%)
History of constipation among parents	35 (46.6)
History of constipation among siblings	32 (42.6%)
Mother's education (Primary school)	34 (45.3)
Mother's education (Secondary school)	17 (22.6)
Mother's education (Higher secondary)	13 (17.3)
Mother's education (Graduation/above)	11 (14.7)

Discussion

75 children with functional constipation who fulfilled Rome IV criteria were evaluated in this study. We observed FC was more prevalent in the age group 6 to 10 years with slight male preponderance (54.75%). Mazumder et al.[7] showed functional constipation was common above 5 years (56.42%) along a bit male dominance (54.75%). Khanna et al.[10] also observed male prevalence with functional constipation. These findings are similar to our one. On the contrary, in Saudi children, females were affected more than males and male to female ratio was 1:3.5.[11] In India, Kondapalli et al. found female predominance in FC.[12]

In our study we observed, children with long duration academic activity (58.6%), unhygienic toilet at academic environment (61.7%), child's embarrassment to use toilet at school (69.1%) and students of madrasa (56%) had higher percentage of constipation. Hasosah et al. noted

lack of cleanliness of school toilets and homework of >3 hours/day as risk factors of functional constipation.[11] Mazumder et al. showed that 39.66% of children refused to defecate at school.[7] Lundblad et al revealed children often affected by negative impression of school toilets and frequently avoid using of toilets during school hours.[13]

In present study most of our children with FC had history of doing indoor games (65.3%) instead of outdoor playing & physical activity. Schryver et al found regular physical activity as a protective element against constipation in adults.[14] Slow gastrointestinal transit time is associated with constipation and it is assumed that exercise influence rapid gastrointestinal transit and thus improve constipation. Masaaki Y et al. reported lack of physical inactivity significantly associated with childhood constipation.[15] Mazumder et al. found constipation in 7.23% children who had history of less physical activity and 2.23% children who were obese.[16]

Children who preferred to use electronic media more than 2 hours/day had higher percentage of constipation (60%) and it is a potential risk factor in modern Bangladesh. Olaru et al. established lack of exercise and television watching more than 3 hours/day as a possible factor of childhood constipation.[17] Children frequently withhold defecation urge during watching television and playing mobile games which initiate vicious cycle of constipation.

Several research suggested positive link up between psychological stress and childhood constipation.[15] Deva Narayana et al reported school and family related stressful evens such as punishment at school or punishment from parents, bullying and domestic violence were associated with higher constipation rates in Sri Lankan children.[18] Frequent irritability, unwillingness to attend school and lack of communication with parents were established as risk factors of constipation by Masaaki Y, Michikazu S and Takashi.[15] In current study we found higher frequency of physical abuse (10.6%), emotional abuse (25.3%) and familial disharmony (18.6%) among children with constipation. Thus, constipation was significantly higher in children exposed to stressful life events. Modulation of gut motility through brain-gut axis probably alters colonic transit and ano-rectal functions causing constipation.[18]

Here we evaluated dietary habits of constipated children. Increased consumption of cow's milk may consider as a risk factor.[19] In our study, children with functional constipation had history of regular cow's milk intake (34.7%). Andiran et al stated constipation may occur due to cow's milk intolerance or cow's milk protein allergy.[19] Young children with chronic constipation and anal fissure consume larger amounts of cow's milk than children with a normal bowel habit.[19] Mazumder et al. also described consumption of cow's milk as one of the risk factors of functional constipation.[16] They found 32.96% constipated children had history of cow's milk intake which is nearly similar to our study.[16]

Our children with functional constipation had history of less fiber (68%) and inadequate fluid intake (58.6%) and habit of regular junk food consumption (50.6%). Wu et al. (2010) found association of constipation with lower intake of vegetables, fruits, soybean products and eggs.[20] Kondapalli et al. monitored vegetables & fruits intake were inadequate in 73.2% children of constipation and 32.7% of them took junk foods in form of fried itemss.[12] Olaru et al. analyzed main food groups of children and revealed constipated children consumed meat products, concentrated sweets and soft beverages more often and they had habit of less fruit and vegetables intake.[17] Findings of these previous studies have much similarity with our one.

We observed children with functional constipation had history of constipation in parents (46.6%) and siblings (42.6%). Similar life style and food habit may explain this familial aggregation. Some researchers suggested presence of genetic and familial connection with constipation.[1,16] Rajindrajith S. et al. reported higher prevalence of constipation (49%) within close family members.[21] Benzamin et al suggested functional constipation of Bangladeshi children had positive familial history.[6]

We marked lower maternal education as one of the risk factors for constipation. In our study, 53.3% mother completed only primary education. Kilincaslan et al. (2014) observed maternal education (elementary) and employment as one of the determinant factors of constipation.[22] J.F. Ludvigsson also figured out relation between low maternal education and constipation.[23] Mazumder et al. stated lower maternal education as a more prevalent problem in Bangladeshi children with FC.[16]

The study was conducted in a single center and it was a cross-sectional study. Further study with large sample and control group would increase reliability of the findings.

Conclusion

Infrequent number and unclean toilet in academic premises, child's embarrassment to use toilet during school hours, long duration educational activity, use of screen time daily two hours or more, preference of indoor games & lack of physical activity, child maltreatment and familial disharmony were found as frequent risk factors. Regular cow's milk ingestion, junk food consumption, inadequate Fiber and fluid intake and regular were frequent dietary risk factors.

Limitation: Single centre study with small sample size which does not represent all children of our country.

Conflict of Interest: The authors have no conflict of interest.

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CASE REPORT

Panhypopituitarism as a Presenting Manifestation of Neurosarcoidosis – A Rare Case Report

Aurpa NN[1], Mark SHK[2], Mahmud R[3], Islam MF[3], Jahan I[3], Sina H[4], Alam I[4], Ahmed KGU[5]

Abstract

Sarcoidosis is a multisystem disease characterized by non-caseating granuloma that affects the nervous system occasionally. When neurosarcoidosis infiltrate the pituitary gland leading to panhypopituitarism, result can be devastating. We present here a case of 30-year-old lady who presented with fever and headache for 6 months along with prolonged period of amenorrhea and forgetfulness. She also had increased thirst and polyuria. Her hormone profiles were suggestive of panhypopituitarism. MRI of brain showed a contrast enhancing lesion in the sellar and suprasellar region along with nodular leptomeningeal enhancement . We retrogradely searched for the underlying reason behin`d this .Her MT was 0 along with ground glass opacity in both lung fields in HRCT chest which made the diagnosis of neurosarcoidosis most likely. We treated her with prednisolone to manage neurosarcoidosis and secondary adrenal insufficiency along with sequential hormone replacement with desmopressin and levothyroxine . Follow up MRI of brain done 3 months later showed near complete resolution of lesion along with significant clinical improvement.

Key words : *neurosarcoidosis, hypopituitarism, panhypopituitarism*

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Introduction

Sarcoidosis is a condition that triggers inflammation in various organs of the body , including the lungs, eye, skin and occasionally nervous system.[1] When sarcoidosis affects the nervous system, it is referred to as neurosarcoidosis, estimated to occur in approximately 5-15% of patients.[2] Pituitary involvement may be present in up to 5% of those cases and can manifest as hypothalamus, adenohypophyses dysfunction or arginine vasopressin deficiency in isolated fashion or variedly combined.[3] When neurosarcoidosis affects the pituitary gland, it can destroy or compress the gland, interfering it's hormone producing capabilities ultimately leading to a life-threatening condition.[1] Hypothalamic-pituitary neurosarcoidosis accounts for 1% of sellar masses and carriesa mortality rate approaching 10%.[4,5,6] We therefore present a rare case of neurosarcoidosis presenting with panhypopituitarism as it's first clinical manifestation.

1. Dr. Nishat Nayla Aurpa, Phase B Resident, Department of Neurology, Dhaka Medical College Hospital, Dhaka
2. Dr. Sayeef Hossain Khan Mark, Registrar, Department of Neurology, Dhaka Medical College Hospital, Dhaka
3. Dr. Reaz Mahmud, Muhammad Fakhrul Islam, Israt Jahan, Assistant Professor, Department of Neurology, Dhaka Medical College Hospital, Dhaka
4. Hashmi Sina, Iftikher Alam, Associate Professor, Department of Neurology, Dhaka Medical College Hospital, Dhaka
5. Professor Kazi Gias Uddin Ahmed, Professor & Head, Department of Neurology, Dhaka Medical College Hospital, Dhaka

Correspondence: Dr. Nishat Nayla Aurpa, Phase B Resident, Department of Neurology, Dhaka Medical College Hospital, Dhaka, Mobile: 01715029675, Email: aurpanishat@gmail.com

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Case presentation

We present the case of 30-year-old lady with complaints of fever along with headache for 6 months and forgetfulness for 3 months. Fever was low grade, irregular with an evening rise of temperature along with global, dull aching headache without any blurring of vision or vomiting. She complained of forgetfulness for recent memory along with fatigability, constipation and cold intolerance for last 3 months. She had amenorrhoea for 18 months with hot flush, pallor and decreased libido. She also had polyuria and polydipsia. She had significant weight loss with anorexia. On general examination, patient was ill-looking, apathetic, pale, mildly anaemic with recorded temperature of 100°F. Nervous system examination revealed she had moderate dementia with MMSE score of 17. Other neurological examination does not reveal any abnormality. Examination of all other systems were unremarkable. Her routine investigations showed reduced haemoglobin along with raised serum sodium level . Hormone profile revealed reduced TSH, FSH, LH, ACTH, basal cortisol and IGF-1 along with raised serum prolactin . Her urine osmolarity was reduced whereas serum osmolarity was maintained. CSF study showed raised protein with negative gene xpert for M. tuberculosis. MRI of brain T1 and T1 contrast sequence revealed a contrast enhancing lesion in sellar and suprasellar region along with nodular leptomeningeal enhancement (Figure 1 & 2). HRCT chest showed ground glass opacity in multiple segments of both lung fields (figure 3) whereas bronchoalveolar lavage was unremarkable.

Table 1

Investigations			Reference range
Full blood count	Hemoglobin (gm/dl)	10	11.5-15.5
	White blood cells (× 10 ^ 9 / L)	13.01	4-11
	Platelets (× 10 ^ 9 / L)	245	150-450
	HCT (%)	30.9	36-46
	ESR (mm in 1st hour)	60	< 20
Renal function	S. Creatinine (mg/dl)	0.99	0.04 – 1.2
	Blood Urea (mg/dl)	4	15-40
Liver function	SGPT (U/L)	16	7-35
	ALP (U/L)	43	40-150
	HBsAGAnti-HCV	Negative	
HbA1C	HbA1c (%)	5	4.5-6.3
Serum electrolyte(mmol/l)	Sodium	149	134-144
	Potassium	3.5	3.3-4.6
	Chloride	111	98-106
	TCO2	24	23-27
Urine R/E		Pus cell: 2-3/ HPF, Albumin, RBC: nil	

Table 2

Test	Result	Reference range
Serum Calcium (mg/dl)	8.6	8.8-10.3
Serum Albumin (mg/dl)	4.0	3.5-5.6
Serum ACE (IU/L)	49	20-70
Serum LDH (IU/L)	222	120-246
Urine osmolarity (mOsm/kg)	71	500-850
Plasma osmolarity (mOsm/kg)	287	282-295
Serum TSH (IU/ml)	0.39	0.7 -4.17
Serum FT4 (pmol/l)	9.17	11.5- 22.7
Serum FSH (mIU/ml)	0.91	3.03-8.08
Serum Prolactin(mIU/ml)	1064.13	59-619
Plasma ACTH (pg/ml)	1.50	8.3-57.8
Basal Cortisol (nmol/L)	25	102-690
IGF-1 (ng/ml)	52	260-350
Urinary electrolyte (mmol/day)		
Urinary sodium	15	25-125
Urinary potassium	18	25-125
Urinary chloride	33	110-250
MT	0	
ANA	Negative	

Table 3

CSF study			Reference range
Cytology	Appearance	Clear	
	Total WBC count(/mm^3)	02	00-05
	Total RBC count(/mm^3)	00	
	Neutrophil (%)	00	
	Lymphocyte(%)	100	
Biochemical	Protein(mg/dl)	67.90	15-48
	Glucose(mg/dl)	59.76	40-70
	ADA (U/L)	2.10	< 10
Gene Xpert		Not detected	

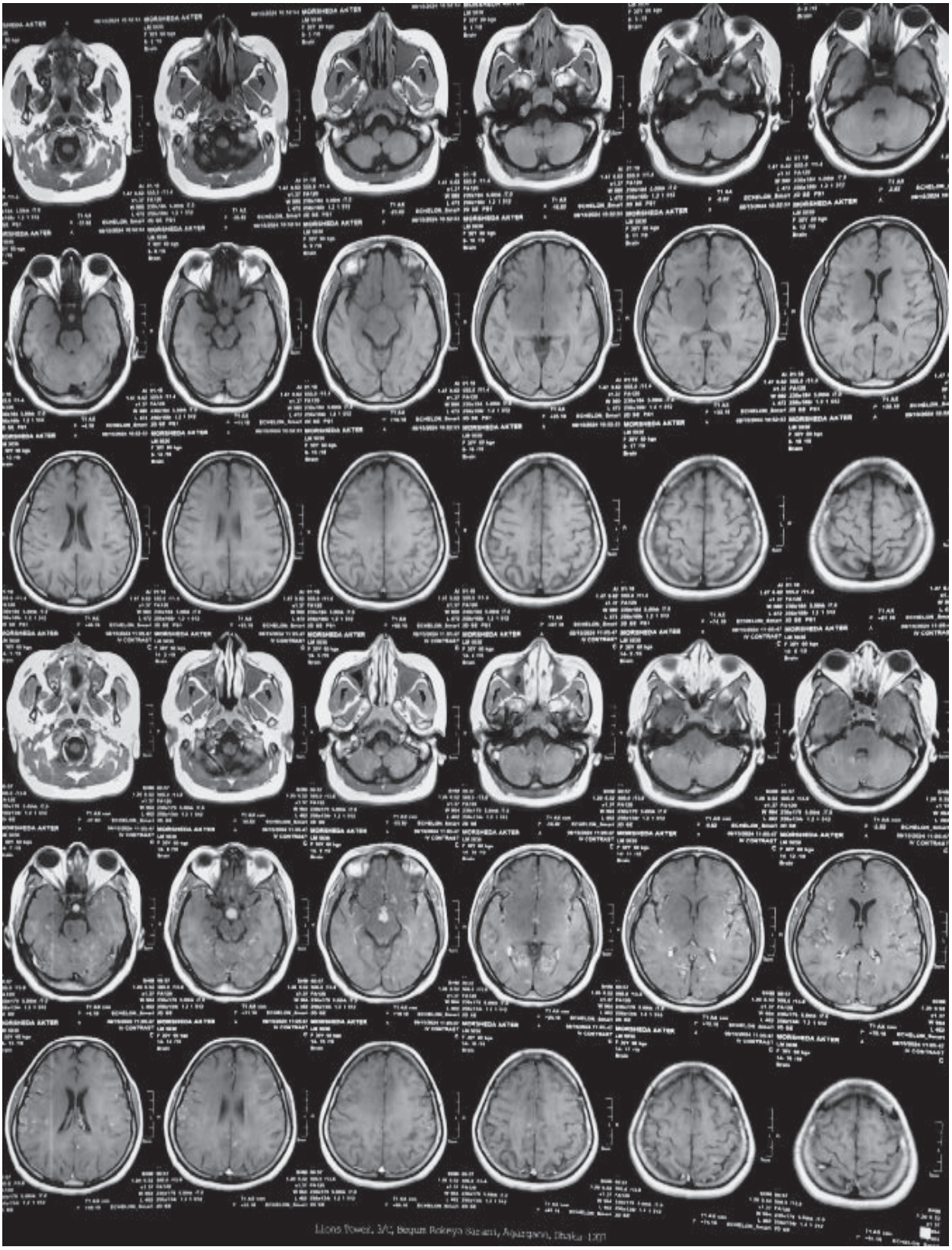

Fig 1: *MRI of brain multiple axial cut T1 and T1 contrast sequence shows a contrast enhancing lesion in sellar and suprasellar region along with nodular leptomeningeal enhancement*

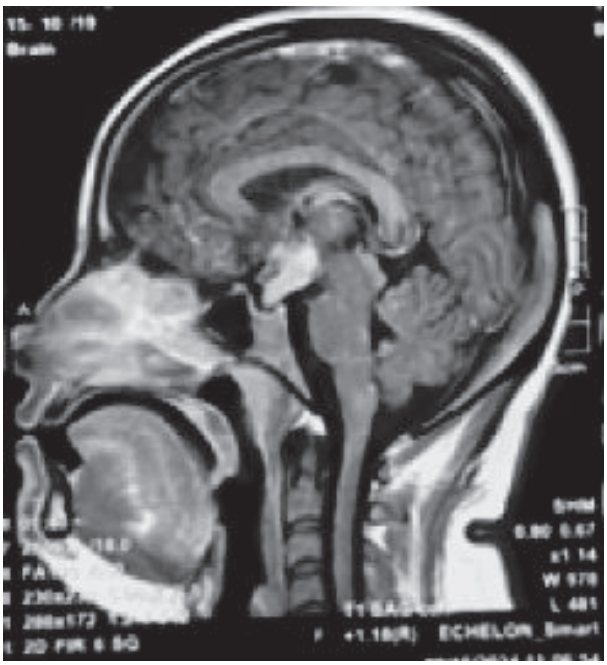

Fig 2a

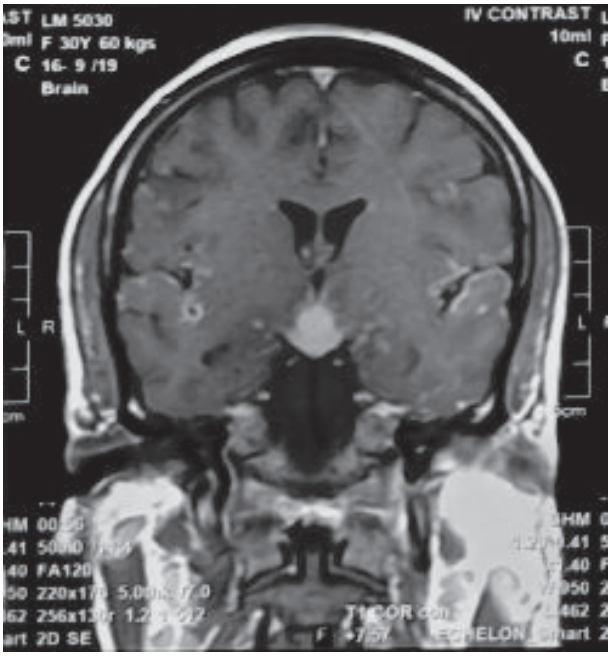

Fig 2b

Fig 2a and 2b showing MRI brain T1 contrast sagittal and coronal section respectively showing a contrast enhancing lesion involving pituitary stalk, pituitary gland, hypothalamus and subependymal portion of third ventricle along with nodular leptomeningeal enhancement

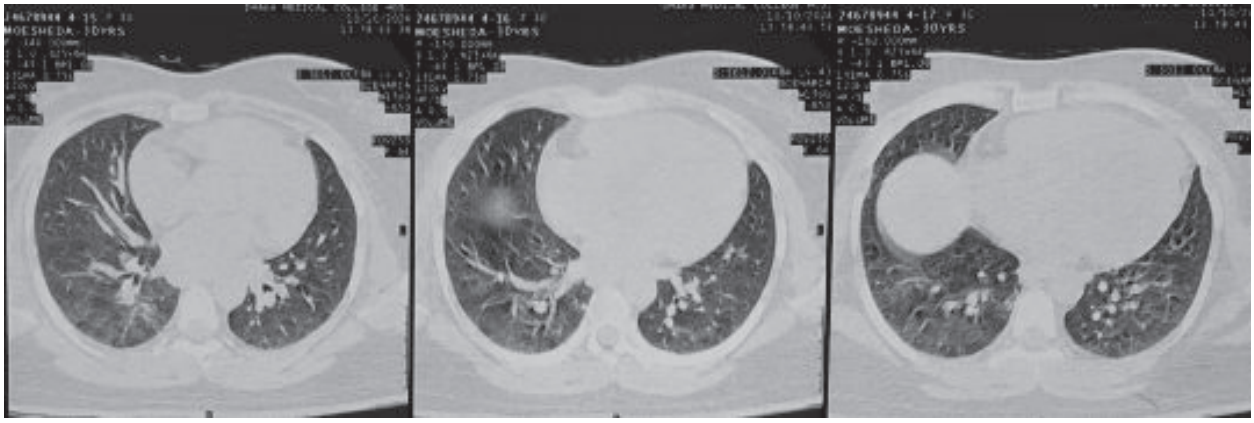

Fig 3 *showing HRCT chest axial section with ground glass opacities involving multiple segments of both lung fields*

On the basis of clinical features, suggestive finding in MRI brain and HRCT chest we diagnosed the case as neurosarcoidosis. We started prednisolone along with other hormone replacements which led to near complete resolution of lesion in follow up MRI brain along with normal s.sodium and TSH level after one month of treatment (Figure 4). Patient was deemed stable for discharge with the plan to schedule a follow-up appointment and reevaluate her pituitary hormones outpatient.

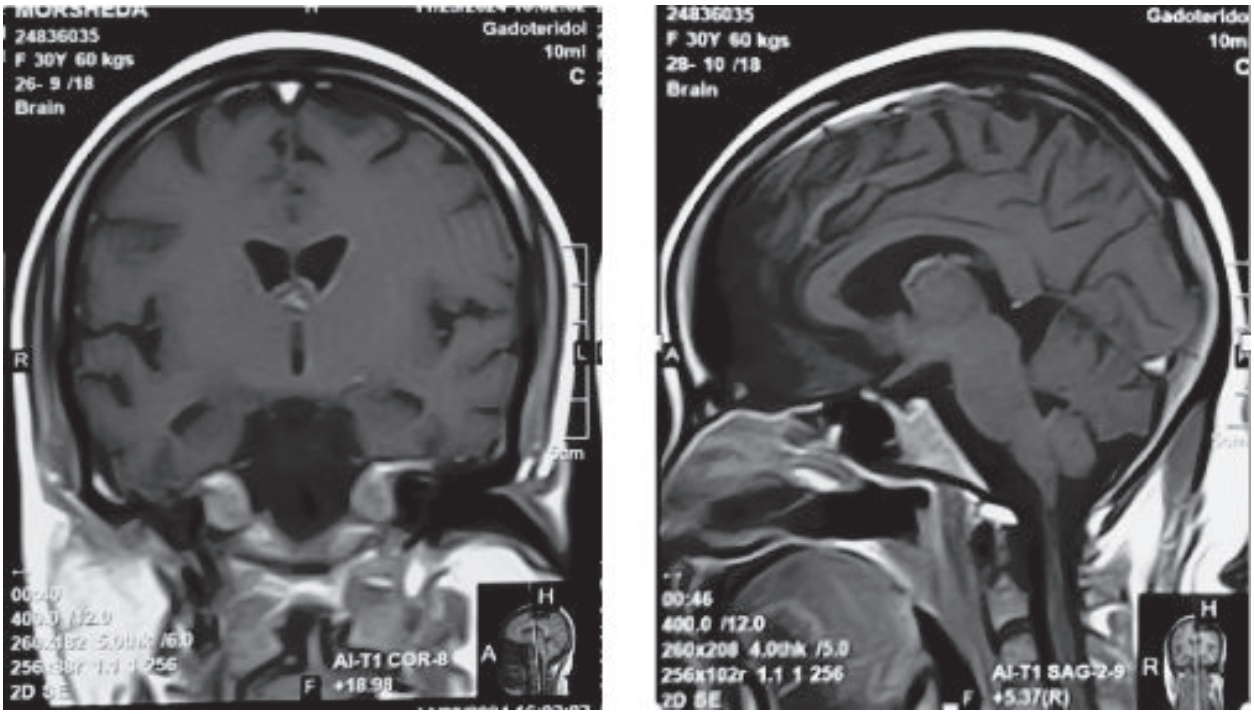

Figure 4 showing follow up MRI brain coronal and sagittal cut T1 contrast sequence showing near complete resolution of lesion after one month treatment with prednisolone.

Discussion

The symptoms of neurosarcoidosis vary depending on the specific anatomic structure affected by sarcoid lesion.[7] Approximately, 5-10% of patients diagnosed with sarcoidosis exhibit neurological symptoms. However, neurosarcoidosis comprises only 1% of all sarcoidosis patients.[8] Diagnosis of neurosarcoidosis on the background of panhypopituitarism is challenging. Occasionally, it may mimic a pituitary mass.[9] In this situation, it may be necessary to undergo biopsy to obtain histological confirmation. Though histological finding of non-caseating granuloma remains the hallmark of the disease, biopsy is not always practical or sufficiently safe as in our case. Neurosarcoidosis diagnosis primarily depends on factors beyond histology such as CSF results or MRI finding.[10,11] The most frequent abnormality observed is raised CSF protein level as in our case. 55% of patients show lymphocytosis in CSF[8] whereas it was normal in our case. MRI brain is very sensitive in detecting abnormality in neurosarcoidosis but it is non-specific.[1] However, it's worth noting that about half of the patients with hypothalamic-pituitary sarcoidosis may appear normal in radiological test.[12]

A literature review done by Ewelina N. et al showed gonadal insufficiency as the most frequent endocrinopathy (85.4%) followed by hypothyroidism (73%) , adrenal insufficiency (51.2%) and growth hormone deficiency (39%).[3] Hypoprolectinemia occurred in 43.9% patients and hyperprolactinemia was seen in 4.8% cases as observed in our case.[3] Clinically apparent HP dysfunction preceded the diagnosis of sarcoidosis in 13 out of 24 HP-NS patients described by Langrand et al.[5] Multiple reports indicated that vast majority of endocrinopathies persist even after resolution of symptoms.[5,13] Notably,Anthony et al found no correlation between neurological improvement radiologically and amelioration of endocrine deficiency.[6] Though beneficial effects of glucocorticoids on HP axis recovery has been proposed , restoration of pituitary function is rare.[14] For instance, on 4 year follow up of NS patients who achieved marked neuroimaging improvement following immunosuppression, only 8% recovered any pituitary function.[5]

In our patient ,there was near complete resolution of radiological finding along with normal thyroid profile and sodium level following one month of treatment with glucocorticoids. However, long term follow up is planned to see complete recovery of hormonal function.

Conclusion

Diagnosis of neurosarcoidosis can create a dilemma in patients presenting with panhypopituitarism. Early diagnosis and treatment is vital to salvage the pituitary function before irreversible damage occurs. Therefore, neurosarcoidosis should be always kept in mind while dealing with patients of panhypipituitarism**.**

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