ISSN 1028-0928 (Print), 2219-7494 (Online)

jDMC

Journal of Dhaka Medical College

• VOLUME 32 • NUMBER 2 • OCTOBER 2023

Indexed in Index Copernicus, DOAJ, ISC, Open J-gate, Socolar, BanglaJOL

OFFICIAL ORGAN OF DHAKA MEDICAL COLLEGE TEACHERS' ASSOCIATION

jDMC
ISSN 1028-0928 (Print)
2219-7494 (Online)
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ISSN 1028-0928 (Print), 2219-7494 (Online)

JOURNAL OF DHAKA MEDICAL COLLEGE

Volume 32, Number 2
October, 2023

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Published biannually (April and October)
By the editorial board on behalf of Dhaka Medical College Teachers' Association

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Indexed in Index Copernicus, DOAJ, ISC, Open J-gate, Socolar, BanglaJOL

JOURNAL OF
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The Journal of Dhaka Medical College [ISSN 1028-0928 (print), 2219-7494 (online)], a biannual (April & October) journal is published by the Editorial board on behalf of Dhaka Medical College Teachers' Association. It is recognized by the Bangladesh Medical and Dental Council (BM&DC). Each issue includes Editorial, Original Articles, Review Articles, Case Reports of exceptional merit on any discipline of medical science.

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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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Basmajian JV, Sloneckcr CE, editors. Grant's method of anatomy. A clinical problem-solving approach. 11th ed. New Dellu : 131 Waverly Pvt Ltd; 1997.p. 180-3.

Organization as author and publisher

World Health Organization. Revised 1990 estimates of maternal mortality - a new approach by WHO and UNICEF. Geneva: World Health Organization;2003:132-51.

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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

WFME Accreditation: A New Era for Medical Graduates in Bangladesh

Quality assurance in undergraduate medical education is crucial in delivering effective healthcare to a nation. The World Federation for Medical Education (WFME) sets global standards to improve basic medical education. It is now essential to achieve this accreditation for rapidly increasing number of medical colleges in Bangladesh to maintain global standards and quality of medical education. This article emphasizes the current status of undergraduate medical education, challenges in maintaining global standards, and implications of WFME accreditation in Bangladesh's future healthcare system.

Introduction

In the current globalized world, quality assurance in undergraduate medical education is essential to ensure that medical graduates will be competent, skilled, and ethically sound to meet the expectations of national and international healthcare. The WFME sets eight key standards to improve the quality of undergraduate medical education by ensuring a standard curriculum, improving infrastructure, standardizing educational resources, faculty development, improving the assessment system, and maintaining good governance and administration.

Background and Rationale

Until the mid-1980's Bangladesh had eight government medical colleges. With the establishment of 1st private medical college in 1986, Bangladesh experienced a rapid increase in the number of medical colleges both in the private and government sectors. Currently, we have 37 government medical colleges and 67 private medical colleges under the Ministry of Health, and also 7 medical colleges under the affiliation of the Bangladesh University of Professionals under the Ministry of Defense. While this explosion in the number of medical colleges reflects the health needs of our nation, it has also compromised the quality and uniformity of undergraduate medical education in our country.[2] Acknowledging this issue, in 2010, the Educational Commission for Foreign Medical Graduates (ECFMG) informed in its website that starting from 2023 (extended to 2024 due to the COVID-19 pandemic), all foreign doctors will need to be graduated from WFME-accredited institutes if they wish to take further postgraduate training or certification in the United States.[2]

Government Response and Policy Action

Recognizing the importance of WFME accreditation of undergraduate medical education, in September 2023, the parliament of Bangladesh approved the 'Bangladesh Medical Education Accreditation Act 2023'. Under this act, the Bangladesh Medical Education Accreditation Council (BMEAC) was formed in 2024. Already, BMEAC has set 11 standards aligned with WFME standards to evaluate the medical colleges for accreditation.

Challenges in Implementation

WFME accreditation is not an easy task to achieve. The key challenge lies in ensuring uniformity in implementation in all medical colleges of our country. Many of the private medical colleges, though, have adequate infrastructure but lack an adequate number of trained faculty and an academic hospital. On the other hand, some public medical colleges suffer from bureaucratic inertia, outdated infrastructure, and a shortage of faculty. So, to achieve WFME accreditation, it needs systemic reforms, investment in capacity building, and a shift from traditional teacher-centred methods to student-centered, outcome-based education.[3]

Implications and Broader Impact

The advantages of WFME accreditation extend beyond mere eligibility for foreign certification and training. This would also increase the reputation of medical education of Bangladesh globally and would create the opportunity for academic collaboration and research. Most importantly, WFME-accredited institutions are likely to produce competent physicians capable of providing standard healthcare both nationally and internationally. The financial stability of many private medical colleges depends on foreign students' tuition fees. Failure to get accreditation will discourage foreign students from getting admitted to these medical colleges, and thus, the survival of private medical colleges will be difficult.[4]

Conclusion

This pursuit of accreditation is not merely inevitable; it is long overdue. In a post-pandemic era where the vulnerability of health systems has been clearly revealed, Bangladesh must allocate resources towards the development of its future health staff. WFME accreditation is a fundamental need for achieving that objective, guaranteeing that Bangladeshi medical graduates are both internationally mobile and locally proficient, empathetic, and dedicated to the best standards of care.

DOI: https://doi.org/10.3329/jdmc.v32i2.83429
J Dhaka Med Coll. 2023; 32(2) : 99-100

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Serum 25-Hydroxy Vitamin D Level in Patients with Alopecia Areata and Its Relationship with Severity of the Disease

Siddika A[1], Alam MS[2], Khan MR[3], Siddika L[4], Sharmin R[5], Nahid A[6], Khan RM[7]

Abstract

Background: *Alopecia areata (AA) is a common autoimmune disease in which autoantigens play an important role in activating T lymphocytes. Vitamin D is associated with various autoimmune diseases and Vitamin D receptors are strongly expressed in hair follicles and their expression in keratinocytes is necessary for the maintenance of the normal hair cycle. Several studies showed that there is an influence of vitamin D on patients with AA.*

Aims and Objectives: *To find out serum 25-Hydroxy vitamin D level in patients with AA and its relationship with severity of the disease in a tertiary care hospital.*

Method: *This cross-sectional study was conducted at the Department of Dermatology and Venereology in Dhaka Medical College Hospital (DMCH), Dhaka, from January 2019 to December 2019. A total of sixty-four subjects were enrolled. Among them thirty-two patients were with clinically diagnosed AA cases (Group A) and thirty-two healthy age and gender matched controls without AA (Group B). Serum 25-Hydroxy vitamin D was analyzed by the automated analyzer. The levels of serum 25-Hydroxy vitamin D were categorized as deficient (<20 ng/ml), insufficient (20 to 29.9 ng/ml) and normal (e"30 ng/ml) and the Severity of Alopecia Tool (SALT) score was used to assess the severity of the disease. p-value <0.05 was taken as significant. Statistical analyses were performed with SPSS version 25.0.*

Results: *The mean age of Group A was 30.56 ± 13.52 years and Group B was 34.97 ± 13.03 years. The mean serum 25-Hydroxy vitamin D level was significantly lower in patients with alopecia areata (13.38± 7.36 ng/mL) as compared to the healthy group (23.16 ± 10.36 ng/mL) (p < 0.0004). Deficient, insufficient and normal Vitamin D levels among Group A vs Group B were (88% vs 44%), (9% vs 41%) and (3% vs 16%) respectively with significant difference (p-value 0.001) between the groups. There was a significant negative correlation between serum 25-Hydroxy vitamin D level and SALT score (r=-.509, p=0.003).*

Conclusions: *This study revealed that the prevalence of serum 25-Hydroxy vitamin D deficiency was significantly higher in alopecia areata group compared to healthy group. There was a significant inverse correlation between its level and alopecia areata disease severity.*

Keywords*: Serum 25-Hydroxy Vitamin D, Alopecia areata, Vitamin D, Severity of Alopecia Tool (SALT).*

DOI: https://doi.org/10.3329/jdmc.v32i2.83430
J Dhaka Med Coll. 2023; 32(2) : 101-106

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Received: *24.01.2023* ***Accepted:*** *28.05.2023*

Introduction

Alopecia areata (AA) is a common nonscarring alopecia which can affect the scalp and/or any hair bearing area of body without any clinical sign of inflammation.[1] There are significant variations in clinical presentation ranging from small well demarcated patches to complete loss of scalp and/or body hair.[2] Nail changes are a common feature of AA, with an average prevalence of 30%. Pitting, trachyonychia, red spotted lunulae, onycholysis, and punctate leukonychia are the reported findings.[3] The prevalence of AA was estimated 0.1 -0.2% and a lifetime risk of 2%.[4] Alopecia areata can begin at any age. Both sexes are equally affected.[5] The histological feature of AA is lymphocyte infiltration, macrophages and langerhans cells around and within affected hair follicles.[6]

Exact etiology is incompletely understood. However, immunological factor is one of the most powerful explanations.[7] The proximal hair follicle constitutes an immune privileged site. This immune privilege is disrupted in alopecia areata.[2] There is an increase in major histocompatibility complex (MHC) I and II molecules and adhesion molecules and correlate with increased leukocyte trafficking into dermis leading to perifollicular inflammation. This peribulbar inflammation adversely affects hair follicle activity resulting in thin dystrophic hair with miniaturization.[8]

Autoimmune etiology has been proposed on the basis of its association with various autoimmune diseases, the presence of autoantibodies, the presence of inflammatory lymphocytes around and within the affected hair follicles, and the ability to promote hair regrowth with the use of immunosuppressive agents.[9] There is increased susceptibility in individuals with HLA DQ3 and increased concordance in monozygotic twins and positive family history.[10] Thus, alopecia areata is considered as a hair follicle-specific autoimmune disease which is triggered by environmental factor in genetically susceptible individual.[8]

Vitamin D is a fat-soluble steroid prohormone mainly produced photochemically in the skin from 7 dehydrocholesterol. Vitamin D consists of two bioequivalent forms: Vitamin D2, also known as ergocalciferol, is obtained from dietary vegetable sources and oral supplements and Vitamin D3, also known as cholecalciferol, is obtained primarily from skin exposure to ultraviolet B (UVB) radiation in sunlight as well as ingestion of food sources.[11]

Vitamin D mediates its effect through vitamin D receptors, which are strongly expressed in the vital structures of hair follicles and its expression is necessary for the maintenance of normal hair cycle.[12] In the immune system, vitamin D suppresses dendritic cell maturation and antigen presentation. If vitamin D level is reduced, regulation of the immune system theoretically can be disrupted possibly by promoting an autoimmune process.[13]

Several studies suggest the role of Vitamin D in pathogenesis of AA and hence a possible role of Vitamin D supplementation in treatment.[1] So, this study was conducted in the Department of Dermatology and Venereology, Dhaka Medical College Hospital, Dhaka to evaluate serum vitamin D level in patients with AA and its relationship with severity of the disease.

Materials and Methods:

This cross-sectional study was conducted in the Department of Dermatology and Venereology, Dhaka Medical College Hospital, Dhaka from January 2019 to December 2019 after taking ethical clearance from Ethical Review Committee of Dhaka Medical College, Dhaka. The study was a hospital-based cross-sectional comparative study involving a series of 32 patients of AA (as Group A) and age and gender matched 32 non-alopecic subjects (as Group B). After fulfilling all inclusion and exclusion criteria, an informed consent was taken from all patients. Patients, who were pregnant and lactating, alcoholic, smoker were excluded. Patients with malignancy, diabetes mellitus, chronic kidney disease, parathyroid disorders, bone metabolic disorders, other autoimmune diseases, and who received therapeutic intervention that might influence vitamin D status including bisphosphonates, systemic corticosteroid, calcium supplements, phototherapy, antitubercular drugs and systemic biologics were also excluded. All

characteristics recorded on a standard proforma. Relevant history was taken regarding present illness, duration of the disease, onset, extension, family history. Then complete dermatological examination was done to ascertain the extent of involvement of the disease. Disease severity of each and every patient were measured by using the severity assessment tools namely the Severity of Alopecia Tool (SALT). The scalp was divided into four areas, namely: Vertex: 40% (0.4) of scalp surface area, Right profile of scalp: 18% (0.18) of scalp surface area, Left profile of scalp: 18% (0.18) of scalp surface area, Posterior aspect of scalp: 24% (0.24) of scalp surface area. Percentage of hair loss in any of these areas was multiplied by the percentage surface area of the scalp in that area. SALT score was the sum of the percentage of hair loss in all the above-mentioned areas. Subgrouping of patients into SALT subclasses was done as follows: Scalp (S): S0, no hair loss; S1, <25% hair loss; S2, 25–49% hair loss; S3, 50–74% hair loss; S4, 75–99% hair loss, and S5, 100% hair loss. Body hair loss was assessed as: B0, no body hair loss; B1, some body hair loss; and B2, 100% body (Excluding scalp) hair loss.

Blood samples were taken from subjects at Department of Biochemistry, BSMMU. Serum 25-hydroxyvitamin D was analyzed by the automated analyzer: Architect Plus ci4100. After collecting all data, association of serum vitamin D level with Alopecia areata was find out by statistical analyses. Statistical analyses were performed with SPSS (statistical package for social science) version 25.0. Continuous parameters were expressed as mean ± SD and com pared with unpaired student's t test or ANOVA test. Categorical parameters were expressed as frequency and percentage and compared by Chi-Square test. Correlation coefficient test was done by Pearson's correlation coefficient test. Statistical significance was set < 0.05 level at 95% confidence interval (CI).

Results:

The mean age of Group A was 30.56 ± 13.52 years and Group B was 34.97 ± 13.03 years. Majority of the study subjects were female both in Group A (72%) and Group B (66%).

Table-I

Comparison of demographic and clinical characteristics of patients and healthy group

Variables	Group A (n=32)	Group B (n= 32)
Age (years)		
Mean ± SD	30.56 ± 13.52 years	34.97 ± 13.03 years
Range	14-65	15-57
Gender		
Female	23 (72%)	21 (66%)
Male	9 (28%)	11 (34%)
Duration of disease		
Mean ± SD	2.09±1.14 (years)	
Range	3 months-7 years	
Pattern of AA		
Single patch	9 (28%)	
Multiple patches	16 (50%)	
Alopecia Totalis	3 (9%)	
Alopecia Universalis	4 (13%)	
Site of involvement		
Scalp	26 (81%)	
Body hair	1 (3%)	
Both Scalp and Body hair	5 (16%)	

Table-II

Disease severity and extension according to SALT scoring (n=32)

SALT	Frequency	Percentage (%)
S1 (<25%)	13	41%
S2 (25-49%)	7	22%
S3 (50-74%)	4	12%
S4 (75-99%)	1	3%
S5 (100%)	7	22%

Table II showed According to SALT scoring severity of AA, maximum 13(41%) patients had severity S1 (<25%), 7 (22%) patients had S2 (25-49%), 4 (12%) patients had S3 (50-74%), 1 (3%) patient had S4 (75-99%) and 7 (22%) patients had S5 (100%).

Table-III

Comparison of serum 25-Hydroxy vitamin D between two groups (N=64)

Serum Vit D level (ng/ml)	Group A(n=32)	Group B(n=32)	p value
Mean	13.38 ± 7.36	23.16 ± 10.36	0.0004*
Range	5.0 – 39.40	7.30 – 61.70	

*Student's t- test

Results were expressed by mean ± SD & percentage.

Table III showed mean of Serum Vit D level in Group A (n=32) is 13.38 ± 7.36 and mean of Serum Vit D level in Group B (n=32) is 23.16 ±10.36 which is statistically highly significant (p value < 0.0004).

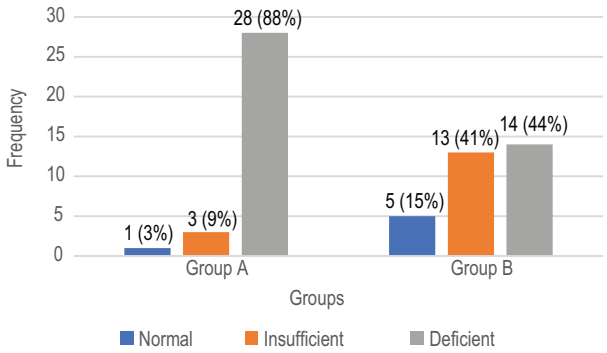

Figure 1: *Comparison of serum vitamin D between two groups (N=64)*

Figure 1 revealed deficient, insufficient and normal Vitamin D level among Group A vs Group B were (88% vs 44%), (9% vs 41%) and (3% vs 16%) respectively with significant difference (p-value 0.001) between the groups.

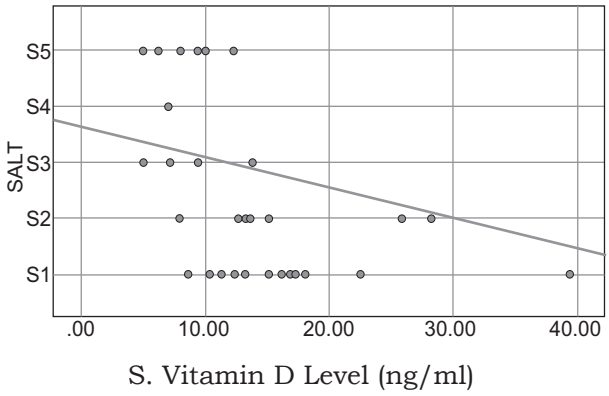

Fig.-2: *Correlation of serum vitamin D level with SALT score. (r=-.509, p=0.003)*

This Scatter diagram showed significant negative correlation (r=-.509, p=0.003) between serum vitamin D level (ng/ml) and SALT score.

Discussion:

In this study the mean age were 30.56 ± 13.52 years for case and 34.97 ± 13.03 years for control. This study included 71.9% female and 28.1% male in case and 65.6% female and 34.4% male in control. Both groups were age gender matched and male: female ratios were 2.5:1 in case and 1.9:1 in control. This result was consistent with the study of Ghafoor and Anwar (2017)[10]. Darwish et al. (2016) also found female predominance in their study.[7]

The present study showed mean duration of the disease is 2.09 ± 1.146 years. Study found that maximum patients 15(46.9%) had multiple alopecic patches followed by single AA patch 8(25.0%). 5(15.6%) patients had alopecia totalis and 4(12.5%) had A. Universalis. Ghafoor and Anwar (2017) in their study found highest patients with multiple pathches 15 (50%) followed by single patch in 6 (20%), a. Totalis in 4 (13.33%) and A. universalis in 2 (6.67%).

Area of highest involvement was scalp 26 (81.3%). Both scalp and body hair loss were involved in 5 (15.6%) and only body hair was involved 1 (3.1%). Dhillon (2013) found scalp to be affected in 38 (76%), beard 5 (10%) and total body hair 7 (14%).[14]

The present study measured the severity of alopecia areata in scalp of 32 patients by SALT scoring. Regarding severity of AA, maximum 13(41%) patients had severity S1(<25%), 7 (22%) patients had S2 (25-49%),4 (12%) patients had S3 (50-74%), 1 (3%) patients had S4 (75-99%) and 7 (22%) patients had S5(100%).Ghafoor and Anwar (2017) found patients 4(13.33%) had S1

grade, 7 (23.33%) in S2 grade, 12 (40%) in S3, 1 (3.33%) in S4, and 6 (20%) cases in S5 grade.[10]

This study showed mean of Serum Vit D3 level in Group A (n=32) is 13.38 ± 7.36 ng/ml and mean of Serum Vit D3 level in Group B (n=32) is 23.16 ±10.36 ng/ml which is statistically highly significant (p value= 0.0004). In their study conducted in southern India, Siddappa, Kumar & Vivekananda (2019) found mean serum vitamin D level was significantly lower in cases as compared to controls (18.90 ± 8.32 vs 28.21 ± 18.32 ng/mL; p < 0.001).[13]

This study result was parallel to Attwa et al. (2016) who performed study on 23 patients with AA and 23 healthy controls to detect their serum 25(OH)D level in Egypt. This was also similar to study made by Bhat et al. (2017).[1] The mean serum 25(OH)D concentration of patients with AA was 16.6 ± 5.9 ng/ml, whereas in control group, the mean concentration was 25.49 ± 1.02. (p < 0.001).[1] On the other hand, Nassiri et al. (2013) and Erpolat et al (2017) differed with this result. They found no statistically significant difference in their study.[4,6] Lin et al. (2019 cited Erpolat et al. 2017) stated that this might be due to the uni-versal tendency toward lower values of 25(OH)D in their geographical area, and they noted that the blood samples were collected only once during the late fall and winter months.[17] Therefore, further studies are needed to confirm the association. There is a seasonal variation in vitamin D level and the effect of vitamin D deficiency on causation of AA seems to be associated mainly through its role in immune system regulation.[10]

This study showed deficient, insufficient and normal Vitamin D3 level among Group A vs Group B were (88% vs 44%), (9% vs 41%) and (3% vs 16%) respectively with significant difference (p-value 0.001) between the groups. In South Asia 80% of apparently healthy population is Vitamin D deficient and up to 40% of the population is severely deficient.[18]. Study showed that women in Bangladesh, were at risk of developing vitamin D deficiency, regardless of different age-groups, lifestyle and clothing.[19]

The study also showed that the mean serum vitamin D level was significantly associated with severity of alopecia areata (p=.041). Mean serum vitamin D level in S1 was 16.32 ± 7.86, S2 was 16.67 ± 7.43, S3 was 9.17 ± 4.33, S4 was 7.0, S5 was 7.98 ± 2.74. No relevant result or discussion was found elsewhere.

The study revealed statistically significant negative correlation (r=-.509, p=0.003) between serum vitamin D3 level (ng/ml) and SALT score. Such inverse correlation between serum vitamin D3 level and SALT score (p <0.05) also found by Siddappa, Kumar & Vivekananda (2018), Cerman et al. (2014), Mahamid et al. (2014), Attwa et al. (2016), Yilmaz et al. (2012), Bhat et al. (2017).[1,12,15,16,20,21] Cerman et al. (2014) reported a significant negative correlation between the degree of AA by (SALT) score and serum 25(OH)D level in AA patients (p <0.001)[20]. Conversely, D'Ovidio et al. (2013) found no correlation between the severity of AA and serum 25(OH)D level.[22] This may be because methodological data e.g. the scoring of AA was not available in this study.

Virtually all immune cells express the VDR, making them susceptible to 1,25(OH)2D3-mediated modulation. As autoimmune diseases are characterized by an overactive immune response, it seems logical that the beneficial effects of vitamin D on autoimmunity are due to effects on the immune system. [23] Promising results were obtained in a few clinical trials but there is still a lack of non-biased large-cohort studies that can sustain the proposed benefits of vitamin D supplementation for optimal immune function.[24]

Limitations:

Small sample size was selected from single tertiary center in Dhaka city, so that the results of the study may not reflect the exact picture of the country.

Conclusion:

Serum vitamin D level in patients with alopecia areata was significantly lower than in participants in the control group. There was a significant inverse correlation between level of serum vitamin D and severity of alopecia areata.

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Characteristics and Outcome at 1 Month of Olfactory Dysfunction in Hospitalized COVID-19 Patients in a Tertiary Care Hospital

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Abstract

Background: *Olfactory dysfunction (OD) is well-established and is a key symptom of COVID-19. Although ample data are available regarding olfactory dysfunction in non-hospitalized COVID-19 patients, there are knowledge gaps about the frequency, severity, and duration of OD in hospitalized COVID-19 patients. So, we conducted the study to determine the outcome of olfactory dysfunction in hospitalized patients with COVID-19.*

Methodology: *This was a hospital-based prospective cohort study conducted in Dhaka Medical College and Hospital. RT-PCR-positive COVID-19 patients who matched the inclusion and exclusion criteria were enrolled in the study. A visual analog scale (VAS, 0-10 cm) assessed the severity of olfactory dysfunction. All the patients were followed up by telephonic interviews on the 10th and 30th day after the onset of olfactory dysfunction to assess the outcome of olfactory dysfunction. Olfactory-specific quality of life (QOL) was assessed in those patients who did not recover olfactory function completely at the 30th day follow-up.*

Results: *We enrolled 277 patients in this study. A total of 90(32%) had olfactory dysfunction. Hyposmia was the most common type of olfactory dysfunction (54.22%), followed by anosmia (40.96%), hyperosmia, and parosmia (2.41%). The Mean age (SD) of the study subjects was 51.8(14.8) years, and the mean age(SD) of the patients with olfactory dysfunction and without olfactory dysfunction was (51.06[10.01]and 52.17[15.34]) years, respectively($p>0.05$). there was no gender discrepancies between the groups (50[60.24%] vs 112[59.89%], $p>0.05$). The majority (53.7%) of the study subjects had severe COVID-19 infection, but olfactory dysfunction was more common among mild COVID-19 patients. In 85.54% of cases, Olfactory dysfunction was associated with taste dysfunction and/or headache. Olfactory dysfunction was completely resolved in 46.99% of cases within 10 days and 87.95% within 30 days. Median (IQR) recovery time from olfactory dysfunction was 14.00 (11.00) days; Recovery time was significantly more in severe COVID-19 patients than in mild COVID-19 patients ($p<0.05$). Ten patients did not recover after 30 days but showed a lower severity of olfactory dysfunction than the 1st survey. The mean (SD) quality of Life (QOL) score in sQOD-NS was 15(4.4), which indicates a higher score reflecting the better olfactory-specific QOL.*

Conclusion: *Olfactory dysfunction was present in about one-third of the hospitalized patients with COVID-19. Most of the patients recovered within 30 days of the onset of dysfunction, suggesting a favorable prognosis.*

Key words: *Olfactory dysfunction; Anosmia; Hyposmia; COVID-19 Outcome.*

DOI: https://doi.org/10.3329/jdmc.v32i2.83432
J Dhaka Med Coll. 2023; 32(2) : 107-116

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Received: *25.01.2023* ***Accepted:*** *28.05.2023*

Introduction

The first cases of the COVID-19 outbreak started in December 2019 in Wuhan City, Hubei Province, China, in patients with complicated pneumonia and quickly spread to the rest of the world.[1] The first case in Bangladesh was detected on 8th March 2020. The most frequent symptoms of COVID-19 are fever, dry cough, sore throat, shortness of breath, fatigue, headache, diarrhea, and conjunctival congestion.[2,3] Initially, olfactory and gustatory dysfunctions were not considered important symptoms of COVID-19. Still, in March 2020, during the pandemic, anecdotal evidence rapidly accumulated from sites around the world that sudden loss of smell (hyposmia) and/or taste (hypogeusia) was also occurring in COVID-19 patients, often without concomitant nasopharyngeal symptoms.[4] After the publication of several studies reporting hyposmia and hypogeusia as frequent symptoms of COVID-19[5], the World Health Organization (WHO) included these symptoms in the case definition.

Major causes of acquired smell loss include upper respiratory tract infection (URTI) by respiratory viruses (adenovirus, rhinovirus, coronavirus, influenza), traumatic brain injury, upper airway inflammation (rhinitis, rhinosinusitis), and neurodegenerative (Parkinson's and Alzheimer's) diseases.[6] It has been suggested that SARS-CoV-2 causes obstructive inflammation of olfactory clefts or targets and damages olfactory epithelium support and stem cells, leading to olfactory disturbances in COVID-19 patients.[7] From March to June 2020, several studies have been conducted on the frequency of loss of smell in many countries and continents. A significant variability has been found (from 5 to 95%) in the incidence of olfactory dysfunction.[8] Variability was also found between hospitalized and non-hospitalized patients. Outpatient COVID-19-positive patients have a higher rate (59-86%) of olfactory dysfunction[5] than hospitalized patients (5-35%).[9,10] There is also a higher frequency of olfactory dysfunction in the European population than in the Indian population.[11] The frequency of olfactory dysfunction in COVID-19 patients in Bangladesh was found to be 38.9%.[12]

As there is variability regarding the frequency of olfactory dysfunction, there is also variability regarding outcomes in COVID-19 patients. Complete olfactory recovery occurred in 51.43% of the patients, and partial recovery occurred in 44.29% of patients on the mean 26th day after the onset of olfactory dysfunction in a group of COVID-19-positive patients[13] (Gorzkowski et al. 2020). Klopfenstein et al.[14] reported that the mean duration of olfactory dysfunction was 8.9±6.3 days (range 1-21 days), and 98% of patients recovered within 28 days after the onset of olfactory dysfunction.

Using either a Visual analog scale (VAS) and/or a disposable olfactory test is recommended for an appropriate and safe quantitative assessment of the loss of smell during COVID-19.[15]

The impact of smell loss as a clinical consequence of COVID-19 has not been adequately addressed. Olfactory dysfunctions have serious health and quality-of-life consequences for patients. Short version Questionnaire for Olfactory Dysfunction Negative Statements (sQOD-NS) is a validated tool to assess olfactory-specific quality of life (QOL).[16]

Information regarding the outcome of olfactory dysfunction in hospitalized COVID-19 patients may be necessary to manage and counsel patients with olfactory dysfunction. So, this study aimed to assess the outcome of olfactory dysfunction in hospitalized patients with COVID-19. This study's findings may help general practitioners, neurologists, and otolaryngologists counsel or reassure patients with olfactory dysfunction in COVID-19.

In this study, we determined the frequency, types, and severity of olfactory dysfunction. We also assessed its duration and reversibility. We assessed olfaction-specific quality of life (QOL) in patients with persistent olfactory dysfunction by sQOD-NS.

Methodology

This was a prospective cohort study conducted in Dhaka Medical College Hospital from January 2021 to December 2021. Before starting this study, the DMCH ethical review committee

(ERC) approved a research protocol. Each patient provided informed written consent (Bengali version).

Sampling technique and Sample size determination:

We employed a consecutive sampling technique to recruit the participants in our study. We used Cochran's formula to calculate the sample size for this study. $n = \frac{z^2 pq}{e^2}$

n = the desired sample size p = 38.7% = 0.387 (prevalence of olfactory dysfunction in COVID-19 in Bangladesh[12]. At 5% level of significance or 95% confidence level, Z = 1.96 and for 5% precision, e = 0.05, n=187. Considering 20% dropout, we consider 225 patients adequate.

Participants:

In this study, we included COVID-19 patients who were admitted to the hospital, had a positive RT-PCR test, were over 18 years old, and were of both gender. We excluded patients who had pre-existing olfactory dysfunction, as well as those with a history of nasal surgery, known allergic rhinitis, sinusitis, nasal polyposis, major head injuries, or any chronic nasal diseases. Additionally, we excluded patients with well-known neurodegenerative diseases, such as Parkinson's disease or dementia, patients experiencing severe respiratory distress who were using high-flow nasal cannula (HFNC), critical COVID-19 patients, and patients with an impaired level of consciousness

Operational definitions:

In this study, COVID-19 patients were defined according to WHO guidelines[14], and the clinical classification of COVID-19 was established as a National Guideline on the Clinical Management of COVID-19, 2020.[18]

Olfactory dysfunction types[19] include i) Hyposmia- reduced ability to detect odors; ii) Anosmia- complete inability to detect odors; iii) Hyperosmia- a heightened sense of odor; iv) Parosmia- change in the normal perception of odors and v) Phantosmia- the sensation of an odor that is not present.

Visual analogue scale (VAS, 0-10 cm)[20]: In this study, a 10 cm analogue scale was used, and quantification included i) Complete smell loss (VAS = 10 cm), ii) Severe smell loss (VAS = 8-9 cm), iii) Moderate smell loss (VAS = 4-7 cm), iv) Mild smell loss (VAS = 1-3 cm) and v) Normal smell (VAS = 0 cm)

Outcome of olfactory dysfunction: In this study, Recovery meant Recovery from olfactory dysfunction, either partial or complete, at 30 days. **Quality of life was assessed with** an Olfactory-specific quality of life (QOL) score by sQOD-NS[21].

Study procedure:

This prospective hospital-based study was conducted in Dhaka Medical College Hospital, Dhaka for 12 months period. A total of 277 patients of both genders and age 18 years or more, admitted in Dhaka Medical College Hospital and diagnosed as COVID-19 on the basis of positive RT-PCR for SARS-Cov-2 and had olfactory dysfunction or not was included in this study. Patients with pre-existing olfactory dysfunction, previous history of nasal surgery, known case of allergic rhinitis, sinusitis, nasal polyposis, major head injury or any chronic nasal disease, patients with neurodegenerative diseases or dementia, patients with severe respiratory distress who is on HFNC, critical COVID-19 patients and patients with impaired level of consciousness were excluded. An informed written consent was taken from all participants, after describing the aim, purpose and procedure of the study. A structured questionnaire was completed by the investigator from answers of the participants, with the help of the relatives, to obtain information on demographic characteristics (e.g., age, gender) and olfactory dysfunction related questions (e.g., presence, types, onset, duration). Severity of olfactory loss was assessed by visual analogue scale (VAS, 0-10 cm). Strict safety measures (proper distancing and appropriate PPE) were ensured to prevent transmission of infection during data collection. All the patients with olfactory dysfunction were followed up by telephonic interview at 10th and 30th day after the onset of olfactory dysfunction to assess the outcome (recovery from olfactory dysfunction

either partial or complete). Olfactory-specific quality of life (QOL) was assessed by short version Questionnaire of Olfactory Disorders-Negative Statements (sQOD-NS) in those patients who did not recover completely at 30th day follow-up. Patients without olfactory dysfunction were inquired about new development of olfactory dysfunction by telephonic interview after 7 days and if olfactory dysfunction developed, they were followed up in the same way as mentioned previously. All information were recorded in a data collection form consisting of relevant questionnaire.

Data analysis:

All data was collected, tabulated and analyzed statistically using a personal computer and the Statistical Package for Social Science (SPSS) version 26.0. (Chicago, Illinois, USA). Each question was coded with a number and all alternative responses for each question was registered to enable a statistic analysis. The data were systematically described, summarized, and presented through descriptive statistics. The normality of the continuous variables was evaluated through the Shapiro-Wilk test. Data with normal distribution, continuous variables was statistically described in terms of mean (SD). Qualitative or categorical variables was described as frequencies and proportions. Non-normally distributed data was expressed as median (IQR). In necessary cases, student's *t* test or chi-square test or non-parametric test was used to establish the association. Statistical significance was defined as P value ≤0.05 and confidence interval set at 95% level.

Results:

This prospective cohort study was conducted in the Department of Neurology, Dhaka Medical College and Hospital among RT-PCR positive hospitalized COVID-19 patients between January 2021 to December 2021 to assess the outcome of olfactory dysfunction. We included 277 patients in this study, 90 patients had olfactory dysfunction and 187 had no olfactory dysfunction.

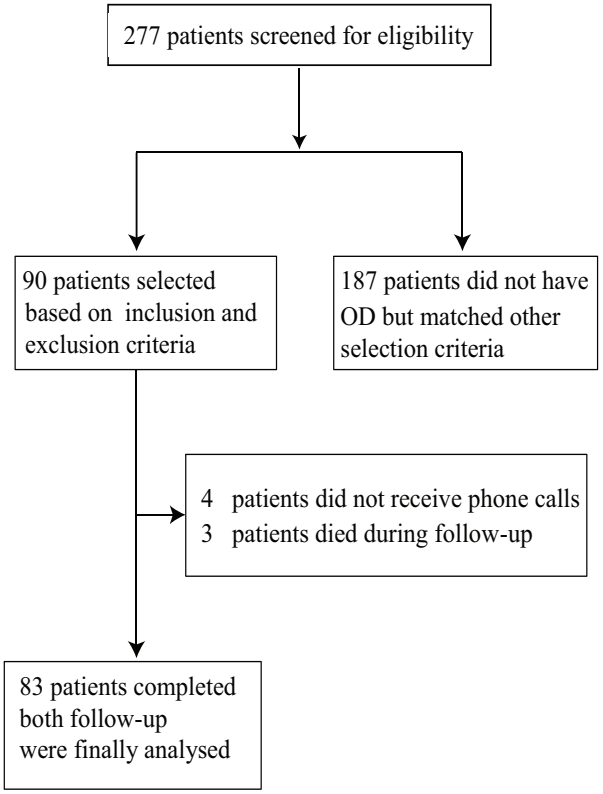

Fig.-1: *Patient selection for this observational study.*

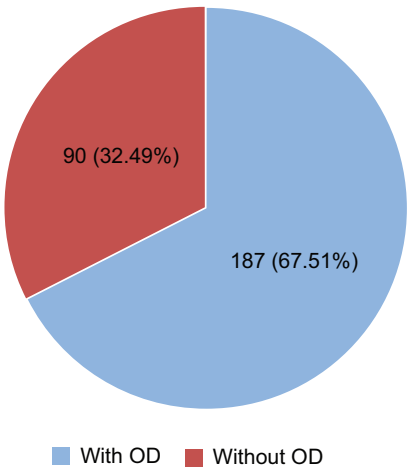

Fig.-2: *Frequency of olfactory dysfunction*

Figure 2 shows frequency of olfactory dysfunction. About one third of the RT PCR COVID-19 patients had olfactory dysfunction.

Table I

Distribution of patients based on demographic characteristics (N=270)

Variable	Olfactory dysfunction present (n=83)	Olfactory dysfunction absent (n=187)	p value
Age group(yrs)			
18-30	7	19	
31-40	14	28	
41-50	22	37	0.3^{ns**}
51-60	19	46	
61-70	16	39	
>70	5	18	
(Mean±SD)	51.06±10.01	52.17±15.34	0.57^{ns*}
Gender			
Male	50(60.24%)	112(59.89%)	0.53^{ns**}
Female	33(39.76%)	75 (40.11%)	

^{ns}= non-significant, $^{*=}$ obtained by unpaired t test, $^{**=}$ obtained by Chi square test

Table I shows distribution of patients based on demographic characteristics. The mean age of the patients with olfactory dysfunction was 51.06±10.01 (SD) years and and without olfactory dysfunction was 52.17±15.34 (SD) years. There was no significant difference in mean age between two groups (p=0.57). Regarding gender, 60.24% male and 39.76% female in patients with olfactory dysfunction and 59.89% male and 40.11% female in patients without olfactory dysfunction. Threre is no significant difference between them regarding gender (p=0.53).

Table II

Distribution of patients according to severity of COVID-19 infection (N=270)

Severity of COVID-19	Olfactory dysfunction present (n=83)	Olfactory dysfunction absent (n=187)	p value
Mild	25 (30.12%)	41 (21.92%)	
Moderate	23 (27.71%)	36 (19.25%)	0.04^{s*}
Severe	35 (42.17%)	110 (58.82%)	

^{s}=significant, *=p value obtained by chi square test

Table II shows distribution of patients according to severity of COVID-19 infection. Olfactory dysfunction was higher among the severe COVID-19 cases (42%) . Severity of COVID-19 was significantly associated with presence of olfactory dysfunction (p=0.04).

Table III

Frequency and types of olfactory dysfunction (n=83)

Olfactory dysfunction types	N	%
Anosmia	34	40.96
Hyposmia	45	54.22
Hyperosmia	2	2.41
Parosmia	2	2.41
Phantosmia	0	0

Table III shows the frequency and types of olfactory dysfunction. Hyposmia was the most common olfactory dysfunction (54.22%) followed by anosmia (40.96).

Table IV

Distribution of patients based on onset of olfactory dysfunction (n=83)

Onset	N	%
Before other COVID symptoms	14	16.87
Concomitant with other COVID symptoms	21	25.30
After the onset of other COVID symptoms	48	57.83

Table IV shows the distribution of patients based on onset of olfactory dysfunction. In most of the cases (57.83%) olfactory dysfunction began after the onset of other COVID symptoms.

Table V

Associated taste dysfunction and headache in patients with olfactory dysfunction (n=83)

	N	%
Headache	2	2.41
Taste dysfunction	45	54.21
Both	24	28.92
None	12	14.46

Table V shows associated taste dysfunction and headache in patients with olfactory dysfunction. Olfactory dysfunction was associated with taste dysfunction in 54.21% of the cases and both taste & headache in 28.92% of cases.

Table VI

Severity of olfactory dysfunction at first survey (n=79)*

Severity	N	%
Complete smell loss (VAS 10)	10	12.65
Severe smell loss (VAS 8-9)	19	24.05
Moderate smell loss(VAS 4-7)	27	34.18
Mild smell loss(VAS 1-3)	14	17.73
Normal smell(VAS 0)	9	11.39

*= 2 patient with hyperosmia and 2 patient with parosmia were not assessed by VAS.

Table VI shows the severity of olfactory dysfunction at 1st survey. Complete smell loss was present only in 12.82% of cases at first survey. Most of the patient had moderate smell loss at the time of first survey (34.62%). Normal smell was present in 8 cases (10.25%) of cases.

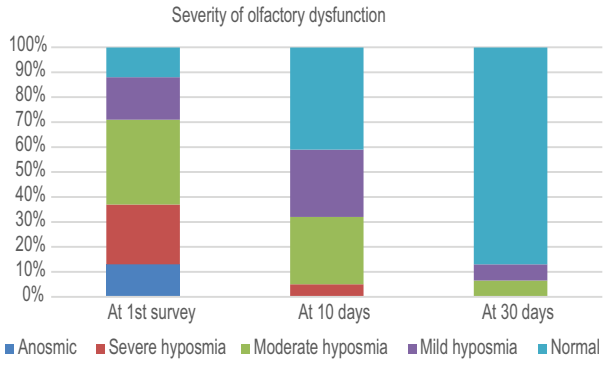

Fig.-3: *Olfactory dysfunction severity sub-group analysis at 1st survey, at 10th day and 30th day after onset of olfactory dysfunction*

Figure 3 shows olfactory dysfunction severity sub-group analysis at different survey periods. There is progressive decrease in the severity of olfactory dysfunction. At 30th day majory of the subjects had normal smell. Only few patients had milder smell loss at the end of the 30 days.

Table VII

Status of smell change at 10th and 30th day of onset of olfactory dysfunction (n=83)

Status	At 10th day		At 30th day	
	N	%	N	%
Completely resolved	39	46.99	73	87.95
Partially resolved	44	53.01	10	12.05
No change	0	0	0	0
Deteriorated	0	0	0	0

Table VII shows status of smell change at 10th and 30th day of onset of olfactory dysfunction. At 10th day 46.99% patient recovered completely from olfactory dysfunction and olfactory dysfunction was partially resolved in 53.01% of cases. At 30th day 87.95% of patients recovered completely from olfactory dysfunction and 12.05% of the cases was partially improved.

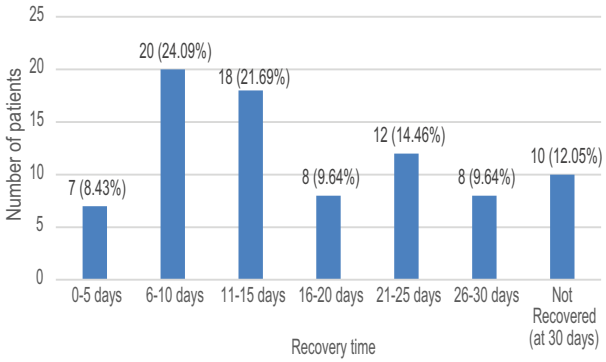

Figure 3: *Recovery time for patients with olfactory dysfunction (n=83, including 10 patients who did not recover after 30 days).*

Figure 3 shows recovery time for patients with olfactory dysfunction. Twenty patient (24.09%) patients recover between 6-10 days time period and 18 (21.69%) patient recover between 11-15 days time period. About 54% of the patients recovered within first 15 days. Ten patient (12.05%) did not recover at 30th day after onset of olfactory dysfunction.

Table VIII

Recovery time for patients with olfactory dysfunction (n=73)

	Median (IQR)	Min-max
Recovery time (days)	14 (10-21)	3-30

Table VIII shows median recovery time for patients with olfactory dysfunction who recovered within 30 days. Median (IQR) recovery time was 14 (10-21) days.

Table IX

Recovery time from olfactory dysfunction based on age and gender of the patients (n=73)

Variables	N	Recovery time Median (IQR) days	P value
Age group			
18-30	7	14 (5)	
31-40	9	15 (12)	
41-50	19	14 (17)	0.806^{ns*}
51-60	18	14 (6.25)	
61-70	16	15 (18)	
>70	4	21 (15.25)	
Gender			
Male	42	14.50 (15)	0.61^{ns**}
Female	31	14 (10)	

^{ns}= non-significant, *= p value obtained by Kruskal-Wallis test, **= p value obtained by Mann-Whitney U test

Table IX shows recovery time from olfactory dysfunction based on age and gender of the patient. Median recovery time was not significantly related to age and gender of the study population (p>0.05).

Table X

Recovery time based on type of olfactory dysfunction and severity of COVID-19

	N	Recovery time Median (IQR) Days	P value
Types of smell loss			
Anosmia	25	20 (15)	
Hyposmia	44	13 (8.75)	0.04^{s*}
Severity of COVID-19			
Mild	24	12 (8)	
Moderate	21	10 (16)	0.004^{s**}
Severe	28	20 (11)	

$^{s=}$ significant, $^{*=}$ p value obtained from Mann-Whitney U test. **= p value obtained from independent
Samples Kruskal-wallis test

Table X shows recovery time based on type of olfactory dysfunction and and severity of COVID-19 infection. Anosmic patients had significantly longer median (IQR) recovery time than hyposmic patients (p=0.04). Patients with severe COVID-19 infection had singnificantly longer median (IQR) recovery time (p=0.004).

Table XI

Demographic and clinical characteristics of subjects who did not recover olfactory dysfunction within 30 days (n=10)

	N	%
Gender		
Male	8	80
Female	2	20
Severity of OD		
Severe (VAS 8-9)	0	0
Moderate (VAS 4-7)	5	50
Mild (VAS 1-3)	5	50
Severity of COVID-19		
Mild	1	10
Moderate	2	20
Severe	7	70

Table XI shows demographic and clinical characteristics of patients who did not recover from olfactory dysfunction at 30 days. Majory was male patient (80%). Olfactory dysfunction was mild to moderate severity in all patients at 30th day of onset of dysfunction. Majoriry of the patient suffered from severe COVID-19 infection (70%).

Table XII

sQOD-NS score in patients with persistent olfactory dysfunction (n=10)

Serial no.	sQOD-NS score	Mean±SD
1	15	
2	18	
3	14	
4	17	
5	13	15±2.05
6	15	
7	14	
8	14	
9	13	
10	18	

Table XII shows sQOD-NS score in patients with persistant olfactory dysfunction at 30th day. Mean sQOD-NS score was 15±2.05 (SD).

Discussion

In this study one third patient had olfactory dysfunction. Hyposmia was the most common type of olfactory dysfunction. The olfactory dysfunction was higher among the severe COVID 19 cases. Olfactory dysfunction was completely resolved within 30 days. Median (IQR) recovery time was two weeks.

Mean age of the study subjects was 51.83±14.76 (SD) years and there was no significant difference in mean age of patients with and without olfactory dysfunction. In a hospital-based study Jalessi et al.[20] found almost similar findings. Study conducted by others[21,22] and most of the other studies took non-hospitalized patients and olfactory dysfunction was more common in younger patients. Younger patients are less likely to suffer from severe COVID-19 infection and less likely to be admitted into hospital. Our study was a hospital-based study and the proportion of younger patient was less. This may explain the lack of association of age with olfactory dysfunction in our study.

Regarding gender 60% of the study subjects were male and 40% were female. Similar gender distribution was found in the study conducted by Jalessi et al.[20] on hospitalized patients. Gender was not significantly associated with presence olfactory dysfunction in their study. Similar finding was found in our study. Association of female gender with olfactory dysfunction was found in other studies, but most of the studies were on outdoor COVID-19 patients. Normally females are less commonly and less severely affected by COVID-19 and less hospitalized. This can explain our study findings.

Majority of the study subjects were severe COVID-19 patients. Severity of COVID-19 infection was significantly associated with presence of olfactory dysfunction being higher among the severe COVID-19 cases. Similar study findings found in a study conducted by Rajos-Lechuga et al.[23] where the frequency of olfactory dysfunction was higher in mild COVID-19 patients.

In our study one-third patients had olfactory dysfunction and hyposmia was the commonest type. Study of Jalessi et al. [20] showed frequency of olfactory dysfunction in hospitalized patients was 23.91%, hyposmia and anosmia was found 59.1% and 40.9% cases respectively. Other studies found diverse findings regarding frequency of olfactory dysfunction, ranging from 5-95% depending upon specific methodology, assessment technique and study population.

Olfactory dysfunction started in 57.83% cases after the onset of other symptoms of COVID-19. Gorzkowski et al.[13] found that in 77.86% of the cases olfactory dysfunction occurred after the onset of other symptoms. Olfactory dysfunction in 85.54% cases was associated with taste dysfunction and/or headache. It can be explained by the fact that both are part of chemosensory system so affection of one system may affect other system by same mechanisms.

Regarding recovery from olfactory dysfunction in this study 46.99% of cases recovered within 10 days and 87.95% within 30 days. Median (IQR) recovery time from olfactory dysfunction was 14 (10-21) days. In a prospective study Martin-Sanz et al.[24] found that 85.4% of the patients recovers from olfactory dysfunction within 15 days. Another study reported mean duration of olfactory dysfunction was 10±6 (SD) days (range 3-31) in patients who completely recovered from olfactory dysfunction[24] Recovery time was significantly more in anosmic patient than hyposmic patients in our study. Study conducted by Rojas-Lechuga et al.[23] found recovery time was more in severe olfactory dysfunction than milder form of olfactory dysfunction. In our study recovery time was significantly more in severe COVID-19 patients than mild COVID-19 patients and also majority of the patients who did not recover at 30th day were severe COVID-19 patients. These findings might indicate that the pathogenesis of olfactory dysfunction in severe COVID-19 patient may be different from that of mild cases. Age and gender was not significantly associated with recovery from olfactory dysfunction in our study.

Ten (12.05%) patient did not recover after 30 days but they showed lower severity of olfactory dysfunction than the 1st survey. In the study of Paderno et al.[26s] a total of 20 (16%) subjects reported ongoing olfactory dysfunction at the end of follow-up, of which 80% reported partial improvements.

Mean quality of Life (QOL) score in sQOD-NS was 15±2.05 (SD) in patients who did not recover from olfactory dysfunction after 30 days, which indicates higher score reflecting the better olfactory specific QOL.

Objective olfactory testing and psychophysical olfactory testing were not conducted in this study. Long-term follow-up for patients with persistent olfactory dysfunction was only carried out for up to 30 days. The final two follow-ups were conducted through telephone interviews, which have limitations regarding proper assessment. Additionally, there was a possibility of recall bias.

Conclusion

Olfactory dysfunction was present in about one-third of the hospitalized patient with COVID-19 and hyposmia was the most common type. Olfactory dysfunction was most commonly associated with taste dysfunction. Most of the patients recovered within 30 days of onset of dysfunction suggesting favorable prognosis.

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Demographic and Clinical Characteristics of Children with Growing Pains

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Abstract

Background: *Growing pains is the most common benign unexplained limb pain in childhood that tends to self-limit once the child reaches adolescence. The present study aimed to get the details knowledge and compare different demographic and clinical characteristics of growing pains (GP).*

Methods: *This cross-sectional study was conducted from August 2021 to September 2022 at National Centre for Control of Rheumatic Fever and Heart Diseases, Dhaka, Bangladesh. Children of 3-12 years irrespective of sex with unexplained limb pain suspected of growing pains were included in the study. Suspicion of growing pains was based on inclusion criteria and exclusion criteria from the definition of Peterson. By collaboration of clinical history, detailed physical examination, result of relevant laboratory and radiological tests confirmatory diagnosis was made.*

Findings: *Among 220 children with unexplained limb pain 73.2% were diagnosed clinically as growing pains. Boys were predominant (52.2%) among children with GP; 60.9% of them were between 5 to 8 years and the mean age was 7.05±2.32 years. The pain was mostly bilateral and calf muscles were the most common sites. Pain was more frequent at night and half of the children complained about pain occurring several times a week. Massaging was the most effective measure followed by oral anti-inflammatory analgesics for pain relieving. The pain was associated with daytime over-activity and a history of GP among siblings.*

Conclusion: *Growing pains was diagnosed among three-fourths of children with unexplained limb pain. Daytime over-activity, obesity, and a positive family history may be the potential risk factors. Demographic and clinical characteristics of growing pains in the Bangladeshi paediatric population were typical as reported in other studies.*

Key words*: Growing pains, children, unexplained limb pain.*

DOI: https://doi.org/10.3329/jdmc.v32i2.83433
J Dhaka Med Coll. 2023; 32(2) : 117-123

Introduction

Growing pains (GP), the most common form of nonspecific, recurrent leg pain syndrome of early childhood, was first described by French physician Marcel Duchamp in medical literature in 1823.[1] Growing pains is one of the most frequent causes of paediatric outpatient visits. It is considered to be a normal occurrence in about 25% to 40% of children with no organic pathology.[2,3] Worldwide the prevalence of growing pains is reported with a wide range estimating from 2.6 to 49.4%.[4] A recent study

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Received: 20.02.2023 ***Accepted:*** 23.06.2023

established the prevalence of growing pains in children aged four to six years as 37%.[3] A study done in Bangladesh shows that the prevalence of growing pains is 19% among school-going children, whereas, among patients of unexplained limb pain, 75% were diagnosed as GP here.[5,6] This variation and discrepancy between the prevalence is mainly due to different and unspecified sample sizes, geographical areas, age ranges, and different types of objective diagnostic criteria adopted in different studies.[5]

Growing pains is confined to childhood; it is usually self-limiting and almost always benign in nature.[7] It does not progress to organic disease and usually resolves by adolescence.[4] GP mainly affects children aged 4-12 years and is most prevalent in those aged 4-6 years.[8] It is typically non-articular, intermittent, bilateral and not associated with limited mobility. It is located in the muscles and predominantly affects the anterior thighs, calves, shins or backs of knees.[9] Pain can be precipitated by exercise and lasts from minutes to hours. GP more often happens at night or evening, but almost always it resolves by morning. The hallmark of growing pains is that it always affects both legs and is gone in the morning.[10] It may sometimes be so severe that can make the kid cry and parents of children may often complain about the association of episodes of growing pains with periods of increased physical activity.[9,10] Frequent painful episodes usually have an important impact on the daily activities of the children and their families.[2]

Correct diagnosis of growing pains requires a careful history and thorough physical examination. Currently, the diagnosis is based only on typical clinical symptoms and exclusion criteria. Its diagnosis remains mainly clinical, based on the criteria described by Peterson; comprising bilateral, non-articular, intermittent pain in lower limbs, characteristically occurring in the evening.[12,13] Treatment is provided through muscle stretching as well as massaging the affected sites or using analgesics.[14,15] Management also focuses on reassurance, education, and healthy sleep hygiene.[16]

In Bangladesh, growing pains is quite common among paediatric population. Being a specialized center for rheumatic fever National Centre for Control of Rheumatic Fever and Heart Diseases (NCCRF&HD) deals with many patients with nonspecific unexplained limb pain. Saha et al reported that 75% of the patient with nonspecific pain in this center was diagnosed clinically as growing pains.[17] Therefore, the present study was conducted to get the details about the demographic and clinical characteristics of growing pains among children of Bangladesh. So that it will increase awareness among the parents and also help the physicians to better manage this kind of patient.

Materials and Methods

This cross-sectional study was conducted at National Centre for Control of Rheumatic Fever & Heart Diseases, Dhaka from August 2021 to September 2022. During this study period, children of 3-12 years irrespective of sex with unexplained limb pain suspected of growing pains attending the outpatient departments of NCCRF&HD were enrolled in the study.

Suspicion of growing pains was based on the inclusion criteria and exclusion criteria according to the definition of growing pains and modified after Peterson.[12,13] Inclusion criteria were children having intermittent, non-articular pain in limbs that generally occurred late in the day or at night. Exclusion criteria were (1) children having persistent pain, unilateral, increasingly intense pain at night that will still present the following morning and joint pain, (2) children having organic causes of pain or signs of inflammation such as local tenderness or swelling, (3) underlying illnesses such as rickets, malnutrition, rheumatologic disorders, celiac disease or other systemic illness. Purposive sampling was used as per inclusions and exclusion criteria.

Paediatric patients with non-specific musculoskeletal pain in limbs suspected of growing pains were enrolled in this study. Specialist physicians attended the patients; clinical history was taken; detailed and

thorough physical examination of the different systems was done and necessary laboratory investigations and radiological tests were done to diagnose growing pains. By collaboration of clinical history, physical examination, and result of the laboratory tests a confirmatory diagnosis was made.

Venous blood sample was collected for laboratory investigations. Complete blood count (CBC) was done in automated cell counter machine (ERBA Lyse, Germany) and ESR was performed in an automated ESR machine (VES mtric 20). Biochemical tests were done in an automated analyzer machine (ERBA Automated XL 200).

Pain severity was evaluated using Visual analog scale (VAS) which is a pain rating linear scale first used by Hayes and Patterson in 1921.[18] Number of centimeters marked was recorded as a score from 0 to 10: no pain= 0, moderate pain= 5, and severe pain intense enough to make the child cry= 10. Children and their families were taught in detail how to use VAS. Children were asked to mark the level of pain they experienced during the most recent attack.

Baseline information was collected from the patient after exploration of different complaints. Data were collected using a preformed data collection form and all information regarding clinical features was recorded.

All the relevant collected data were compiled on a master chart first and then statistical analysis was done using Microsoft Excel program.

Results

This study included 220 children with unexplained limb pain; among them, 161(73.2%) were diagnosed as growing pains and 59(26.8%) children had diseases other than GP. Juvenile Fibromyalgia syndrome was found in 11(5%), 8(3.6%) were Juvenile chronic arthritis and possible rheumatic fever each. Legg Calve Perthes disease and transient synovitis of hip were diagnosed in 5(2.3%) children. (Table I)

Table I

Diagnosis of unexplained limb pain (n=220).

Diagnosed diseases	Number	Percentage
Growing pains	161	73.2
Juvenile Fibromyalgia syndrome	11	5.0
Juvenile chronic arthritis	8	3.6
Possible rheumatic fever	8	3.6
Legg Calve Perthes disease	5	2.3
Transient synovitis of hip	5	2.3
Fracture	4	1.8
Accidents and sports injuries	4	1.8
Pronated feet	3	1.4
Flat foot	2	0.9
Osgood Schlatter disease	2	0.9
Undiagnosed	7	3.2
Total	220	100.0

A total of 161 children were diagnosed clinically as growing pains; among which boys were predominant (84 boys/ 77 girls); 52.2% children with GP were boys. Sixty percent of children with GP were between 5 to 8 years with a maximum 54(33.5%) in 5-6 years and 44(27.3%) in 7-8 years age group. The mean (mean ±SD) age of the study population was 7.05±2.32 years (range 3-12 years). (Figure 1).

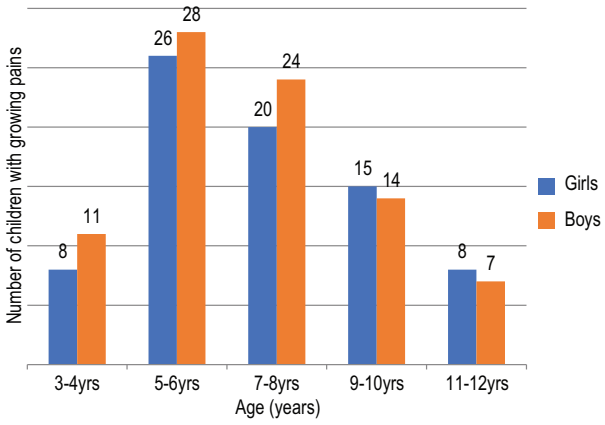

Figure 1: *Age and sex distribution of children with growing pains (n=161)*

Regarding the location of pain, 81(50.3%) children complained about pain over calf muscles followed by pain felt in popliteal regions 34(21.1%), over shins 23(14.3%) and front of

Table II

Clinical characteristics of growing pains (n=161).

Characteristics of pain	Frequency	Percentage
Site of pain		
Calf muscles	81	50.3
Popliteal	34	21.1
Shin	23	14.3
Front of thighs	21	13.0
Upper limbs	11	6.8
Joints	7	4.3
Foot	3	1.9
Timing of pain		
Night	108	67.1
Evening	47	29.2
Afternoon	6	3.7
Frequency of painful episodes		
Daily	54	33.5
Weekly	79	49.1
Monthly	23	14.3
3 monthly	5	3.1
Intensity of pain		
Mild	24	14.9
Moderate	96	59.6
Severe	41	25.5
Total duration of disease		
≤6 months	13	8.1
7-12 months	103	64.0
> I year	45	28.0
Duration of persistence of pain		
<30 minutes	51	31.7
30-60 minutes	61	37.9
>1 hour	49	30.4
Therapeutic modalities adopted		
Massaging	136	84.5
Oral anti-inflammatory analgesics	129	80.1
Warm compression	55	34.2
Rest	30	18.6
Stretching exercise	21	13.0
Topical analgesics	19	11.8
Application of bandage	12	7.5
Application of ice	9	5.6

thighs 21(13%). There was also overlapping of sites in some cases. Pain was more frequent at night time (in 67.1% children) and 29.1% experienced pain during evening. Painful episodes were experienced daily in 54(33.5%) children and 79(49.1%) complained about pain occurring several times a week. Intensity of pain was moderate in 96(59.6%) children whereas pain was severe enough to make the child cry in 41(25.5%) cases. Duration of the disease was 7-12 months in 103(64%) children followed by duration of more than one year in 45(28%). Painful episodes persisted for 30-60 minutes in 61(37.9%) children and duration was less than 30 minutes and more than one hour in 51(31.7%) and 49(30.4%) cases respectively. Massaging the affected site was the most effective measure adopted by 136(84.5%) for pain relieving followed by medication with oral anti-inflammatory analgesics 129(80.1%). Warm compression (34.2%), rest (18.6%), stretching exercise (13%), and application of topical analgesics (11.8%) were also adopted by the guardians (Table II).

Pain was associated with increased day-time physical activity among 63(39.1%) children and 14(8.7%) children were obese. History of unexplained limb pain or GP among siblings was positive in 39(24.2%) cases. Restlessness, headache, and abdominal pain were commonly associated problems occurring in 16(9.9%), 14(8.7%) and 5(3.1%) children respectively. Pain hampered the daily activities of 113(70.2%) patients with GP. Guardians complained that pain caused problems in sleep in 65(40.4%) children; normal schooling and sports were hampered in 29(18%) and 15(9.3%) children respectively (Table III).

Table III

Association of growing pains with other factors

Relationship with	Frequency	Percentage
other factors		
Obesity (BMI ≥95th centile)	14	8.7
Over-activity	63	39.1
History among siblings	39	24.2
Associated problems (n=35)		
Restlessness	16	9.9
Headache	14	8.7
Abdominal pain	5	3.1
Pain hampering activities (n=113)		
Sleep	65	40.4
Schooling	29	18.0
Sports	15	9.3
Feeding	4	2.5

BMI- Body mass index

Discussion

Growing pains was a frequent presenting complaint in paediatric outpatient departments in our study. Majority of the children with unexplained limb pain were diagnosed as growing pains and their demographic and clinical characteristics mostly correlated with reports of other studies.

Our study included 220 children with unexplained limb pain among whom about three-fourths (73.2%) were diagnosed as GP. This type of high frequency of growing pains in children with unexplained limb pain was also observed by Yousuf et al and Saha et al in Bangladesh and the frequency was even higher reported by Liao et al in Taiwan.[6,17,19] However, clinicians should be cautious in differentiating GP from other chronic musculoskeletal pain.

Growing pains mostly occurs in children between the ages of 3-12 years and the peak of incidence is found at 8-12 years.[10] In our study, one-third of children with GP were between 5 to 6 years of age and about 80% of children were between 5-10 years. The mean age of the study population was 7.05±2.32 years. There was a predominance of boys over girls (84/77). This finding correlates with the report of Haque et al, Liao et al and Li et al but is in contrast to girls' predominance reported by Saha et al, Yousuf et al and Asadi-Pooya et al.[5,6,17,19-21] Sex ratio may vary between studies due to the difference between the age range of the study population, and also lack the diagnostic criteria of GP adopted by different authors. In our settings, social background may also be a factor for male predominance where boys sometimes receive more attention regarding treatment seeking than girls in the family.

Pain was found bilateral in most of the cases. Majority of the children complained about pain over calf muscles; the other common sites were popliteal regions, over shins and front of thighs. This finding regarding the sites of pain is consistent with the reports of studies done in Bangladesh and other regions.[5,6,21] Pain intensity was assessed by VAS whenever possible from children who have adequate cognitive and physical development for understanding it or as complained by the attending guardians. Pain intensity was moderate in about sixty percent of children but in more than one-fourth of children, it was severe enough to make them cry in pain.

Among the therapeutic modalities adopted by the parents massaging the affected site and use of oral analgesics like acetaminophen or non-steroidal anti-inflammatory drugs (NSAIDs) were the most common ones. Different studies showed that massage was the most common method (66.6%-94%) for relieving pain which is consistent with the findings of our study where four out of five children needed this intervention.[5,6,21-23] Both oral and topical medication usage increased in the present study compared to previous studies in Bangladesh which mentioned that 52-57% of children used oral medication to relieve their pain.[5,24] The availability of these 'over-the-counter' drugs may be a logical reason behind this. On many occasions, the medications were advised by the guardians themselves and some were prescribed by local physicians. In about half of the patient massage and analgesics were used in combination.

About forty percent of parents reported that there were episodes of pain on the days of increased physical activities or sports. This finding signifies the theory that growing pains may represent local overuse syndrome leading to bone fatigue.[25] Normal daily activities were hampered by pain to some extent in about seventy percent of the study population especially in boys. Most guardians complained that pain caused problems in sleep and schooling of the children as they could not rise early to attend school in time and also learning time was hampered due to pain occurring at evening hours. Night-time feeding was found difficult occasionally in some children during painful episodes. The same type of disturbance in daily activities was reported in a study among school children by Haque et al in Bangladesh.[5] Findings of this study support that obesity, over-activity, and positive family history may be possible risk factors for GP in children.

Conclusion

Growing pains was the most common disease diagnosed among 73% of children with

unexplained limb pain. It was found prevalent in children of 4-8 years and more in boys. GP was mostly bilateral and pain felt over calf muscles. Daytime over-activity, obesity and positive family history may be the potential risk factors. Other demographic and clinical characteristics found in our study had similarities with the reports of other authors.

Acknowledgment
We thankfully acknowledge NCCRF&HD for providing data collection and entire laboratory facilities.

Ethical Consideration
The protocol of this study was approved by the Ethical Review Committee of NCCRF&HD. Informed written consent was taken from authorized legal guardian of each child. Anonymity of patients and confidentiality of information were maintained strictly.

Funding for the work
No financial support was taken for this study.

Conflict of interest
We do not have any conflicts of interest.

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Maternal Outcome of Admitted Obstetric Patient in Intensive Care Unit of Dhaka Medical College Hospital, Bangladesh

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Abstract

Background: *The obstetric patient may suffer with any surgical/ medical condition necessitating intensive care unit (ICU) admission. When admission ctiteria is fulfilled then early admission to Intensive Care Unit can reduce the maternal mortality.*

Aim: *To observe the causes of Intensive Care Unit admissions, interventions, complications and maternal outcome.*

Materials and Methods: The study was a prospective longitudinal study conducted in the ICU of Dhaka medical college hospital Dhaka Bangladesh. The study period was 01/05/ 2019 to 30/04/2020. All the patient who had obstetric related complication were enrolled in this study. Data was collected from patient, patient's attendants, patient's clinical parameter and hospital documents (history sheet, investigation sheet and treatment sheet) and written in the pre-formed data sheet. The information obtained was type of admission, antenatal or postpartum, age, parity, obstetric status, primary diagnosis, associated medical and surgical condition, referral or inpatient shift to ICU, reason for ICU admission, mode of delivery, details of supportive interventions, complications.

Results: *The total admissions to the ICU were 272 obstetric patients. The mean maternal age was 24 ± 4. 2 years. Most of them were house wives (70%), daily laborers 10% and others contribute to 20%. Majority of the patients were multipara (68%). The more common indications of ICU admission were septic shock (26%) antepartum eclampsia (21.6%), hypovolemic shock (17%), post-partum eclampsia (8%), AKI following LUCS (8.8%), Peripartum cardiomyopathy (5. 8%).Highest number of patient (58.08%) come from obstetric ward and lowest number patient (4.41%) from medicine ward. 55.88 % patients required mechanical ventilation and mean duration of mechanical ventilation is 3 days. The duration of ICU stay varied from 2 -5 days in 191 cases ,6 to 10 days in 40 cases and more than 31days in 1 cases. Transfusion of Blood and blood products was needed in 66. 8% of patients and 11.39% patient required haemodialysis. 75 patient developed complications among those septicaemia (21 patient) was the highest, 11 patient AKI ,13 patient ARDS, 9 patient DIC and 4 patient pneumothorax. The survival rate is 61.01%.*

Conclusion: *Septic shock was the major cause of ICU admission. About two third patients discharged alive.*

Key wards: *Maternal outcome; Critical care; Obstetric patient.*

DOI: https://doi.org/10.3329/jdmc.v32i2.83434
J Dhaka Med Coll. 2023; 32(2) : 124-130

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Received: *22.02.2023* ***Accepted:*** *25. 07.2023*

Introduction

Critically ill obstetric patients are always a challenge to Intensive Care Unit (ICU) physicians and account for as much as 7% of the ICU admissions in developing countries, while they account for a smaller proportion in developed countries.[1] The care of these patients poses a challenge in our environment due to the need for highly specialized care and equipment where the people are still grappling with poverty, ignorance and scarcity of skilled attendants. Admission of obstetric patients occurs approximately at 0.1- 0.9% of the deliveries.[2] The overall maternal death rate in the ICU varies from 3.4-21%.[3] Inadequate knowledge about the illness and infrequent admission of the obstetric patients results in high mortality and morbidity. WHO states that, "there is a story behind every maternal death or life-threatening complication".[4] So a better knowledge of the spectrum, characteristics, and outcomes of the disease involving this group of patients is the first step towards achieving prevention and hence, reduction of both maternal morbidity and mortality.[5] Maternal mortality is a primary health care indicator that reflects the health care adequacy of a country. It remains unacceptably high in many developing countries like Bangladesh unlike the developed nations and many pregnant women in these countries require critical care during pregnancy and need intensive care support. This difference is very likely related to improved socioeconomic conditions, availability of comprehensive antenatal, obstetric, anaesthetic and intensive care services, as well as access to more advanced treatment modalities in the developed countries.[5] The primary objective of this study is to evaluate the reason of admission, pattern of surgical & other interventions and maternal outcome of obstetric patients admitted into the intensive care unit (ICU) of the Dhaka medical college hospital.

Materials and Methods

The study was a prospective longitudinal study conducted in the ICU of Dhaka medical college hospital Dhaka Bangladesh. The study period was 01/05/2019 to 30/04/2020. All the patient who were admitted in the ICU and had obstetric related complication were enrolled in this study. Total 272 patients were admitted in the ICU during the study period. Data was collected from patients, patient's attendant, patient's clinical records and hospital documents (history sheet, investigation sheet and treatment sheet) and written in the pre-formed data sheet. Then data was analyzed in SPSS.

Results:

Table I

Age distribution of patients

Age (year)	Number	Percentage	Mean age (Years)	(SD)
≤20	81	29.77	24.80	(4.2)
21-30	133	48.89		
31-40	54	19.85		
41-51	04	1.47		

Table II

Indication for admission in ICU

Diagnosis	No of patient	Percentage of total pt	Survive	Percent of survival	Death
Septic shock following D & C	22	8.00	13	59.09	9
Septic shock following NVD	17	6.25	12	70.58	5
Septic shock with IUD	14	5.14	8	57.14	6
Septic shock following LUCS	20	7.32	10	50.00	10
Pre eclamsia	4	1.47	4	100	0
Antepartum eclampsia with LUCS	59	21.69	37	62.71	22
Postpartum Eclampsia with LUCS	24	8.82	18	75	6
Hypovolemic shock due to ruptured ectopic pregnancy with laparotomy	16	5.82	9	56.25	7
Hypovolemic shock due to ruptured uterus with laparotomy	4	1.47	1	25	3

Table II

Indication for admission in ICU

Diagnosis	No of patient	Percentage of total pt	Survive	Percent of survival	Death
Hypovolemic shock due to LUCS	16	5.88	10	62.50	6
Hypovolemic shock due to PPH	12	4.41	6	50	6
Peripartum cardiomyopathy	16	5.88	10	62.50	6
Pregnancy with valvular heart disease	7	2.57	3	42.85	4
Pregnancy with anaemic heart failure	3	1.10	2	66.66	1
AKI following LUCS	35	12.86	20	57.14	15
Delayed reversal from anesthesia	2	0.73	2	100	0
Hypersensitivity to Anaesthetic drug	1	0.366	1	100	0

Highest number of patients admitted in the ICU due to Septicemia, then pre-eclampsia, then eclampsia, then hypovolemic shock and others.

Table III

Causes of death

Cause	Total patient	Number of death	Percentage**(%)**
Septic shock	73	30	41.58
Antepartum eclamsia	59	22	37.28
Postpartum eclamsia	24	6	25.00
Hypovoemic shock	48	22	45.83
Peripartum cardiomyopathy	16	6	37.50
Valvular heart disease	7	4	57.14
Anaemic heart failure	3	1	33.33
AKI following LUCS	35	15	42.85

Septic shock antepartum eclamsia an Hypovolemic shock are the major causes of death.

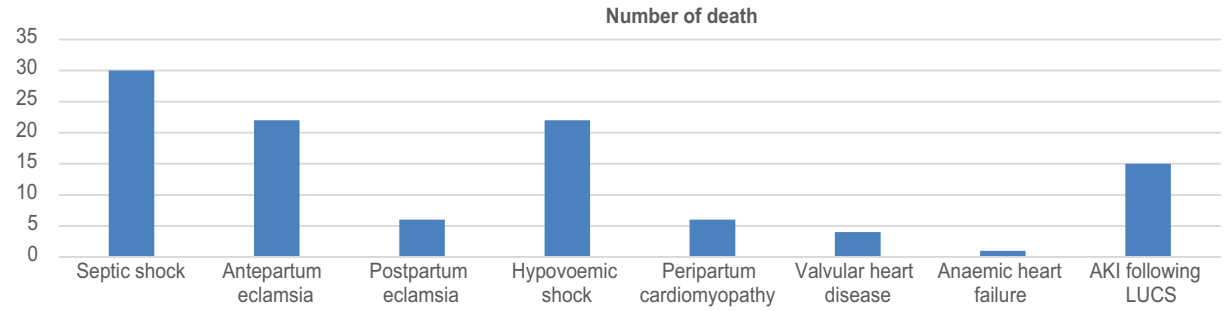

Fig.-1: *Causes of death*

Table IV

Referring ward to ICU

From	No of pt	Percentage (%)	Survive	Percentage (%)	Death	Percentage(%)
Obstetric ward	158	58.08%	99	62.65	59	37.34
Post operative ward	60	22.05	34	56.66	26	43.33
Operation theatre	25	9.19	14	56.00	11	44.00
One stop emergency center (OSEC)	17	6.25	12	70.82	5	29.41
Medicine ward	12	4.41	4	33.33	5	41.66

Most of the patients were referred from obstetric ward and least from medicine ward.

Table V

Duration of ICU stay

Number of patient	Duration	Mean duration(days)
12	<1 day (24 hours)	5.00
191	1 - 5 day	
40	6 - 10 day	
20	11 - 15 day	
5	16 - 20 day	
2	21 - 25 day	
1	26 - 30 day	
1	> 31 day	

Maximum patient required short duration (1 to 5 days) of ICU stay, highest duration of ICU stay was more than 31 days.

Intervention required:

Table-VI

Mechanical ventilation: Mean duration mechanical ventilation 3 days.

		Survive	Percentage	Death	Percentage
Ventilation required	152	56	36.84%	106	63.15%
Non ventilation	120	120	100%	00	00%
Dialysis required	31 (11.2%)	21	67.74%	10	32.25%

Among the patients 31(11.2%) required dialysis and 21 patients were survived.

Table VII: Complications during ICU period:

Outcome:

Results

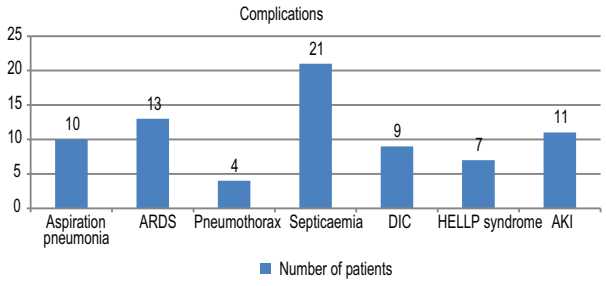

Fig.-2: *Among the patients is the highest number patient developed septicemia, then ARDS, then AKI, then aspiration pneumonia, then DIC, then HELLP syndrome, then pneumothorax.*

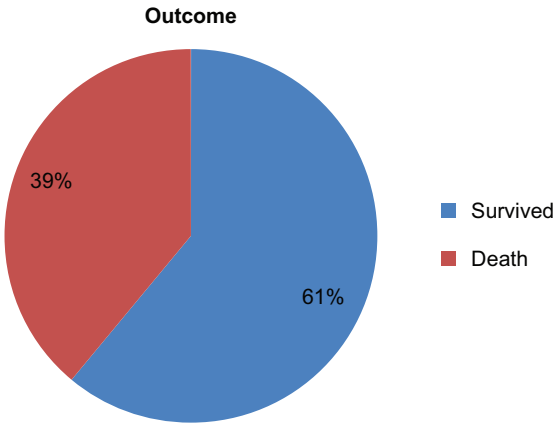

Fig.-3: *Among the admitted patient in ICU, survival was 61% and death rate was 39%.*

The total admissions to the ICU were 272 obstetric patients. The mean maternal age was 24 ± 4. 2 years (Table I). Most of them were house wives (70%), daily laborers 10% and others contribute to 20%. Majority of the patients were multipara (68%). The more common indications of ICU admission were septic shock (26%) antepartum eclampsia (21.6%), hypovolemic shock (17%), post-partum eclampsia (8%), AKI following LUCS (8.8%), Peripartum cardiomyopathy (5. 8%).Highest number of patient (58.08%) come from obstetric ward and lowest number patient (4.41%) from medicine ward (Trable IV). 55.88% patients required mechanical ventilation and mean duration of mechanical ventilation is 3 days. The duration of ICU stay varied from 2 -5 days in 191 cases,6 to 10 days in 40 cases and more than 31days in 1 cases (Table-V). Transfusion of Blood and blood products was needed in 66.8% of patients 11.39% patient required haemodialysis. 75 patient developed complications among those septicaemia (21 patient) was the highest, 11 patient AKI, 13 patient ARDS, 9 patient DIC and 4 patient pneumothorax (Figure 1). The survival rate is 61% and death rate is 39%. Frequency of deaths high among Vulvular heart disease(57.14%), Hypovolemic shock (45.83%), AKI following LUCS (42.85%), Septic shock(41.58%) peripartum cardiomyopathy (37.50%), Antepartum Eclamsia (37.28%), Anaemic heart failure (33.33%), Postpartum eclamsia (25.00%).

Discussion

Any pregnant woman can develop life threatening complications with little or no advance warning. The complications of pregnancy and labor are essentially of two types the first set of complications include obstetric complications like Postpartum Hemorrhage (PPH), Pre eclampsia/Eclampsia (PE/E) etc. which require intensive obstetric care by specially trained providers, and the second set of complications include multi organ involvement/failure which necessitates care provision by intensivist and super specialists such as those from nephrology, neurology, cardiology, pulmonology etc.[26] This can be achieved with patient management at ICU. Understanding the epidemiology of severe obstetric morbidity and "near miss events" may help target interventions aimed at improving the full range of maternal outcomes. Analyzing intensive care unit (ICU) utilization during pregnancy is an accepted approach to identifying severe and "near-miss" maternal morbidity.[27]

During the study period total 7312 patients were admitted in the obstetric ward which was recorded from obstetric ward admission registered book and total 272 obstetric patients was admitted in ICU. The rate of ICU admissions in this study was 3.73% of all obstetric admissions. It varies from place to place and availability and admission to ICU. This is higher than other studies[6, 27] lesser than others.[7-9] In the United States each year, 1 to 3 percent of pregnant women require critical care services, and the risk of death during such admission ranges from 2 to 11 percent (American Academy of Pediatrics and the American College of Obstetricians and Gynecologists, 2012). In our study antenatal and antepartum admissions were 62% which is more than postnatal, which is more than study.[23] But in this study antepartum haemorhage and haemo-peritoneum, haemorhagic shock due to rupture uterus and ruptured ectopic with delayed admissions which correlates with few studies.[10,11,23] In our study, the more common condition requiring ICU admission were septic shock (26%) followed by antepartum eclampsia (21.6%), hypovolemic shock(17%), post-partum eclampsia (8%), AKI following LUCS(8.8%), Peripartum cardiomyopathy(5.8%) which is nearer to study.[12-16,23] The other major conditions were vulvular heart disease(2.57%), anaemic heart failure (1.11%), delayed reversal of anaesthesia, Anaesthetic drug hyper-sensitivity. Studies have found hypertensive disorders as the commonest condition.[17-19] In this study cardiac diseases accounted to 9% which more than other study.[23] 2.57% was vulvular heart disease in these series with 4 maternal deaths and 5.88% peripartum cardiomyopathy patients with 6 maternal deaths. Peripartum cardiomyopathy is a rare pregnancy-specific condition of uncertain aetiology which accounts for less than 1% of all cardiovascular events related to pregnancy.[20]

In this study most of the patients (58.8%) came from obstetric ward followed by post-operative ward (22%), operation theatre (9.1%), one stop emergency center (6.25%) and medicine ward (4,4%). In our study, interventions included blood transfusion 66.3%, inotropes in 72%, mechanical ventilator support in 55% and haemodialysis 11.39% apart from antihypertensive and anticonvulsive nearer to study.[21] The mean duration of mechanical ventilation was 3 days. The duration of ICU stay varied from 2 -5 days in 191 cases ,6 to 10 days in 40 cases and more than 31days in 1 cases (Table-V). Patients need ventilator support for a higher PaO_2 or SpO_2 than normal to reduce the risk of fetal hypoxia in a potentially compromised feto-placental circulation.[22] The survival rate is 61.01% and death rate is 38.97%. In this study the patient who required mechanical ventilation survival rate was 36.84%. where non ventilated patient's survival rate was 100%.

During the study period 31 patients required haemodialysis, among them 21 patients survived and 10 patients died. Maternal mortality accounted to 38.97% with pyrexia, wound infection, sepsis, multiorgan failure, renal failure, ARDS, pnumonitis which is more than the study.[23] Indirect maternal deaths were due to heart disease like severe mitral stenosis with PAH, peripartum cardiomyopathy, infective jaundice with septicemia, hepatorenal syndrome and multiorgan failure. This is nearer to other study.[24] but higher than other studies.[8,12,25]

Conclusion

Obstetric patients admitted into the ICU, especially the unbooked patients had severe morbidities and a high mortality rate. Septicemia, Obstetric haemorrhage with haemodynamic instability and eclamptic disorders are major causes of ICU admissions. Septicemia is the highest complication after admission to ICU.

Limitations of Study

1. This prospective observational study was conducted in a single center government tertiary hospital in the centre of the capital of Bangladesh hence, the results cannot be generalized.
2. It is a short duration of study, only 12-month study.
3. Small sample population and direct admissions to ICU without HDU.

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Clinical Features and Functional Outcome of Patients with Non-compressive Myelopathy: A Hospital Based Cross Sectional Study from a Tertiary Care Center of Dhaka

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Abstract

Background: *Non-compressive myelopathy (NCM) has a wide temporal and clinical profile with etiology that varies over different geographical locations. The etiology may vary according to age, sex, geographical location and other associated factors. There remains a great deal of heterogeneity in clinical features and imaging findings. The functional outcome also differ according to etiology, extent of involvement and rapidity of the management.*

Aims: *To evaluate the clinical features and functional outcome of patients with non-compressive myelopathy.*

Methods: *This observational study was carried out in the Department of Neurology, Neurosurgery and Medicine of Dhaka Medical College Hospital, Dhaka, during January2018 to December 2019. A total of 84 patients suffering from non-compressive myelopathy were included in this study. Age >18 years, both male and female patients with features of myelopathy admitted within 14 days of onset were enrolled in this study and followed up for 180 days.*

Results: *40 (47.5%) patients had acute transeverse myelitis (ATM) without spinal shock followed by 26(30.9%) had ATM with spinal shock, 9(10.8%) had multiple sclerosis (MS), 6(7.2%) had neuromyelitis optica (NMO) and 3(3.6%) had neuromyelitis optica specterum disorders (NMOSD). More than one third (38.2%) patients belonged to age 18-20 years followed by 22(26.3%) in 21-30 years, 20 (23.9%) in 31-40 years, 6(7.2%) in 41-50 years and 4(4.8%) in >50 years. Male to female ratio was almost 2:1. Almost two third (63.1%) patients had paraplegia and 31(36.9%) had quadriplegia. Three fourth (75.0%) patients had sudden onset and 21(25.0%) had insidious onset. More than three fourth (84.5%) patients had sensory involvement. Two third (65.5%) patients had bowel and bladder involvement. The mean Modified Rankin Scale (MRS) score on admission was 4.3±0.86 and 3.13±1.15 at 180 days. The difference was statistically significant ($p<0.05$) between MRS score on admission and MRS score at 180 days. Almost half (48.0%) patients had improved MRS score, followed by 20(20.0%) static, 16(16.0%) worse. The mean barthel index was 34.35±16.71 and 50.06±19.75 on admission and at 180 days (p value <0.01). More than half (53.0%) patients had improved barthel index, followed by 22(22.0%) worse, 16(16.0%) lost to follow up and 9(9.0%) static.*

Conclusion: *ATM was the most common diagnosis among non-compressive myelopathy; with the 2nd decade of the life being the most common age group and predominantly affecting male. Patients with non compressive myelopathy most commonly presented with paraplegia, sudden onset symptoms, sensory involvement, bowel and bladder dysfunction. More than half of the patient improved at day 180.*

Keywords: *Non Compressive Myelopathy (NCM).*

DOI: https://doi.org/10.3329/jdmc.v32i2.83435
J Dhaka Med Coll. 2023; 32(2) : 131-138

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Received: *2.02.2023* ***Accepted:*** *12.06.2023*

Introduction

Myelopathies commonly present with motor and sensory deficits along with sphincter disturbances. The clinical presentation and causes of compressive myelopathies characteristically differ from those of non-compressive myelopathies, although rare presentations in either category can mimic each other and pose a diagnostic dilemma to the astute clinician.[11]The management strategies between compressive and non-compressive myelopathies differ dramatically, as compressive lesions usually require urgent neurosurgical intervention and decompression of the spinal cord,[2] whereas non compressive myelopathies are usually amenable to medical treatment itself.[3] Myelopathies usually present with devastating neurological consequences like para/quadriparesis, neurogenic bladder, decubitus ulcers, spasticity, etc which can impair the quality of life and independence of the affected individual. The sequelae of spinal cord disorders are myriad, with few diseases like subacute combined degeneration showing dramatic response to treatment, producing only a mild impact on the patients daily life, whereas some cases of acute transverse myelitis or cord compression can hamper the vital functions of mobility, sensation, bladder and bowel control, making the patient completely dependent on their caregivers.[4-6] The disease spectrum varies and is somewhat different in Asian countries. Infectious and nutritional diseases are common in this part of the world while demyelinating and HIV associated diseases are common in western and African countries respectively. Quadriparesis and paraparesis due to nontraumatic myelopathies are common neurological diseases with high morbidity (up to 79% of patients was definitely remain disabled) and mortality.[7,8] An increasing understanding of the underlying etiological factors were beneficial in managing spinal cord diseases more comprehensively. Adherence to the following practice was enhance the probability of early detection of important myelopathies and thereby was reduce the morbidity and economic burden of the diseases.[9]

As far the knowledge goes relatively small numbers of studies have focused on the clinical pattern of involvement in non-compressive myelopathies and their functional outcome in this country. So, this study would help us in finding the pattern of involvement, etiological profiles and functional outcome of patients with non-compressive myelopathies and thereby helps in their management.

In this study we assessed the clinical presentations of patients admitted with non-compressive myelopathy (NCM) and determined the functional outcome of the patients according to Modified Rankin Scale (MRS) and Barthel index (BI) at 180 days.

Methodology

This was Hospital-based observational cross-sectional study, carried out in the departments of Neurology, Neurosurgery and Medicine of Dhaka Medical college Hospital from January 2018 to December 2019. Following admission, patients with non-compressive myelopathies were sorted out according to inclusion & exclusion criteria. All of the study population was counselled regarding the aim, objective & significance of the study. Written informed consent was obtained from each patient and the researcher personally conducted interviews using a semi-structured questionnaire. Information regarding the demographic profile (age, sex) and clinical presentation was recorded in the questionnaire. Patients admitted within 14 days of onset of event and treated with i.v methylprednisolone for 5 days were included in this study. Upon admission functional outcomes were quantified using the Modified Rankin Scale (MRS) and Barthel Index (BI). MRI findings, CSF analysis results and other laboratory reports were recorded. The functional outcome of the patients was reassessed by the principal investigator on day 180 (via telephone for discharged patients).

Inclusion and exclusion criteria

We included patients with age more than 18 years, both male and female patients with features of myelopathy (paraplegia or quadriplegia with or without bowel and bladder disturbances), with or without spinal shock and

admitted within 14 days of onset were included in this study. All the patients gave informed written consent. Patients with history of trauma, spinal cord compression on MRI associated peripheral neuropathy, myopathy and stroke were excluded from the study.

Operational definition

Non-Compressive Myelopathy[7] was described as non-compressive myelopathy encompasses a large range of disease entities ranging from demyelination, infection, nutritional, toxic, heredo-familial to degenerative conditions. ATM was diagnosed as per criteria proposed by Transverse Myelitis Consortium Working Group (TMCWG 2002).[10] The diagnosis of multiple sclerosis (MS) was based on 2010 Revised McDonald Criteria.[11] NMO & NMO spectrum disorder (NMOSD) was diagnosed based on 2015 International Panel for NMO Diagnosis criteria.[12] The term "Spinal shock" applies to all phenomena surrounding physiologic or anatomic transection of the spinal cord that results in temporary loss or depression of all or most spinal reflex activity below the level of the injury.[13]

Ethical clearance

Ethical approval was also obtained from the ethical review committee of the study hospital.

Results

In this study, total 84 patients were evaluated, 53 males and 31 females with a male to female ratio 1.7:1(Table I).

Table I

Distribution of the study patients by sex (n=84)

Sex	Number of patients	Percentage
Male	53	63.1
Female	31	36.9

It was observed that more than one third (38.2%) patients belonged to age ≤20 years followed by 22(26.3%) in 21-30 years, 20 (23.9%) in 31-40 years, 6(7.2%) in 41-50 years and 4(4.8%) in >50 years. The mean age was 27.74±13.39 years with range from 18 to 72 years (Table II).

Table II

Distribution of the study patients by age (n=84)

Age (years)	Number of patients	Percentage
≤20	32	38.2
21-30	22	26.3
31-40	20	23.9
41-50	6	7.2
>50	4	4.8
Mean ± SD	27.74 ± 13.39	
Range(min-max)	18-72	

It was observed that 40(47.5%) patients had ATM followed by 26(30.9%) had ATM with spinal shock, 9(10.8%) had MS, 6(7.2%) NMO and 3(3.6%) NMOSD (Table III).

Table III

Distribution of the study patients by Etiology (n=84)

Etiology	Frequency	Percent
ATM without spinal shock	40	47.5
ATM with spinal shock	26	30.9
MS	9	10.8
NMO	6	7.2
NMOSD	3	3.6
Total	84	100

This study also observed that almost two third 53(63.1%) patients had paraplegia and 31(36.9%) had quadriplegia. It was also observed that more than three fourth (84.5%) patients had sensory involvement and two third (65.5%) patients had bowel and bladder involvement (Table IV).

Table IV

Clinical Profile

Clinical features	Frequency	Percentage
Paraplegia/Paraperesis	53	63.1
Quadriplegia/quadriperesis	31	36.9
Sensory symptoms present	71	84.5
Sensory symptoms absent	13	15.5
Bowel & Bladder involvement present	55	65.5
Bowel & Bladder involvement absent	29	34.5

Table V showed the most common sites of involvement were dorsal 33(39.5%) and cervical 26(30.9%) of study subjects. In MRI findings T2 WI signal changes were present in 78(92.8%) of study populations, among them 3 or more segments of vertebral length were involved in 64(76.2%) patients (Table V).

Table V

MRI findings in the study subjects (n=84)

Level of involvement n (%)	MRI features n (%)
Normal 6(7.1%)	T_2 Hyperintesity 78(92.8%)
Cervical 26(30.9%)	
Dorsal 33(39.5%)	Length of involvement
Cervicodorsal 13(15.4%)	a. ≥3 segments: 64(76.2%)
Dorsolumbar 6(7.1%)	b. <3 segments: 14(16.6%)

The mean MRS score on admission was 4.3±0.86 with range from 2 to 5. More than half (53.6%) patients belonged to MRS score 5 on admission. Almost half (47.6%) patients belonged to MRS score 4 at 180 days. The mean MRS score at 180 days was 3.13±1.15 with range from 1 to 5. The difference was statistically significant (p<0.05) between two groups (Table VI).

Table VI

Distribution of the study patients by MRS score (n=84)

MRS score	On admission n	%	At 180 days n	%	P value
1	0	0.0	9	10.7	
2	2	2.4	19	22.6	
3	16	19.0	12	14.3	0.001[s]
4	21	25.0	40	47.6	
5	45	53.6	4	4.8	
Mean±SD	4.3±0.86		3.13±1.15		

Table VII

Distribution of the study patients by barthel index (n=84)

Barthel index	On admission n	%	At 180 days n	%	P value
1-20	22	26.2	4	4.8	
21-40	35	41.7	31	36.8	0.001[s]
41-60	21	25.0	25	29.7	
61-80	6	7.1	24	28.7	
Mean±SD	34.35±16.71		50.06±19.75		0.001[s]

The mean barthel index on admission was 34.35±16.71 with range from 5 to 80. More than one third (41.7%) patients belonged to barthel index 21-40 on admission. More than one third (36.8%) patients belonged to barthel index 21-40 at 180 days. The mean barthel index at 180 days was 50.06±19.75 with range from 20 to 90. The difference was statistically significant (p<0.05) between two groups (Table VII).

Discussion

A total of 84 pastients suffering from non-compressive myelopathy attended in the Neurology, Neurosurgery & Medicine department of Dhaka Medical College Hospital, Dhaka, during January 2018 to December 2019 were included in this study. ATM is a monophasic illness and represents a localized form of post infectious encephalomyelitis. In this study acute transverse myelitis is more likely to cause paraparesis than quadriparesis (56.94% cases VS 21.05%) cases. Overall incidence of ATM causing quadriparesis and

paraparesis was 13.0% and compatible with the findings.[14] Regarding the diagnosis, in this present study, it was observed that 47.5% patients had ATM followed by 30.9% had ATM with spinal shock, 10.8% had MS, 7.2% NMO and 3.6% had NMOSD. Anusha study findings showed that acute transverse myelitis comprised 47.91% of the cases.[15] Another Indian study describing the spectrum of compressive myelopathies also showed that spinal tuberculosis was the commonest cause 24.6% followed by spinal metastases 17.4%.[16] According to Transverse myelitis consortium working group (TMCWG), ATM is classified according to Idiopathic and secondary to diseases like MS, NMOSD and connective tissue disorders.[17] In one study rather than making broad diagnosis of ATM, patients were classified according to etiology of ATM, because treatment and prognosis differ according to etiology of ATM.[18] In their study, patient was diagnosed as post-infectious ATM if had a clear history of febrile illness within 30 days preceding onset of myelitis. Another Indian studied 43 patients of ATM and found that 17 had tetraplegia, 26 had paraplegia and 36 had bladder involvement.[19]

A study observed 30 patients, out of which 41.1% had ATM cases.[20] Cord myelomalacia was seen in two patients who presented very late after clinical onset. A study conducted by on patients of non-compressive myelopathies who underwent MRI showed ATM to be the most common cause of NCM and long segment changes in cord as the most common MRI finding.[21] A Indian study mentioned that the etiologies of myelopathy were MS, neuro-degenerative, systemic lupus erythematosus, spinal cord infarction and idiopathic ATM was diagnosed in 29.3% patients.[20] In this current study, it was observed that 38.2% patients belonged to age ≤20 years followed by 26.3% in 21-30 years, 23.9% in 31-40 years, 7.2% in 41-50 years and 4.8% in >50 years. The mean age was 27.74±13.39 years with range from 18 to 72 years. A Bangladeshi study found age range varied from 15 to 74 years and the highest number of patients (26.0%) was in the age group 51-60 years, followed by 24% patients in the age group 31-40 years, which is comparable with the current study.[22] The age range in this study are similar to other studies.[7,14] In another study observed that age of presentation varied from 14 to 75 years, which also support the present study.[23] However, Thangaraj and Jayasankar found that the mean age of their patients was 34.5 years.[24] In another study Kamble et al. showed the median age of their study population was 38 years, which is higher with the present study.[14] Prabhakar et al. reported the clinical and radiological findings in 57 Indian patients with non-compressive myelopathy having a mean age of 34.45 years which was also higher than the present study.[7] The higher mean age and age range obtained by the above authors may be due to geographical variations, racial, ethnic differences, and genetic causes may have significant influence in their study subjects.

World Health Organization (WHO) reported that the incidence of non-traumatic myelopathies is higher in male than females and incidence steadily increases with age (World Health Organization and International Spinal Cord Society, 2013).[25] Similarly, in this present study, it was observed that non compressive myelopathy was more common in male subjects, which is consistent with Anusha study, where they found 59.0% were males and the rest 41.0% were females.[15] Male predominance may be due to the culture of our society where male are more likely admitted in the hospital and more bed for male patients in the ward. Similarly, Thangaraj and Jayasankar also showed predominant male affection, i.e male to female ratio was 1.9:1.[24] Similar observations regarding the male predominant were also observed in other stufies.[18,22,23]

In this current study, it was observed that 56.0% patients were rural and 44.0% were urban. Similarly, Singh et al. found that 58.9% and 41.1% patents came from Urban and rural area respectively.[20]

In this present study, it was observed that 63.1% patients had paraplegia and 36.9% had quadriplegia. Kamble et al. found quadriparesis in 67.5%, Paraparesis 30.0% and Bibrachial

weakness 1.3% in their studied patients[18]. Thangaraj and Jayasankar observed that bibrachial weakness in 6.9% and Quadriparesis had 28.8% of the patients.[24] Haleem et al. also observed that 92.3% presented with paraplegia and 7.7% presented with quadriplegia.[22] Watson et al. showed that 79.6% had weakness of lower limbs (paraplegia) on presentation while 20.3% patients had involvement of all four limbs (quadriplegia).[23] Anusha observed in patients with nontraumatic myelopathy had paraparesis at presentation whereas 46.0% were quadriparetic. One patient presented with brachial monoparesis, 8.3% patients did not manifest with any weakness and had presented to the hospital with non-motor complaints only.[15]The above studies findings are comparable with the present study. In this current study, it was observed that 75.0% patients had sudden onset and 25.0% had insidious onset. He also observed that onset of illness was acute in 22.0% patients. Subacute onset was noted in another 20.0% whereas 58 patients had a chronic and progressive course prior to presenting to the hospital.[15]

In this present study, it was observed that 84.5% patients had sensory involvement. Thangaraj and Jayasankar found that posterior column sensory loss had 26.7% and Spinothalamic sensory loss had 24.4%.[24] Kamble et al. observed that posterior column sensory loss had 51.3% and spinothalamic sensory loss 45.0%[18]. Haleem et al. study showed that 90.3% cases had some sort of sensory symptoms and 51.6% had involvement of bowel and bladder.[22] In another study Anusha observed that sensory complaints were present in 69.0% of their study patients. In those patients, 44.0% patients presented with a sensory level, 10.0% patients manifested with glove and stocking type of sensory loss, 8.0% patients had radicular pattern of sensory loss, 5.0% patients manifested with diffuse funicular pain, and only 2.0% patients had hemi sensory loss.[15]

Regarding the bowel & bladder involvement in this current study, it was observed that 65.5% patients had bowel & bladder involvement. Haleem et al. showed that more than half (51.6%) of the patients had involvement of bowel and bladder.[22] Ozkan et al. studied 50 patients, among them, 12.0 cases having bladder and bowel dysfunction.[27] Kalita et al. found that bladder involvement in 50.0% cases.[6] Milross et al. observed that bladder dysfunction in 44.68% cases and bowel dysfunction in 38.29% cases.[26] In their study 91.7% patient had sensory symptoms and involvement of both bowel and bladder. This result is higher than the present study. This may be because of selection criteria, diagnosis far too late and less awareness of cancer metastasis.

Regarding the MRS Score on admission in this present study, it was observed that 53.6% patients belonged to MRS score 5 on admission and 47.6% patients belonged to MRS score 4 at 180 days. The mean MRS score on admission was 4.3±0.86 with range from 2 to 5 and 3.13±1.15 with range from 1 to 5 MRS score at 180 days. The difference was statistically significant ($p<0.05$) between MRS score on admission and at 180 days. In this present study, it was observed that 48.0% patients had improved MRS score, followed by 20.0% static, 16.0% worse and lost to follow up respectively. Christensen et al. (1990) described the long-term follow-up of 29 cases of acute transverse myelopathy and noted that one third had a good outcome, while one third had poor outcome. Back-pain and signs of spinal shock were found to indicate worse outcome in his study. Anusha showed improvement in 25.0% and worsening in 3.0%, whereas Barthel index showed improvement in 40.0% and worsening in 8.0% of the patients.[15]

Regarding the Barthel index on admission in this current study, it was observed that 41.7% patients belonged to barthel index 21-40 on admission and 36.8% patients belonged to 21-40 at 180 days. The mean barthel index on admission was 34.35±16.71 with range from 5 to 80 and 50.06±19.75 with range from 20 to 90 at 180 days. The difference was statistically significant ($p<0.05$) between Barthel index on admission and at 180 days. In this current study, it was observed that 53.0% patients had improved barthel index, followed by 22.0% worse, 16.0% lost to follow up and 9.0% static.

Anusha study observed that the mean Barthel index score at initial presentation was 51.15±19.67 with a ranged from 5 to 100. The corresponding mean MRS score was 3.29±0.81 with values ranging between 0 and 5 in the patients with non traumatic myelopathy.[15]

There was some limitation of this study, includes the small sample size, short duration of the study period, follow up was done over phone most of the patients. The study population was selected from one hospital in Dhaka city, so that the results of the study may not reflect the exact picture of the country.

Conclusion

ATM was the most common diagnosis. Non-compressive myelopathy affected people across all adult age groups but most of them were in 2nd decade and male predominant. Paraplegia, sudden onset, sensory involvement, bowel & bladder involvement were more common in patients with non-compressive myelopathy. Nearly a half improved according to MRS Score and more than a half improved according to Barthel index.

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CASE REPORT

A Clinical Exploration of SSPE in Adolescents : A Case Series

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Abstract:

Subacute Sclerosing Panencephalitis (SSPE) is a rare but devastating slowly progressive neurological disorder that typically occurs 6 to 10 years following an initial measles virus infection. SSPE remains a critical concern in the context of historical measles infections, particularly in unvaccinated populations. This case-based review focuses on the clinical features and diagnostic challenges for SSPE. Here, we demonstrate two cases that highlight the variability in presentation and progression of the disease.

The distinctive feature of SSPE is the gradual deterioration of neurological function, with progressive cognitive impairment, seizure and motor dysfunction leading to severe disability. But the clinical presentation of SSPE can often be subtle, and initial symptoms may be mistaken for other developmental disorders that leading to diagnostic difficulty. Thus, a high index of suspicion is essential. The combination of clinical features, EEG findings, and CSF analysis can provide a comprehensive approach to diagnosis. Enhanced EEG techniques and CSF analysis have been emphasized for early detection, with several studies showing that early intervention can lead to better outcomes. Atypical presentation of SSPE must be recognized in area with high incidence. EEG findings were found to be the most important indicator for diagnosis.

The review emphasizes the importance of early recognition and diagnosis to manage the progression of SSPE. While there is currently no curative treatment, symptomatic management and supportive care can improve quality of life for affected individuals. Increased awareness among clinicians regarding the late sequelae of measles virus infection is important for timely diagnosis and intervention. Ongoing research is needed to refine diagnostic methodologies and explore potential therapeutic modalities.

Keywords*: Subacute sclerosing panencephalitis, measles virus, neurological disorder, clinical features, diagnosis.*

DOI: https://doi.org/10.3329/jdmc.v32i2.83436
J Dhaka Med Coll. 2023; 32(2) : 139-144

Introduction:

Subacute sclerosing panencephalitis (SSPE) is a slowly progressive brain disorder, present as a late complication of measles infection, caused by mutant measles virus. Clinically, SSPE is characterized by florid panencephalitis. It is invariably fatal in most cases. Recent studies suggest that mutations in the F protein confer hyperfusogenic properties to the measles virus facilitating transneuronal viral spread. The inflammatory response in the brain leads to extensive tissue damage. SSPE usually has a prediction for children and younger adults. Early aged males from lower socioeconomic conditions suffer from SSPE. The male-to-female ratio of SSPE is approximately 3:1.[1,2,3] SSPE has broadly distinguished into typical and atypical SSPE. The typical SSPE usually occurs over a slow course of 6-10 years after primary measles infection as compared to the atypical form usually has a more fulminant course occurring within 1-6 months with a few occasional cases with deterioration occurring over a small span of 15 days. Although in the post-vaccination era there has been a substantial decline in the incidence of the

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Received: *24.01.2023* ***Accepted:*** *28.06.2023*

disease, it is still higher in the developing countries. An annual incidence of 21 per million populations in India in comparison with 2.4 per million populations in the Middle East.[4,5] A World Health Organization (WHO) expert group reported the global incidence of four to 11 SSPE patients per 100,000 measles cases. In developing countries, the incidence seems to be much higher with up to 27.9 SSPE patients per 100,000 cases of measles.[6,7] Measles infection is still common in Bangladesh. So, the chances of SSPE is still high in this country. There is no data about the incidence of SSPE in Bangladesh but it can be indirectly presumed from the high prevalence of measles despite wide vaccination coverage.[2] SSPE usually presents with the symptoms of motor involvement such as jerking movements, muscle spasms, ataxia, tremor, seizure, cognitive impairment etc.[8] However, several atypical presentations are also noted.[9-12] A wide spectrum of movement disorders is also observed throughout the clinical stages of SSPE.[8] The clinical manifestations of SSPE are not always typical and that may cause a delay in the diagnosis. Diagnosis of SSPE typically involves a combination of clinical history with various diagnostic tests that include EEG findings, CSF (cerebrospinal fluid) study, and neuroimaging. This article reviews the clinical features of SSPE, examines current investigation methodologies, and summarizes the findings from recent studies to further understand the disease's progression and diagnostic challenges. In this case-based review, we discuss two cases of SSPE one presenting with myoclonus with cognitive decline and another with psychiatric manifestations with seizure.

Case Finding:

Case 1

A 16-year-old male with a past medical history of Measles infection presented with a 2-years history of walking difficulty, repeated jerky movement of limbs and trunk, and generalized tonicclonic seizures occurring in both wakefulness and sleep. During illness, progressive cognitive decline and behavioral change were also observed. Family history was noncontributory. The birth was a full-term normal vaginal delivery without perinatal complications. He is developmentally normal and he was immunized according to the EPI schedule.

Neurological examination reveals a decline in cognitive function, MMSE 12, speech was slurred, and muscle power MRC (Medical Research Council) grade 4 in both upper and lower limbs with myoclonus. Deep tendon reflexes were brisk in all extremities, Babinski's signs were present bilaterally. Cranial nerve and sensory function were all normal. No incoordination or signs of meningeal irritation was noted.

EEG showed a generalized periodic high voltage complex. CSF study reveals CSF was clear and cytology revealed predominant lymphocytes and no red blood cells, anti-measles antibodies titer was markedly elevated (590.9mIU/ml, normal< 150mIU/ml). Magnetic resonance imaging (MRI) of the brain fluid-attenuated inversion recovery (FLAIR) showed multiple discrete

periventricular white matter hyperintensities.

Case 2

Kawser, a 15-year-old boy of nonconsanguineous parents with no significant birth and developmental history presented to the psychiatric department with low mood, personality, and behavioral change and gradual worsening of school performance. Later on, he developed generalized seizures and tremulous movement of both hands but no history of myoclonus or recurrent fall. No history of measles infection in childhood was reported by the parents.

Neurological examination revealed he was fully oriented and able to speak with labile mood, action, and intension tremor present, he had muscle power MRC (Medical Research Council) grade 4, ataxic gait with brisk reflex. Cranial nerve and sensory function were all normal.

On investigations, EEG showed generalized periodic spike-wave discharge, CSF study reveals CSF was clear and cytology revealed predominant lymphocytes, protein mildly raised, demonstrating positive anti-measles antibodies in high titer. Magnetic resonance imaging (MRI) of the brain was normal.

Discussion:

SSPE is a rare but serious neurodegenerative disorder that typically occurs in children and young adults as a late complication of measles virus infection. It is caused by persistent defective measles virus. SSPE is a commonly encountered disease in poor and resource-constrained countries.[13] The WHO has estimated its incidence to be approximately 4–11 cases per 100,000 measles cases.[15] Measles infection acquired very early in life is associated with a much higher risk.[16] The diagnosis of SSPE is based upon clinical manifestations, characteristic periodic EEG discharges, and demonstration of raised antibody titer against measles in the plasma and cerebrospinal fluid. SSPE is still common in developing and underdeveloped countries. One of the most important limitations in the treatment of SSPE is the difficulty in recognizing the early manifestation of the disease. The management of SSPE focuses on improvement of quality of life and prolongation of survival which can be achieved with the use of supportive care modalities and immunomodulators, respectively. Diagnosis is especially problematic in adult patients with SSPE.

Pathogenesis:

The occurrence of SSPE represents a defective cell-mediated immune response in the primary measles infection by mounting a premature humoral immunity and facilitating intraneuronal infection. Certain genetic polymorphisms have been attributed to this.[16] A persistent measles infection of brain clinically manifests several years after the acute measles infection. The brain infection leads to an exaggerated mononuclear inflammatory reaction to persisting measles virus. The mononuclear inflammatory response in the brain is mediated by CD4+ and CD8+ T cells along with monocytes and antibody secreting B lymphocytes. The antibody response against the measles virus is aggravated by high production of measles virus specific antibodies by plasma cells inhabiting the brain[17]. The parieto occipital cortex is most dominantly affected. Anterior parts of the cerebral cortex, periventricular white matter, thalamus, brainstem, and spinal cord are less severely involved.[18-19]

Clinical Feature:

Literature review shows that clinical presentation may vary from case to case. This includes progressive mental decline, behavioral abnormality, different types of movement disorders both hyperkinetic and hypokinetic, seizures including myoclonic, generalized, focal, and multiple types of seizure[20-21]. SSPE has four clinical stages[22] (Table 1). Here, between our two cases first one is present with some typical feature like myoclonus and cognitive decline. While the second case was presented with psychiatric feature in the psychiatry department, later he developed generalized convulsion and after EEG periodic discharge was found and thereafter CSF showed high titre of anti-measles antibodies. A comparison of the clinical spectrum of these two patients is shown in Table II.

Table I

Clinical staging of subacute sclerosing panencephalitis (SSPE)

Stages	Clinical features	Disability Status
Stage 1	Subtle decline in mental and scholastic performance	No or mild disability, no or mild impairment to walking
Stage 2	Periodic myoclonus and severe mental decline	Moderate disability with significant impairment to walking
Stage 3	Akinetic mutism with generalized spasticity	Confined to bed and totally dependent
Stage 4	Vegetative state	Impaired consciousness and requires 24 h nursing care

Table II
Clinical spectrum of SSPE patients

	Case 1	Case 2
Age of patient	16 years	15 years
P/H of Measles	Present	Absent
Measles vaccination	Vaccinated	Not vaccinated
Clinical Features	Walking difficulty	Depression and Personality
	Myoclonus	change
	Seizure	Emotional lability
	Progressive cognitive decline	Decrease school performance
		Seizure
		Tremor
MRI of brain	multiple discrete periventricular white matter hyperintensities (in FLAIR)	Normal
EEG Findings	generalized periodic spike-wave complex	generalized periodic spike-wave discharge
CSF Anti-measles Antibody	Positive in high titre (590.9 mIU/ml)	Positive in high titre (445.3 mIU/ml)

Diagnosis:
The diagnosis of SSPE relies on the modified Dyken's criteria that consist of major and minor criteria. Two major and one minor criterion must be satisfied to confirm the diagnosis of SSPE. The major criteria include clinical history and CSF measles antibody titers while minor criteria include EEG, MRI, and brain biopsy. Brain biopsy given its invasive nature, is incompatible with routine use and is therefore restricted to cases where clinical suspicion is high and the antibody titer is negative in a subacute sclerosing.[23]

Electroencephalography:
Almost all the patients of SSPE showed periodic high-voltage complexes, which usually occur in patients with a disease duration of more than four months. EEG in SSPE includes generalized periodic complexes or discharges[24]. Periodic EEG complexes consist of giant slow wave with several sharp wave. A typical discharge is polyphasic with duration varying from 0.5 to 2 seconds, high voltage (300 1500 mV), and repetitive (occurring every 4 to 15 s). Periodic discharges persist during sleep.[25-27] The typical pattern of EEG is more common in SSPE; however, we should also keep in mind that atypical and normal patterns of EEG can also occur in SSPE.[24] In the developing world with limited resources, EEG can be used as a good diagnostic tool for the suspected cases of SSPE. Figure 1 shows the EEG of an SSPE patient.

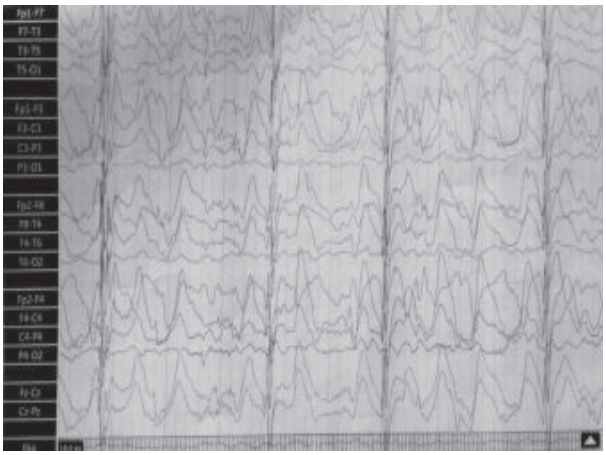

Figure 1: *Electroencephalogram of a patient with SSPE stage- ii showing periodic discharge appearing every 3 seconds and lasting for 1 second.*

CSF Examination:

The detection of CSF IgG against the measles virus using the Enzyme-linked immunosorbent assay (ELISA) technique has a very high sensitivity and specificity value which explains why it is a major criterion in the diagnosis of SSPEA high titer of measles antibodies, in the CSF and serum, is the gold standard for the diagnosis of SSPE. Other CSF findings are oligoclonal bands and lymphocytosis, protein may be normal or mildly elevated [28,29]. Here, anti-measles antibody titer was markedly elevated in both cases, the value was 590.9 mIU/ml in case 1 and 445.3 mIU/ml in case 2 where the normal value was normal < 150mIU/ml.

Neuroimaging:

Neuroimaging modalities may include a CT or MRI brain:

CT Scan:

It is normal in the early stages of SSPE. Later, focal white matter hypodensities in parietooccipital regions can be seen.[30]

Magnetic resonance imaging:

MRI is a better imaging modality for showing brain abnormalities of SSPE. MRI may be normal in the initial stage of SSPE. At later stages, abnormalities are usually located in subcortical, periventricular, and cortical gray matter. Corpus callosum, basal ganglia, cerebellum, and brainstem are less frequently affected. A typical neuroimaging picture shows bilateral asymmetric periventricular and subcortical white matter hyperintensity. Classical T2 weighted images or fluid attenuated inversion recovery (FLAIR) images show hyperintense signals.[31,32]

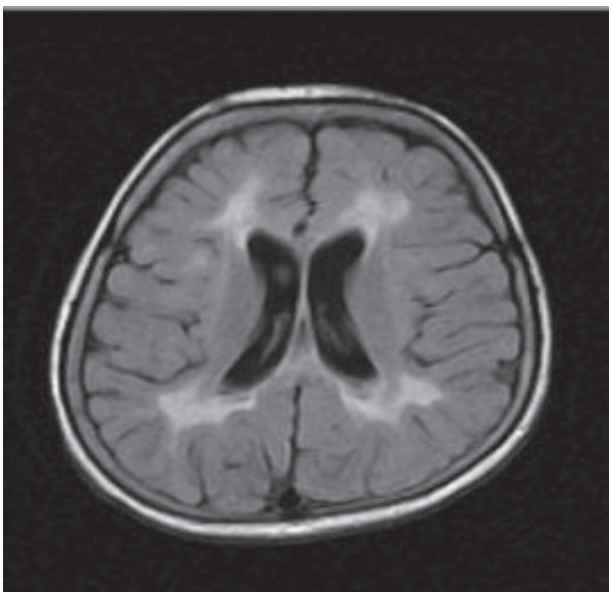

Figure 2: *MRI of an SSPE patient showing bilateral periventricular and subcortical hyperintensities in T2, FLAIR image.*

Conclusion

SSPE is a complex and devastating neurological condition that requires a high index of suspicion for diagnosis, particularly in individuals with a history of measles. EEG is particularly valuable in diagnosis, especially for developing countries like us. Early identification and clinical intervention are crucial, although effective treatments remain limited and primarily focus on managing symptoms and providing supportive care. While SSPE remains a challenging condition with no definite cure, ongoing research is necessary to better understand its pathogenesis and explore potential therapeutic options.

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