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Original Article

Factors Affecting Work Productivity and Activity Impairment in Axial Spondyloarthritis Patients

Ahmed S¹, *Islam MA², Abdal SJ³, Shahin MA⁴

ABSTRACT

Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease that commonly affects individuals during their economically productive years and may substantially impair physical function, quality of life, and participation in work. A systematic review and meta-analysis reported that more than half of employed patients with active axSpA experienced work impairment, with presenteeism accounting for a major component of productivity loss. Evidence reported mean absenteeism, presenteeism, overall work productivity loss, and activity impairment of 4.5%, 24.9%, 27.6%, and 35.2%, respectively. However, evidence concerning occupational outcomes and their determinants among patients with axSpA in Bangladesh remains limited. This study aimed to assess work productivity and activity impairment (WPAI) and to identify demographic, clinical, functional, and psychosocial factors associated with employment status among patients with axSpA in Bangladesh. This analytical cross-sectional study was conducted at the Department of Rheumatology, Bangladesh Medical University (BMU), Dhaka, from June 2023 to June 2024. Of 222 patients aged 18-55 years with axSpA fulfilling the Assessment of SpondyloArthritis International Society (ASAS) classification criteria were included. Participants were recruited using purposive consecutive sampling. Work productivity and activity impairment were assessed using the WPAI questionnaire for axSpA (WPAI-axSpA). Disease activity, functional limitation, spinal mobility, health-related quality of life and psychological well-being were assessed using BASDAI, BASFI, BASMI, ASDAS-CRP, ASQoL, SF-12 and GHQ-12, respectively. Continuous and categorical variables were compared using appropriate parametric or non-parametric and categorical tests. Associations between

WPAI domains and patient-reported outcomes were examined using Spearman's rank correlation. Multivariable logistic regression was performed to identify factors independently associated with unemployment. Statistical significance was defined as $p < 0.05$. The mean age was 34.0 ± 8.5 years, and 66.7% of participants were male (male-to-female ratio 2:1), with 38.7% unemployed. Mean disease duration was 6.31 ± 3.40 years; peripheral arthritis (72.1%) and enthesitis (45.0%) were the most frequent musculoskeletal manifestations. Activity impairment (AI) was significantly greater among unemployed than employed participants ($59.39 \pm 18.19\%$ vs $50.46 \pm 16.33\%$; $p = 0.006$), whereas absenteeism, presenteeism and overall work productivity loss (OWPL) did not differ significantly by employment status. Among employed participants, education was associated with presenteeism ($p = 0.016$) and OWPL ($p = 0.011$), while smoking was also associated with OWPL ($p = 0.030$). AI differed significantly across BMI categories ($p = 0.031$). Spearman's analysis demonstrated positive correlations between disease activity and functional limitation and all WPAI domains, with the strongest correlations observed for BASDAI and BASFI with OWPL ($\rho = 0.71$ for both; $p < 0.001$). PCS-12 was inversely correlated with all WPAI domains, most strongly with OWPL ($\rho = -0.74$; $p < 0.001$). In multivariable logistic regression, age, male sex, married status, NRS pain score and PCS-12 were independently associated with unemployment, whereas education, BASDAI, ASDAS-CRP ≥ 3.5 , ASQoL and GHQ-12 were not independently associated. AxSpA was associated with a substantial burden of unemployment and AI in this Bangladeshi tertiary-care facility. Work-related impairment was closely associated with disease activity, functional limitation and physical health, while employment status was additionally associated with demographic characteristics. Management strategies should therefore address disease control, functional capacity and preservation of participation in work and daily activities.

Keywords: Axial spondyloarthritis; work productivity; activity impairment; employment; absenteeism; presenteeism.

INTRODUCTION

Axial spondyloarthritis (axSpA) is a chronic immune-mediated inflammatory rheumatic disease that predominantly affects the sacroiliac joints and the axial skeleton.^{1, 4} Because symptom onset commonly occurs during the third decade of life and generally before 45 years

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of age, axSpA can affect individuals during their most economically productive years.³

The epidemiology of axSpA varies by geographic region, ethnicity, HLA-B27 prevalence, and classification criteria. Reported global prevalence ranges from approximately 0.1% to 1.4%.¹ Available Asian data show marked regional variation, from approximately 0.03% in India to around 1.2% in Bangladesh.² A national Bangladeshi survey has also demonstrated a substantial burden of musculoskeletal conditions and related disability among adults.² Family history and HLA-B27 are important determinants of susceptibility, and the multinational ASAS-PerSpA study has demonstrated substantial geographic variation in family history of SpA and its relationship with HLA-B27 status.¹⁴

Chronic pain, fatigue, morning stiffness, restricted spinal mobility, peripheral arthritis, enthesitis and extra-articular manifestations can interfere with physical functioning and participation in everyday activities.^{1, 4} These limitations usually translate into absenteeism, presenteeism, reduced overall work productivity and impaired participation in non-work activities. The WPAI questionnaire specific for axSpA (WPAI-axSpA) provides a structured assessment of these consequences over the preceding seven days, including absenteeism, presenteeism, OWPL and AI.^{5, 10}

A systematic review and meta-analysis found that more than half of employed patients with active axSpA experienced work impairment, with presenteeism representing an important component of productivity loss.⁵ In Singapore, mean absenteeism, presenteeism, overall work productivity loss and activity impairment were reported as 4.5%, 24.9%, 27.6% and 35.2%, respectively; poorer work outcomes were associated with higher disease activity, impaired physical function, fatigue and lower educational attainment.⁶ A Turkish study similarly found significant positive correlations between BASDAI and WPAI domains, where greater work impairment was associated with poorer quality of life.⁷

International studies have identified work-related and psychosocial burdens among patients with axSpA, including persistent pain, fatigue, reduced mobility and psychological distress.^{8,9,17} Work disability may also be influenced by socioeconomic circumstances, educational attainment, healthcare access and social support.¹² Evidence from chronic inflammatory rheumatic diseases indicates that employment outcomes can differ substantially from those of the general population.¹³ In addition, comorbidities are common in axSpA and usually contribute to disability, poorer quality of life and reduced productivity.¹⁶

Although advances in biologic and targeted synthetic disease-modifying antirheumatic therapy have improved

disease control and functional outcomes, work disability and activity impairment remain clinically important problems.^{3,5} This burden may be particularly relevant in low- and middle-income settings, where delayed diagnosis, restricted access to advanced therapies, financial constraints and socioeconomic barriers can influence long-term outcomes. Despite the established international evidence, information on work productivity, activity impairment and their determinants among Bangladeshi patients with axSpA remains limited; therefore, this study was undertaken to evaluate WPAI among patients with axSpA and to identify demographic, clinical, functional and psychosocial factors associated with employment status.

MATERIALS AND METHODS

Study Design and Setting: This analytical cross-sectional study was conducted in the Department of Rheumatology, BMU, Dhaka, Bangladesh, over a one-year period from June 2023 to June 2024. The study evaluated work productivity and activity impairment among patients with axSpA and examined demographic, clinical, laboratory, functional, and psychosocial factors associated with employment status.

Study Population and Participant Selection: Adults aged 18-55 years with a confirmed diagnosis of axSpA according to the ASAS classification criteria were eligible. Participants were required to have experienced paid employment or regular occupational activity at some point after disease onset and to be able to complete the study questionnaires independently or with minimal assistance. Patients were excluded if they had an inflammatory rheumatic disease other than axSpA, severe neurological or psychiatric illness interfering with questionnaire completion, advanced medical illness unrelated to axSpA causing substantial disability, pregnancy, incomplete clinical or laboratory information, or refusal to provide written informed consent. A total of 300 patients were screened, of whom 222 fulfilled the eligibility criteria and were included in the final analysis. Participants were recruited using purposive consecutive sampling from patients attending the rheumatology service during the study period.

Data Collection: Demographic and socioeconomic information, including age, sex, marital status, education, residence, smoking/tobacco use and occupational status, was collected using a pretested semi-structured questionnaire. Clinical information included disease duration, pain severity, family history of spondyloarthritis, peripheral arthritis, enthesitis, hip involvement, uveitis, sacroiliitis and comorbidities. Clinical examination included assessment of spinal mobility and peripheral musculoskeletal manifestations. Disease activity was

assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score based on C-reactive protein (ASDAS-CRP). Functional limitation was assessed using the Bath Ankylosing Spondylitis Functional Index (BASFI), while spinal mobility was evaluated using the Bath Ankylosing Spondylitis Metrology Index (BASMI). Health-related quality of life was assessed using the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire and the Short Form-12 (SF-12), from which Physical Component Summary (PCS-12) and Mental Component Summary (MCS-12) scores were derived. Psychological well-being was assessed using the 12-item General Health Questionnaire (GHQ-12). Laboratory investigations included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and HLA-B27 status where available. Clinical and laboratory assessments were performed according to the standard procedures of the rheumatology centre.

Assessment of Work Productivity and Activity Impairment: The primary outcome was work productivity and activity impairment measured using the WPAI questionnaire for axSpA (WPAI-axSpA). The instrument assesses impairment during the preceding seven days in four domains:

1. Absenteeism: percentage of work time missed because of axSpA;
2. Presenteeism: percentage reduction in productivity while working;
3. Overall work productivity loss (OWPL): combined effect of absenteeism and presenteeism; and
4. Activity impairment (AI): percentage impairment in regular non-work activities.

Scores range from 0% to 100%, with higher scores indicating greater impairment.^{5,10}

Work-related WPAI domains were analyzed among participants with valid employment-related responses. Because absenteeism does not apply to participants without work hours during the assessment period, analyses of absenteeism were restricted to respondents for whom the relevant WPAI responses were available. AI was analyzed among participants with valid responses to the relevant WPAI item. Employment status was coded as employed=0 and unemployed=1 for the multivariable logistic regression analysis. In the final dataset, 136 participants were employed, and 86 were unemployed.

Statistical Analysis: Data were entered, cleaned, and analysed using SPSS version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarised as mean±SD, while categorical variables were presented as

frequencies and percentages. Comparisons between employed and unemployed participants were performed using the independent-samples t test for normally distributed continuous variables and the χ^2 test or Fisher's exact test, as appropriate, for categorical variables. Differences in WPAI scores across BMI categories were assessed using one-way analysis of variance (ANOVA). Associations between age and WPAI domains and between patient-reported outcome measures and WPAI domains were assessed using Spearman's rank correlation coefficient (ρ) because several variables were not normally distributed. Correlations were calculated using pairwise-complete observations, and the number of observations therefore varied between WPAI domains according to the availability of valid responses. Two-sided p values were reported, with $p < 0.05$ considered statistically significant.

A multivariable binary logistic regression model was used to identify factors independently associated with unemployment (unemployed=1; employed=0). The model included age, sex, educational attainment, marital status, NRS pain score, BASDAI, ASDAS-CRP category (≥ 3.5 vs < 3.5), ASQoL, PCS-12 and GHQ-12. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported. The final regression analysis included 212 participants with complete data for the model variables. Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC), and model fit was assessed using the likelihood-ratio statistic and McFadden pseudo- R^2 . Statistical significance was defined as a two-tailed $p < 0.05$.

Ethical Clearance: The study protocol was reviewed and approved by the Institutional Review Board of BMU. Written informed consent was obtained from all participants before enrolment. Participation was voluntary, and participants were informed of their right to withdraw at any stage without affecting their clinical care. Confidentiality and anonymity of participant information were maintained throughout the study in accordance with the ethical principles of the Declaration of Helsinki and its subsequent amendments.

RESULTS

A total of 222 adult patients with axSpA were included in the final analysis. Baseline data included sociodemographic characteristics, clinical and laboratory findings, disease activity indices, patient-reported outcome measures, and WPAI scores.

Baseline Sociodemographic Characteristics

Table I shows that the mean age of the participants was 34.0 ± 8.5 years (range 18-55 years), and 148 (66.7%).

Most participants were married (73.4%) and had completed HSC or higher education (61.3%). Urban residents constituted 61.3% of the study population. Regarding BMI, 68.5% had normal weight, 24.3% were obese, and 7.2% were underweight. A positive family history of SpA was reported by 20.3%, while 69.4% were non-smokers.

Table I: Baseline Sociodemographic Characteristics of Patients with axSpA (n=222)

Variable	Category	n (%) / Mean±SD
Age (years)	Mean ± SD	34.0 ± 8.5
Gender	Male	148 (66.7)
	Female	74 (33.3)
Marital status	Married	163 (73.4)
	Unmarried	59 (26.6)
Education	Up to SSC	86 (38.7)
	HSC and above	136 (61.3)
Residence	Urban	136 (61.3)
	Rural	86 (38.7)
BMI	Underweight	16(7.2)
	Normal	152(68.5)
	Obese	54 (24.3)
Family history of SpA	Yes	45 (20.3)
	No	177 (79.7)
Tobacco use	Non-smoker	154 (69.4)
	Smoker	60 (27.0)
	Smokeless tobacco	8 (3.6)

Data are presented as frequency (percentage) or mean ± standard deviation.

Figure 1, the pie chart illustrates the employment status of the study population. Of the 222 participants, 136 (61.3%) were employed, and 86 (38.7%) were unemployed.

Employment Status of Patients with Axial Spondyloarthritis (n = 222)

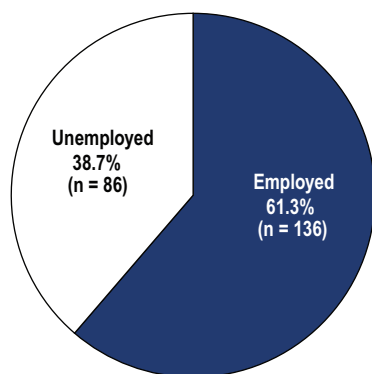


Figure 1: Employment Status of Patients with axSpA (n=222).

Clinical, Laboratory, and Functional Descriptive Statistics

Table II presents that the mean disease duration was 6.31 ± 3.40 years, with an average pain score of 4.84 ± 1.10 on the visual analogue scale. Peripheral arthritis was present in 72.1% of patients, enthesitis in 45.0%, hip involvement in 29.7%, and previous or current uveitis in 8.1%. Sacroiliitis was demonstrated in 95.0%, and 43.2% were HLA-B27- positive. Mean inflammatory markers were ESR 47.68 ± 22.22 mm/hour and CRP 18.13 ± 27.60 mg/L. The mean BASDAI, BASFI, BASMI and ASDAS-CRP scores indicated overall moderate disease activity and functional impairment. Patient-reported outcome measures also suggested impaired quality of life and moderate psychological distress.

Table II: Clinical, Laboratory and Functional Characteristics of Patients with axSpA (n=222)

Variables	n (%) / Mean ± SD
Disease duration (years)	6.31 ± 3.40
Pain (VAS)	4.84 ± 1.10
Peripheral arthritis	160 (72.1)
Enthesitis	100 (45.0)
Hip involvement	66 (29.7)
Uveitis	18 (8.1)
Sacroiliitis	211 (95.0)
HLA-B27 positive	96 (43.2%)
Comorbidity	47 (21.2)
ESR (mm/hr)	47.68 ± 22.22
CRP (mg/L)	18.13 ± 27.60
Current treatment	
TsDMARD	87 (39.2)
CsDMARD	81 (36.5)
NSAIDs only	54 (24.3)
Disease activity indices	
BASFI	1.83 ± 1.32
BASMI	3.33 ± 0.96
BASDAI	2.70 ± 1.06
ASDAS-CRP	2.95 ± 0.86
Patient-reported outcomes	
ASQoL	6.90 ± 4.32
PCS-12	35.58 ± 9.89
MCS-12	51.82 ± 8.02
GHQ-12	11.39 ± 5.25

Data are presented as n (%) for categorical variables and mean±SD for continuous variables.

Comparison According to Employment Status

Table III shows that among the 222 participants, 38.7% were employed, and they were significantly older than unemployed patients (35.8 ± 7.4 vs. 31.0 ± 9.3 years, $p < 0.001$). Employment status also differed significantly by gender, marital status, smoking status, disease duration,

hip involvement, and BMI. No significant differences were observed in education, inflammatory markers, treatment categories, or most disease activity indices, although GHQ-12 ($p = 0.066$), CRP ($p = 0.083$), and BASDAI ($p = 0.096$) showed a borderline association with employment status ($p = 0.096$).

Table III. Sociodemographic, Clinical and Disease Characteristics According to Employment Status among Patients with axSpA

Variable	Employed (n=136) n (%) / Mean $\pm$ SD	Unemployed (=86) n (%) / Mean $\pm$ SD	p-value
Age (years)	35.8 $\pm$ 7.4	31.0 $\pm$ 9.3	<0.001
Male sex	114 (83.8%)	34 (39.5%)	<0.001
Married	116 (85.3%)	47 (54.7%)	<0.001
Smoking	54 (39.7%)	6 (7.0%)	<0.001
BMI			0.033
Underweight	6 (4.4%)	10 (11.6%)	
Normal weight	101 (74.3%)	51 (59.3%)	
Overweight/obese	29 (21.3%)	25 (29.1%)	
FH SpA positive	24 (17.6%)	21 (24.4%)	0.293
DD (years)	7.2 $\pm$ 4.4	4.9 $\pm$ 2.8	<0.001
Peripheral arthritis	94 (69.1%)	66 (76.7%)	0.217
Hip involvement	49 (36.0%)	17 (19.8%)	0.014
HLA-B27 positive	59 (43.4%)	37 (43.0%)	0.734
Pain VAS	4.9 $\pm$ 1.1	4.7 $\pm$ 1.1	0.268
ESR	47.2 $\pm$ 21.7	48.4 $\pm$ 23.2	0.704
CRP	15.4 $\pm$ 24.0	22.4 $\pm$ 32.2	0.083
BASFI	1.7 $\pm$ 1.0	2.0 $\pm$ 1.6	0.121
BASMI	3.4 $\pm$ 1.0	3.3 $\pm$ 0.9	0.359
BASDAI	2.6 $\pm$ 0.8	2.9 $\pm$ 1.3	0.096
ASDAS-CRP	2.9 $\pm$ 0.8	3.0 $\pm$ 0.9	0.258
ASQoL	6.8 $\pm$ 4.8	7.1 $\pm$ 3.9	0.627
PCS-12	36.2 $\pm$ 10.3	34.7 $\pm$ 9.5	0.286
MCS-12	52.5 $\pm$ 7.3	51.2 $\pm$ 8.8	0.266
GHQ-12	10.8 $\pm$ 5.3	12.2 $\pm$ 5.2	0.066

FH SpA= Family history of SpA; DD= Disease duration

Data are presented as n (%) or Mean $\pm$ SD. Percentages are calculated within employment-status groups. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate, and continuous variables using the independent-samples *t* test. A two-sided $p < 0.05$ was considered statistically significant.

Relationship of WPAI and Sociodemographic Factors

Table IV presents WPAI scores and socio-demographic factors among employed participants. Education was significantly associated with presenteeism ($p = 0.016$) and overall work productivity loss ($p = 0.011$), with higher impairment among participants with education up to SSC. Smoking status was also associated with overall work productivity loss ($p = 0.03$). Among employed participants, WPAI scores of all 4 domains did not differ significantly according to gender, marital status, or residence.

Table IV: WPAI Scores According to Sociodemographic Characteristics among Employed Patients with axSpA
(N = 136).

Socio-demographic factors (Employed)	Absenteeism		Presenteeism		OWPL		AI	
	Mean±SD	p value	Mean±SD	p value	Mean±SD	p value	Mean±SD	p value
Gender								
Male	21.06±13.15	0.692	54.23±13.93	0.141	57.72±16.05	0.103	50.46±15.24	0.511
Female	19.79±7.27		48.82±14.95		51.00±16.83		49.05±13.75	
Marital Status								
Married	20.69±12.40	0.677	53.52±14.62	0.792	57.12±16.81	0.442	51.44±14.49	0.189
Unmarried	22.73±15.62		52.63±11.15		54.14±16.92		54.50±16.92	
Education								
Up to SSC	23.34±16.81	0.162	57.72±16.25	0.016	61.86±18.40	0.011	53.15±17.40	0.505
Above SSC	18.66±6.33		50.96±12.16		53.74±14.15		51.67±13.60	
Residence								
Rural	23.81±16.39	0.110	54.73±15.56	0.356	58.40±18.01	0.297	52.36±15.90	0.932
Urban	18.38±7.54		52.40±12.93		55.37±14.76		52.18±14.89	
Smoking								
Smoker	19.35±7.52	0.327	56.23 ±12.13	0.054	60.33 ±14.10	0.03	53.79±14.13	0.369
Non-smoker	22.62±16.48		51.39±15.05		54.07±17.14		51.69±15.57	

AI = Activity Impairment; Values reported as mean ± SD; Significant ($p < 0.05$).

WPAI scores are expressed as percentages, with higher scores indicating greater impairment. Values are presented as Mean±SD. p values were obtained using Welch's t test or Mann-Whitney U test, as appropriate; Significant ($p < 0.05$). OWPL, Overall Work Productivity Loss; AI, activity impairment.

Employment status and activity impairment (AI)

Table V states the AI according to employment status among patients with axSpA. AI was significantly greater among unemployed participants than among employed participants (59.39±18.19% vs 50.46±16.33%, $p=0.006$).

Table V: AI According to Employment Status among Patients with axSpA (n=222)

Employment status		Activity Impairment Mean±SD	P value
Employment	Employed	50.46±16.33	0.006
	Unemployed	59.39±18.19	

Values are Mean±SD. WPAI activity impairment is expressed as percentage impairment (0–100%), with higher values indicating greater impairment. p -value obtained using the independent-samples t test.

BMI and WPAI

Table VI shows the WPAI scores according to body mass index (BMI). AI differed significantly according to BMI category ($p=0.031$), with the highest mean AI observed among underweight participants. No statistically significant differences across BMI categories were observed for absenteeism, presenteeism, or OWPL.

Table VI: Work Productivity and AI Scores According to BMI Category (One-way ANOVA).

Nutritional Status (BMI)	Absenteeism		Presenteeism		OWPL		AI	
	Mean±SD	P value	Mean±SD	P value	Mean±SD	P value	Mean±SD	P value
Underweight	33.32±15.92	0.119	64.29±20.71	0.065	67.70±23.80	0.128	61.25±21.87	0.031
Normal weight	20.51±13.43		53.42±13.85		56.64±16.01		50.95±13.74	
Overweight / Obese	18.55±5.62		50.37±11.92		53.78±13.92		53.15±16.00	

Values are presented as Mean±SD. *p* values were obtained using one-way analysis of variance. WPAI scores are expressed as percentage impairment (0-100%), with higher values indicating greater impairment. WPL, work productivity loss.

Correlation of Age with WPAI Domains

Table VII shows the correlation between age and WPAI domains; here, age showed no statistically significant correlation with absenteeism, presenteeism, or AI. A positive correlation was observed between age and OWPL ($r=0.174$, $p=0.049$).

Table VII: Correlation between age and WPAI Domains

WPAI Domains	ρ	P value
Absenteeism	-0.241	0.062
Presenteeism	0.146	0.099
Work Productivity loss	0.174	0.049
Activity impairment	-0.015	0.820

Spearman's ρ rank correlation was used.

Patient-Reported Outcome (PRO) correlations

Table VIII displays the correlation between patient-reported outcomes and WPAI domains. BASDAI, ASDAS-CRP, and BASFI show strong positive correlations with all three work-related WPAI domains ($\rho \approx 0.45$ - 0.71 , all $p < 0.001$),

and moderate-to-strong correlations with activity impairment ($\rho \approx 0.55$ - 0.65). This confirms that higher disease activity, whether measured by symptoms (BASDAI), a composite inflammatory score (ASDAS-CRP), or functional capacity (BASFI), is associated with greater lost productivity at work and in daily life.

PCS-12 shows strong inverse correlations across all four WPAI domains (strongest with work productivity loss: $\rho = -0.74$). MCS-12, by contrast, is essentially independent of work productivity ($\rho \approx -0.11$ to -0.24 , all $p > 0.05$) and only weakly correlated with activity impairment ($\rho = -0.18$, $p = 0.008$), suggesting that among patients, psychological wellbeing (as captured by MCS) does not drive work-presenteeism or absenteeism.

ASQoL and GHQ-12 both correlate strongly with every WPAI domain ($\rho \approx 0.52$ - 0.70 , all $p < 0.001$), both of which co-move with productivity impairment. Spinal mobility (BASMI) correlates only moderately with presenteeism, work productivity loss, and activity impairment ($\rho \approx 0.33$ - 0.34), and is unrelated to absenteeism ($\rho = 0.16$, $p = 0.23$).

Table VIII: Spearman's Rank Correlations between PRO Measures and WPAI Domains among Patients with axSpA

Patient-Reported Outcome	Absenteeism n = 52–61 ρ (p)	Presenteeism n = 112–129 ρ (p)	WPL n = 112–129 ρ (p)	AI n = 182–218 ρ (p)
Disease activity and functional limitation				
BASFI	+0.50 ($p < .001$)	+0.69 ($p < .001$)	+0.71 ($p < .001$)	+0.55 ($p < .001$)
BASMI	+0.16 ($p = 0.230$)	+0.33 ($p < .001$)	+0.33 ($p < .001$)	+0.34 ($p < .001$)
ASDAS-CRP	+0.45 ($p < .001$)	+0.69 ($p < .001$)	+0.70 ($p < .001$)	+0.59 ($p < .001$)
BASDAI	+0.53 ($p < .001$)	+0.67 ($p < .001$)	+0.71 ($p < .001$)	+0.65 ($p < .001$)
Health-Related Quality of Life (SF-12)				
PCS-12	-0.48 ($p < .001$)	-0.69 ($p < .001$)	-0.74 ($p < .001$)	-0.54 ($p < .001$)
MCS-12	-0.24 ($p = 0.062$)	-0.12 ($p = 0.199$)	-0.11 ($p = 0.241$)	-0.18 ($p = 0.008$)
Disease-Specific Quality of Life & Psychological Distress				
ASQoL	+0.59 ($p < .001$)	+0.68 ($p < .001$)	+0.70 ($p < .001$)	+0.64 ($p < .001$)
GHQ-12	+0.52 ($p < .001$)	+0.65 ($p < .001$)	+0.69 ($p < .001$)	+0.58 ($p < .001$)

WPL= Work Productivity Loss; AI= Activity Impairment.

Spearman's rank correlation coefficients (ρ) were calculated using pairwise-complete observations, and Correlation magnitude bands: $|\rho| < 0.30$ weak, 0.30–0.50 moderate, 0.50–0.70 strong, > 0.70 very strong. WPAI work-related domains were restricted to participants with valid employment-related responses, whereas activity impairment was analyzed among participants with valid responses. Two-sided *p* values are reported; both positive and negative, significant ($p < 0.05$).

Table IX shows the multivariable logistic regression analysis that identified several independent predictors of unemployment among patients with axSpA. Multivariable logistic regression identified five independent factors associated with unemployment (Table IX). Older age, male sex, married status and higher PCS-12 scores were associated with lower odds of unemployment, whereas higher NRS pain scores were also independently associated with lower odds of unemployment after adjustment. Education, BASDAI, ASDAS-CRP ≥ 3.5 , ASQoL and GHQ-12 were not independently associated with unemployment.

Table IX: Multivariable Logistic Regression Analysis of Factors Independently Associated with Unemployment among Patients with axSpA

Predictor	Adjusted OR	95% CI	p value
Age, per 1-year increase	0.92	0.86–0.98	0.016
Male sex	0.04	0.01–0.10	<0.001
Education $\leq$ SSC	1.69	0.70–4.09	0.248
Married status	0.12	0.04–0.39	<0.001
NRS pain score, per 1-point increase	0.48	0.28–0.81	0.006
BASDAI	1.63	0.90–2.95	0.109
ASDAS-CRP ≥ 3.5	0.99	0.32–3.11	0.987
ASQoL	0.89	0.78–1.00	0.054
PCS-12, per 1-point increase	0.93	0.87–0.98	0.011
GHQ-12	1.08	0.98–1.20	0.128

The dependent variable was unemployment (unemployed=1, employed=0). Adjusted ORs were obtained from a multivariable logistic regression model including age, sex, education, marital status, pain score, BASDAI, ASDAS-CRP category, ASQoL, PCS-12 and GHQ-12. An adjusted OR <1 indicates lower odds of unemployment. CI, confidence interval; OR, odds ratio; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score based on C-reactive protein; ASQoL, Ankylosing Spondylitis Quality of Life; PCS-12, Physical Component Summary score of the Short Form-12; GHQ-12, General Health Questionnaire-12.

DISCUSSION

This study examined WPAI among 222 patients with axSpA attending a tertiary rheumatology facility in Bangladesh. The study population was relatively young (mean age 34.0 ± 8.5 years), predominantly male (66.7%), and had a mean disease duration of 6.31 ± 3.40 years. Despite this relatively young age, 38.7% of participants

were unemployed, indicating a substantial employment burden in this cohort. Among employed participants, WI was considerable, while activity impairment was significantly greater among unemployed than employed participants ($59.39 \pm 18.19\%$ vs $50.46 \pm 16.33\%$, $p=0.006$). These findings suggest that the functional consequences of axSpA extend beyond disease activity to occupational participation and everyday activities.

The clinical profile also demonstrated a substantial burden of disease. Peripheral arthritis was present in 72.1%, enthesitis in 45.0%, hip involvement in 29.7%, and sacroiliitis in 95.0%; HLA-B27 was positive in 43.2%. Mean BASDAI, BASFI and ASDAS-CRP scores were 2.70 ± 1.06 , 1.83 ± 1.32 and 2.95 ± 0.86 , respectively. Importantly, employed participants were older and had longer disease duration than unemployed participants, while sex, marital status, smoking, BMI and hip involvement also differed significantly between employment groups. These associations indicate that employment status in axSpA is influenced by a combination of demographic, social and clinical characteristics rather than by disease activity alone.

The substantial occupational burden observed in this study is consistent with the established impact of axSpA on employment and work participation. Chronic inflammatory rheumatic diseases are associated with impaired employment compared with the general population, with disability and functional limitation contributing importantly to work loss.¹³ Previous international studies have similarly demonstrated that axSpA can adversely affect work productivity, particularly through presenteeism and reduced functional capacity.^{5, 6, 10, 11}

The present findings extend this evidence to a Bangladeshi tertiary-care facility. Among employed participants, presenteeism and OWPL were significantly greater among those with education up to SSC than among those with higher education, while smoking was associated with greater OWPL. These observations suggest that social and behavioural characteristics may modify the occupational consequences of axSpA. International studies have also highlighted the importance of socioeconomic circumstances and work-related factors in determining outcomes among patients with axSpA.^{8, 12}

The strong correlations between disease activity, functional limitation and WPAI outcomes provide further evidence that clinical status is closely linked to productivity.

BASDAI, BASFI and ASDAS-CRP demonstrated moderate-to-very-strong positive correlations with work-related impairment, with the strongest associations observed for BASFI and BASDAI with OWPL ($p=0.71$ for both). Similarly, ASQoL and GHQ-12 correlated positively with all WPAI domains, whereas PCS-12 showed consistently strong inverse correlations, reaching $p=-0.74$ with OWPL. These findings accord with evidence that disease activity, functional disability, comorbidity and quality of life are interrelated determinants of the overall burden of axSpA.^{10,16,18}

The relatively weaker associations involving MCS-12 are noteworthy. Although MCS-12 was not significantly associated with absenteeism, presenteeism or OWPL, it showed a weak inverse correlation with activity impairment ($p=-0.18$, $p=0.008$). In contrast, GHQ-12 demonstrated stronger positive correlations across all WPAI domains. This difference may reflect the greater sensitivity of a disease-specific psychological distress measure to functional consequences than a generic mental health summary score. BMI also showed a significant association with AI ($p=0.031$), with the highest mean AI among underweight participants. However, absenteeism, presenteeism and OWPL did not differ significantly across BMI categories.

The strong relationships between BASFI, BASDAI, ASDAS-CRP, ASQoL, PCS-12 and WPAI measures suggest that improving functional capacity and health-related quality of life may be particularly relevant to maintaining productivity. International evidence similarly supports the importance of effective disease management in reducing work impairment.^{5,6,11}

The multivariable analysis provides an important additional perspective. Age, male sex, marital status, pain score and PCS-12 were independently associated with unemployment, whereas BASDAI, ASDAS-CRP, ASQoL and GHQ-12 were not independently associated after adjustment. Thus, the bivariate relationships between disease measures and employment should not be interpreted as evidence that disease activity alone determines employment status. The observational design also prevents causal interpretation of the inverse associations observed for pain and PCS-12. These findings reinforce the need to consider demographic and socioeconomic circumstances when assessing occupational vulnerability.

LIMITATION OF THE STUDY

The single-centre, hospital-based design limits generalisability to the broader Bangladeshi axSpA population. The cross-sectional nature of the analysis precludes determination of temporal or causal relationships between disease characteristics and employment. WPAI outcomes were based on participant-reported information and therefore may be affected by recall or reporting bias. Furthermore, the work-related WPAI analyses had variable numbers of valid observations, as reflected by the pairwise sample sizes in the correlation analysis.

CONCLUSION

Axial spondyloarthritis was associated with a substantial occupational and functional burden in this Bangladeshi tertiary-care cohort, with 38.7% of participants being unemployed and activity impairment significantly greater among unemployed than employed participants. Work productivity impairment was closely related to disease activity, functional limitation and physical health status, particularly BASDAI, BASFI, ASDAS-CRP and PCS-12. However, after multivariable adjustment, age, sex, marital status, pain score and PCS-12 were independently associated with unemployment, whereas BASDAI, ASDAS-CRP, ASQoL and GHQ-12 were not. These findings indicate that employment outcomes in axSpA are determined by interacting clinical, functional and sociodemographic factors rather than inflammatory disease activity alone. Early recognition, effective disease management, functional rehabilitation and attention to occupational and social circumstances may help preserve work participation and reduce activity impairment. Further multicentre longitudinal studies are warranted to clarify causal pathways and evaluate interventions aimed at improving employment and productivity outcomes in Bangladeshi patients with axSpA.

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Original Article

Complementary Feeding Practices and Associated Maternal Factors among Children Aged 6–24 Months Attending Dinajpur Medical College Hospital, Bangladesh

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Abstract

Complementary feeding during the first two years of life is critical for growth, nutrition, and neurodevelopment. While timely initiation has improved in many low and middle income countries, inadequate dietary diversity and inappropriate practices remain major concerns in Bangladesh. Maternal knowledge, education, and socioeconomic status are known to influence feeding practices, but evidence from northern Bangladesh is limited. This study was conducted to assess complementary feeding practices and maternal factors among children aged 6–24 months attending a tertiary health facility. A cross-sectional study was conducted in the Department of Paediatrics, Dinajpur Medical College Hospital (DjMCH) between December 2025 and May 2026. One hundred mother–child pairs were consecutively recruited. Data were collected using a structured, pretested questionnaire based on WHO recommendations. Maternal knowledge was assessed using a six-item scoring system. Descriptive statistics were presented as mean $\pm$ SD, frequencies, and percentages. Associations were evaluated using Chi-square tests, and univariate logistic regression estimated crude odds ratios (ORs) with 95% confidence intervals (CIs) for factors associated with early initiation (<6 months). Most mothers (46%) were aged 20–30 years, resided in rural areas (66%), and had completed secondary education (58%). The mean age of children was 14.2 ± 5.1 months; 56% were female. Cesarean delivery was common (61%). Exclusive breastfeeding, followed by complementary feeding at 6 months, was reported by 84%,

while 16% introduced foods earlier. Continued breastfeeding after initiation was practiced by 94%. Complementary feeding was dominated by cereal-based foods such as khichuri (28%), with limited animal-source foods (14%) and fruits/vegetables (8%), reflecting poor dietary diversity. Maternal knowledge was generally good (70%). Bivariate analysis showed significant associations between complementary feeding practices and monthly household income ($p=0.017$), but no significant associations were found between age, education, residence, employment, or knowledge. However, in univariate logistic regression, compared with households earning $\leq$ BDT 10,000 per month, the odds of early initiation were significantly higher among households earning BDT >10,000–20,000 and BDT >40,001–60,000, but other maternal factors were not significant. Although most mothers initiated complementary feeding and continued breastfeeding, dietary diversity and nutritional quality remained inadequate. Household income was the only factor significantly associated with early initiation, underscoring the role of socioeconomic circumstances. Strengthening nutrition education and targeted interventions may improve complementary feeding practices in Bangladesh.

Keywords: Complementary feeding; infant and young child feeding; dietary diversity; maternal knowledge.

INTRODUCTION

Appropriate complementary feeding is a critical intervention for ensuring optimal growth, neurodevelopment, and long-term health in early childhood. Exclusive breastfeeding is recommended for the first six months; however, breast milk alone becomes insufficient thereafter to meet infants' increasing nutritional needs. Thus, nutritionally adequate, safe, and age-appropriate complementary foods should be introduced while breastfeeding continues up to two years of age.^{1–4} Timely initiation of complementary feeding, alongside continued breastfeeding, supports physical growth, cognitive development, immune function, and healthy dietary habits throughout childhood.^{2–8}

The World Health Organization (WHO) defines complementary feeding as the process that begins when breast milk alone no longer satisfies nutritional

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requirements, necessitating other foods and liquids alongside breastfeeding.^{3,4} The complementary feeding period (6–24 months) is a critical window for growth and development, during which infants acquire the physiological and neuromuscular abilities for chewing, swallowing, digestion, and acceptance of diverse foods.^{3–8} Complementary foods should provide adequate energy, protein, iron, zinc, calcium, essential fatty acids, and vitamins, while ensuring appropriate consistency, diversity, frequency, and hygienic preparation.^{5–10}

Despite clear international recommendations, practices remain suboptimal in many low- and middle-income countries. Early or delayed introduction of foods, inadequate meal frequency, poor dietary diversity, and reliance on cereal-based diets contribute to undernutrition and micronutrient deficiencies.^{5–10} International studies show limited inclusion of animal-source foods, fruits, and vegetables, thereby reducing dietary quality during this vulnerable period.^{8–10} These practices heighten the risk of growth faltering, recurrent infections, impaired cognitive development, and long-term adverse health outcomes.^{3–10}

Maternal knowledge, education, socioeconomic status, cultural beliefs, family support, and access to counselling are key determinants of feeding practices.^{9,10} Mothers with better knowledge are more likely to initiate feeding at the recommended age and provide diverse diets. Yet knowledge alone does not guarantee optimal behaviour, as financial constraints, food insecurity, traditional practices, limited availability of nutrient-rich foods, and inadequate family support often shape decisions.^{9,10,21,22,26–28} Understanding maternal knowledge alongside socioeconomic context is therefore essential for designing effective interventions.

Globally, complementary feeding indicators remain unsatisfactory. WHO/UNICEF and the Global Nutrition Report highlight that only a minority of children aged 6–23 months receive a minimum acceptable diet, with inadequate dietary diversity widespread.^{7,11} Similar findings are reported across South Asia, where national surveys reveal persistent deficiencies in dietary diversity and meal adequacy despite improvements in maternal education and child health services.¹² In Bangladesh, surveys such as the Bangladesh Demographic and Health Survey (BDHS) and the Multiple Indicator Cluster Survey (MICS) show progress in breastfeeding practices but continued gaps in complementary feeding, particularly regarding dietary diversity, animal-source food consumption, and achievement of a minimum acceptable diet.^{13–17}

Studies in Bangladesh and neighbouring countries consistently demonstrate associations between feeding practices and maternal education, household income, residence, autonomy, and access to health information.^{15–28} However, regional variation persists due to differences in socioeconomic conditions, food availability, cultural practices, and healthcare access. Most evidence derives from national surveys or community-based studies, while hospital-based data from northern Bangladesh remains limited. Few studies have simultaneously examined the timing of initiation, types of foods, maternal knowledge, and socioeconomic characteristics within the same population.

Dinajpur Medical College Hospital serves a large population in northern Bangladesh, including rural and socio-economically disadvantaged families where childhood malnutrition remains a pressing concern. Generating local evidence from this setting may help identify context-specific gaps in feeding practices and inform targeted counselling and public health interventions. Therefore, this study aimed to assess complementary feeding practices among children aged 6–24 months attending Dinajpur Medical College Hospital and to examine maternal socioeconomic and knowledge-related factors associated with these practices.

MATERIALS AND METHODS

Study Design and Setting: This cross-sectional study was conducted in the Department of Paediatrics, Dinajpur Medical College Hospital (DjMCH), northern Bangladesh, between December 2025 and May 2026. DjMCH is a tertiary referral hospital serving both urban and rural populations, including socioeconomically disadvantaged families where childhood malnutrition is a major concern.

Study Population: Participants included children aged 6–24 months attending the Paediatric Outpatient Department (OPD) during the study period. Mothers or primary caregivers accompanying the children were interviewed, as they were directly responsible for feeding practices.

Sample Size and Sampling Technique: The calculated sample size was 384 mother–child pairs using standard formulae. Due to time and resource constraints, 100 consecutive eligible pairs were recruited, ensuring every child meeting the criteria during data collection was included.

Eligibility Criteria: Inclusion criteria were children aged 6–24 months attending the OPD with mothers who

provided written informed consent. Exclusion criteria included children younger than 6 months or older than 24 months, adopted children, those with major congenital anomalies or severe developmental disorders affecting feeding, and mothers unwilling to participate.

Study Variables: The primary outcome was complementary feeding practice, including timing of initiation, continuation of breastfeeding, and types of foods provided. Explanatory variables included maternal age, education, occupation, residence, household income, parity, and knowledge of complementary feeding. Child-related variables such as age, sex, gestational age, birth weight, mode of delivery, and exclusive breastfeeding history were also collected.

Data Collection Instrument and Procedure: Data were gathered through face-to-face interviews using a structured, pretested questionnaire administered by the principal investigator. The tool was developed after reviewing WHO recommendations and relevant literature, then adapted to the local context. Pretesting was conducted among ten mother–child pairs not included in the final study.

Assessment of Maternal Knowledge: Maternal knowledge was assessed using six questions based on WHO guidelines and published literature. Items covered recommended age of initiation, appropriate foods, continued breastfeeding, meal frequency, and consequences of inappropriate feeding. Each correct answer scored one point; incorrect or “don’t know” responses scored zero. The maximum score was six. Mothers scoring ≥ 4 were classified as having good knowledge, while those scoring < 4 were categorized as having poor knowledge. Four additional questions assessed practices but were analyzed separately.

Statistical Analysis: Data were coded, checked, and entered into SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD), while categorical variables were presented as frequencies and percentages. Associations between categorical variables were tested using Chi-square or Fisher’s exact test. Crude odds ratios (ORs) with 95% confidence intervals (CIs) were estimated via univariate logistic regression to identify maternal factors associated with early initiation (< 6 months) compared with timely initiation. Statistical significance was set at $p < 0.05$. Due to the small sample size and limited outcome events, multivariable regression was not performed.

Ethical Clearance: Ethical approval was obtained from the Institutional Review Board of DjMCH prior to data collection. Written informed consent was secured from all participating mothers or caregivers after explaining study objectives and procedures. Participation was voluntary,

with assurances that refusal or withdrawal would not affect medical care. Confidentiality and anonymity were maintained using unique identification numbers, and access to data was restricted to investigators.

RESULTS

A total of 100 children aged 6–24 months were included in the study.

Maternal Sociodemographic and Economic Characteristics

Table I outlines the socio demographic and economic characteristics of the mothers. Among these mothers, 46.0% were 21 to 25 years old, 35.0% were 20 years or younger, and 19% were over 25 years. Regarding educational status, 35% had completed HSC or were graduates, 30% had completed SSC, 28% had reached high school level, and 7% were either illiterate or had only primary education. Among the mothers, 66.0% resided in rural areas, and 34% in urban areas. Notably, 89.0% were housewives, with 11% being self-employed or employed. Monthly household income for 42.0% of the mothers was $\leq 10,000$ BDT, while 37%, 12%, 4%, and 5% had $> 10,000$ to 20,000; $> 20,001$ to 40,000; $> 40,000$ to 60,000; and $> 60,000$ BDT, respectively.

Table I: Sociodemographic and Economic Characteristics of Mothers (N=100)

Characteristics	Category	Percentage
Maternal age	In years	
	≤ 20	35%
	21-25	46%
	> 25	19%
Mother’s education status	Level of education	
	Illiterate and Primary level	7%
	High school level + SSC pass	58%
	HSC Pass and graduate	35%
Residence of mother	Resident	
	Rural	66%
	Urban	34%
Employment status	Service	
	House wife	89%
	Self-employed and job holder	11%
Family income (in taka)	Bangladeshi Taka (BDT) per month	
	$\leq 10,000$ BDT	42%
	$> 10,000$ –20,000	37%
	$> 20,001$ –40,000	12%
	$> 40,001$ –60,000	4%
	$> 60,000$	5%

Secondary School Certificate (SSC); Higher Secondary Certificate (HSC).

Child Characteristics

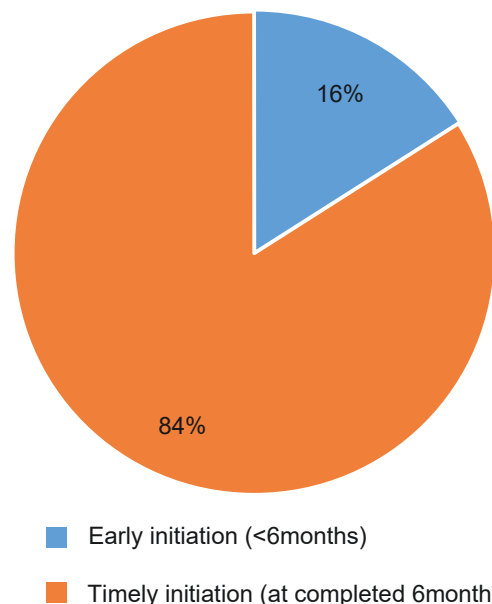
Table II provides a summary of the characteristics of the children. Among them, 55.0% were in the age group of 6 to 12 months, with 56% of females. A notable 97.0% were born at term (between 37 to 42 weeks of gestational age), and 89.0% had a normal birth weight of 2500 to 4000 grams. Deliveries occurred in health facilities, with 61.0% by caesarean section and 39.0% by vaginal delivery. Exclusive breastfeeding for six months was reported in 84.0% of children.

Table II: Characteristics of Children (N=100)

Characteristics	Category	Percentage
Age of the child	Months	
	6-12	55%
	13-18	28%
	19-24	17%
Sex	Female	56%
	Male	44%
Gestational age at delivery	Weeks	
	37-42	97%
	<37	3%
Birth weight	Grams	
	<2500	7%
	2500-4000	89%
	>4000	4%
Mode of institutional delivery	Normal vaginal delivery	39%
	Cesarean section	61%
Exclusive breastfeeding	Yes	84%
	No	16%

Timing of Complementary Feeding Initiation

Figure 1 illustrates the timing of complementary feeding initiation. Complementary foods at the recommended age of 6 completed months were introduced to 84.0% of children, while early initiation (<6 months) was found in 16.0%.



Early initiation is defined as <6 months; timely initiation is defined as exactly six completed months.

Figure 1: Timing of Complementary Feeding Initiation among Children Aged 6–24 Months (N=100)

Types of Complementary Feeding Initiation

Table III shows the types of complementary foods provided. Khichuri was initiated among 28.0% of children as a complementary food, followed by suji (18.0%) and rice gruel (17.0%). Only 14.0% received animal source foods (fish, meat, eggs), 8.0% fruits or vegetables, and 3.0% received milk other than breast milk (formula, cow, or goat milk).

Table III: Types of Complementary Feeding Initiation (N=100)

Types of food	Percentage (%)
Milk (formula, cow or goat milk)	3%
Suji	18%
Haluwa	12%
Khichuri	28%
Rice or rice gruel	17%
Animal protein (fish, meat, egg)	14%
Others (Fruit or vegetable puree)	8%

Maternal Knowledge and Practices Regarding Complementary Feeding

Table IV displays maternal knowledge and practices. Here, 94.0% of mothers recognized that breast milk is more easily digested than other foods, whereas 84.0% knew both that complementary feeding should begin at six months and that children need to consume 2 or more meals per day, along with breast milk. However, 83% recognized that a late start of complementary feeding has physical risks, and 69.0% identified malnutrition as the main

consequence of late initiation of complementary feeding. A single mother (1%) subscribed to the misconception that "the health advantages of breast milk are equivalent to those offered by other food sources."

Regarding practices, Exclusive breastfeeding up to 6 months was reported by 84.0% of mothers, 94.0% continued breastfeeding with complementary feeding, 79.0% reported feeding ≥ 4 times per day, 69% used family food as complementary feeding, and 60% maintained proper hygiene during the preparation of complementary food.

Table IV: Maternal Knowledge and Practices Regarding Complementary Feeding (N=100)

Variables	Response	Percentage (%)
Knowledge of complementary feeding		
Breast milk is more easily digested than any other food	True	94%
Semi-solid, solid, and soft foods should be introduced at 6 months	True	84%
Any other food and breast milk have the same health benefits	True	1%
Late start of complementary feeding has physical risks	True	83%
Malnutrition is the main consequence of the late initiation of complementary feeding	True	69%
Children need to consume two meals or more per day, along with breast milk	True	84%
Practice of complementary feeding		
Exclusive breastfeeding up to 6 months	Yes	84%
Maintaining proper hygiene during the preparation of complementary food	Yes	60%
Using family food as complementary feeding	Yes	69%
Continued breastfeeding with complementary feeding	Yes	94%
Feeding ≥ 4 times a day	Yes	79%

Inferential Statistical Analysis

Relationship between Maternal Factors and Feeding Practices

Table V shows the associations between the maternal factors and the timing of complementary feeding initiation. Maternal age, education, residence, employment status, and knowledge were not significantly associated with the timing of complementary feeding initiation. Timely initiation was most frequently observed among mothers aged 21–25 years (45.2%), followed by those with a high school+SSC pass education level (59.5%), rural residents

(64.3%), employed as housewives (88.1%), and belonged to good knowledge (69.0%). Monthly household income was the only socio-demographic and economic factor significantly associated with complementary feeding practices ($p=0.017$). Early initiation was most common among households with a monthly income of BDT >10,000–20,000 (56.2%), whereas timely initiation was highest among families earning $\leq 10,000$ BDT (47.6%). Here, timely initiation was more frequent among mothers with good knowledge (69.0%) than among those with poor knowledge (31.0%).

Table V: Relationship between Maternal Sociodemographic and Economic Factors and Timing of Complementary Feeding Initiation (N=100)

Variables	Early initiation n (%)	Timely initiation n (%)	Exact p-value
Maternal age (years)			0.551
≤20 (n=35)	4 (25.0)	31 (36.9)	
21–25 (n=46)	8 (50.0)	38 (45.2)	
>25 (n=19)	4 (25.0)	15 (17.9)	
Mother's education status			0.468
Illiterate + primary level (n=7)	2 (12.5)	5 (6.0)	
High school level + SSC pass (n=58)	8 (50.0)	50 (59.5)	
HSC pass + graduate (n=35)	6 (37.5)	29 (34.5)	
Residence			0.567
Rural (n=66)	12 (75.0)	54 (64.3)	
Urban (n=34)	4 (25.0)	30 (35.7)	
Employment status			1.000
Housewife (n=89)	15 (93.8)	74 (88.1)	
Self-employed + job holder (n=11)	1 (6.2)	10 (11.9)	
Monthly family income (BDT)			0.017
≤10,000 (n=42)	2 (12.5)	40 (47.6)	
>10,000-20,000 (n=37)	9 (56.2)	28 (33.3)	
>20,000-40,000 (n=12)	3 (18.8)	9 (10.7)	
>40,000-60,000 (n=4)	2 (12.5)	2 (2.4)	
>60,000 (n=5)	0	5 (6.0)	
Maternal knowledge			
Poor (n=30)	4 (25.0)	26 (31.0)	0.711
Good (n=70)	12 (75.0)	58 (69.0)	

Early initiation: <6 months; timely initiation: 6 completed months. Percentages are row percentages. Exact tests were used because of small cell counts.

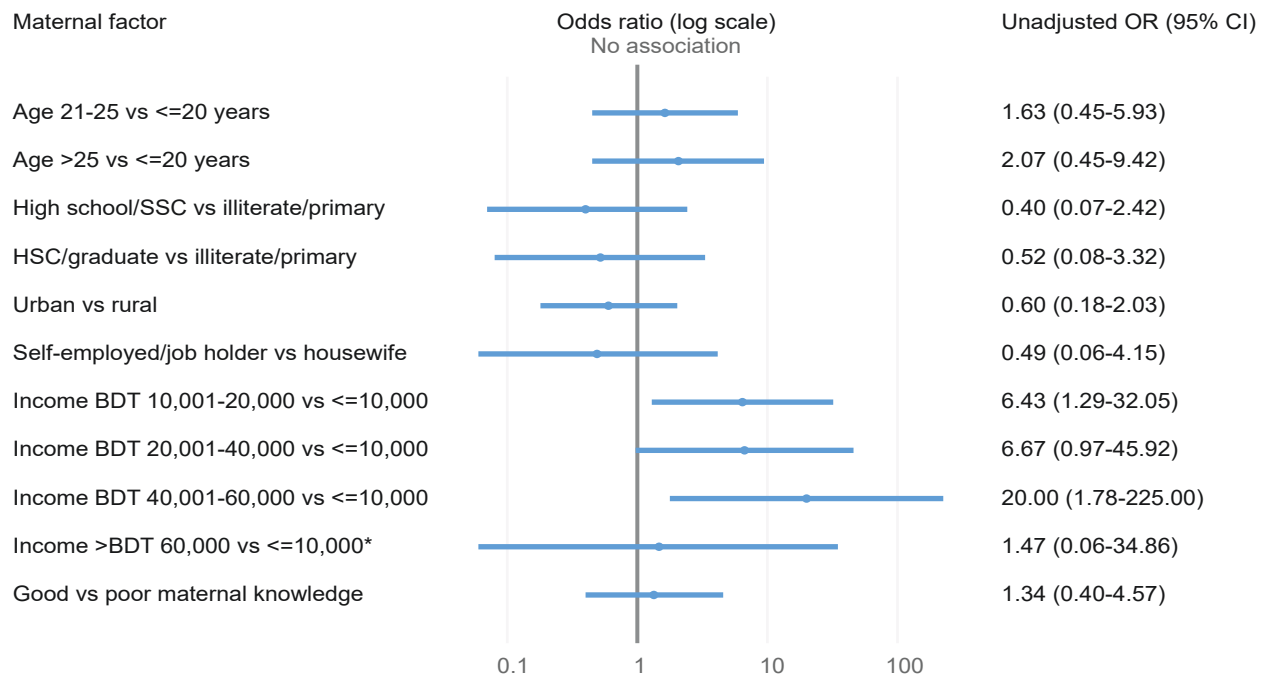
Logistic Regression Analysis

Table VI presents unadjusted logistic regression estimates for early initiation of complementary feeding (<6 months), with timely initiation at 6 completed months as the comparison group. Compared with households earning ≤ BDT 10,000 per month, the odds of early initiation were

significantly higher among households earning BDT >10,000-20,000 (OR 6.43, 95% CI 1.29-32.05; $p=0.023$) and BDT >40,001-60,000 (OR 20.00, 95% CI 1.78–225.00; $p=0.015$). Other maternal factors were not statistically significant. The estimate for income >BDT 60,000 used a 0.5 continuity correction because no early-initiation event occurred in that group.

Table VI: Unadjusted Logistic Regression Analysis of Maternal Factors Associated with Early Initiation of Complementary Feeding (N=100)

Variable	Category	Unadjusted OR (95% CI)	p-value
Maternal age (years)	≤20	Ref.	
	21–25	1.63 (0.45–5.93)	0.457
	>25	2.07 (0.45–9.42)	0.348
Mother's education status	Illiterate + primary level	Ref.	
	High school level + SSC pass	0.40 (0.07–2.42)	0.319
	HSC pass + graduate	0.52 (0.08–3.32)	0.487
Residence	Rural	Ref.	
	Urban	0.60 (0.18–2.03)	0.410
Employment status	Housewife	Ref.	
	Self-employed + job holder	0.49 (0.06–4.15)	0.515
Monthly family income (BDT)	≤10,000	Ref.	
	>10,000–20,000	6.43 (1.29–32.05)	0.023
	>20,000–40,000	6.67 (0.97–45.92)	0.054
	>40,000–60,000	20.00 (1.78–225.00)	0.015
	>60,000	1.47 (0.06–34.86)	0.811
Maternal knowledge	Poor	Ref.	
	Good	1.34 (0.40–4.57)	0.635



*Estimate uses a 0.5 continuity correction because there were no early-initiation events in this group.

Figure 2: Forest Plot of Unadjusted Logistic Regression Analysis of Maternal Factors Associated with Early Initiation of Complementary Feeding

Figure 2, the forest plot, presents unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) for early initiation of complementary feeding before 6 months of age. The vertical line at OR=1 represents no association. Most maternal factors were not significantly associated with early initiation. Compared with households earning $\leq$ BDT 10,000 per month, households' monthly incomes of BDT >10,000–20,000 and BDT >40,000–60,000 had significantly higher unadjusted odds of early initiation. The confidence intervals were wide, reflecting the small number of early-initiation events ($n=16$); therefore, the estimates should be interpreted cautiously.

DISCUSSION

This hospital-based cross-sectional study assessed complementary feeding practices and maternal factors among 100 children aged 6–24 months at DjMCH. Findings showed encouraging adherence to WHO recommendations, i.e., 84.0% of children received complementary foods at six completed months, and 94.0% continued breastfeeding thereafter. However, nutritional quality was suboptimal, with diets dominated by cereal-based foods and limited intake of animal-source foods (14.0%) and fruits/vegetables (8.0%). Although 70.0% of mothers demonstrated good knowledge, gaps persisted regarding dietary diversity and the consequences of inappropriate feeding.

Bivariate analysis identified significant associations between feeding practices and maternal monthly household income; then logistic regression revealed household income as the only significant factor for early initiation, underscoring socioeconomic influence despite satisfactory maternal awareness.

The socio-demographic profile of participants- mean child age 14.2 ± 5.1 months, 56.0% female, the majority of mothers aged 20–30 years, 66.0% rural, and 58.0% with secondary education (High school level + SSC pass) resembles national surveys such as BDHS and other Bangladeshi studies.^{13–17,19} Despite improvements in maternal education, many households remained low-income, reflecting persistent inequalities that may affect feeding behaviour.

Compliance with WHO recommendations was notable: 84.0% initiated complementary feeding at six months, consistent with reports from Bangladesh, Pakistan, Malaysia, Saudi Arabia, and the UAE, where maternal and child health programmes have improved timely initiation.^{1,6,10,15–17,26} Yet 16.0% introduced foods earlier, a concern given associations with diarrhoeal disease,

reduced breast milk intake, and poor nutritional balance.^{3,4,7} Continued breastfeeding by 94.0% of mothers aligns with WHO guidance to maintain breastfeeding up to two years or beyond.^{3,4,7}

Despite timely initiation, dietary quality was poor. Cereal-based foods, especially khichuri (28.0%), predominated, while animal-source foods and fruits/vegetables were rarely consumed. Similar patterns are reported in Bangladesh and other LMICs, where carbohydrate-rich staples dominate complementary diets with limited diversity and micronutrient adequacy.^{5,8,15,17,25} Such practices risk deficiencies in iron, zinc, vitamin A, and other micronutrients, contributing to impaired growth and development.^{3,5,7,8}

Maternal knowledge was generally satisfactory, with 70.0% scoring well and most identifying six months as the correct initiation age. Comparable findings have been reported in Bangladesh, Saudi Arabia, and Malaysia, reflecting improved awareness through antenatal care and nutrition education.^{10,19,21,22,26} This gap between knowledge and practice has been noted previously, suggesting that awareness alone is insufficient when constrained by financial limitations, food insecurity, cultural beliefs, and restricted access to diverse foods.^{9,21,22,26–28}

Bivariate analysis showed a relationship between feeding practices and maternal education, knowledge, and household income, consistent with findings from Bangladesh, Ethiopia, Nepal, and other South Asian countries, where higher education and socioeconomic status improve adherence to recommended practices.^{15–19,21–23,27}

Univariate logistic regression highlighted household income as the only significant factor for early initiation (<6 months), while maternal age, education, residence, occupation, parity, and knowledge were not significant. This distinction reflects crude odds ratios without multivariable adjustment. Thus, maternal education or knowledge cannot be considered an independent predictor in this study. The small sample size and limited early initiation cases ($n=16$) reduced statistical power, producing wide confidence intervals. Household income therefore emerged as the strongest correlate in this sample, though not necessarily a causal determinant.

LIMITATIONS OF THE STUDY

Limitations include the small sample size, single-centre design, limited generalizability, reliance on maternal recall (risking recall and social desirability bias), and absence of multivariable regression to adjust for confounding.

CONCLUSION

Complementary feeding practices among children aged 6–24 months at Dinajpur Medical College Hospital were generally satisfactory, with 84.0% timely initiation and 94.0% continued breastfeeding, reflecting adherence to WHO recommendations. However, dietary diversity was poor, with limited intake of animal-source foods, fruits, and vegetables despite good maternal knowledge. Bivariate analysis linked practices to maternal education, knowledge, and income, but logistic regression identified household income as the only significant factor for early initiation, underscoring socioeconomic influence. Strengthening nutrition programmes should combine maternal education with counselling on dietary diversity while addressing economic barriers. Larger multicentre studies are recommended. Larger multicentre community-based studies with multivariable analyses are needed to clarify independent factors influencing complementary feeding practices in Bangladesh.

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Original Article

Sociodemographic Profile, Treatment-Seeking Patterns, and Psycho-Social Factors Related to Corrosive Poisoning in Adults: A Hospital-Based Study in Bangladesh

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Abstract

Corrosive poisoning remains an important public health problem in Bangladesh and other low and middle income countries, contributing substantially to morbidity, healthcare utilization, and socioeconomic burden. Unlike agricultural poisoning, corrosive ingestion is frequently associated with psycho-social stress, deliberate self harm, and easy household access to caustic cleaning agents. However, contemporary evidence describing the sociodemographic characteristics, treatment-seeking behaviour, and precipitating psychosocial factors of corrosive poisoning in Bangladesh remains limited to describe the socio demographic profile, treatment-seeking behaviour, corrosive exposure pattern, and causal factors

among adult patients admitted with corrosive poisoning to a tertiary care hospital. This hospital-based cross-sectional observational study was conducted among 50 adult patients with corrosive poisoning in the Department of Medicine at Dhaka Medical College Hospital, Bangladesh, from October 2013 to April 2014. Data on demographic characteristics, education, residence, socioeconomic status, type of corrosive agent, treatment-seeking behavior, and psychosocial factors were collected through structured interviews. Descriptive statistics summarized the findings, and categorical variables were compared using the Chi-square test. A p-value <0.05 was considered statistically significant. The mean age of the study population (Mean±SD=26.4±6.1) was concentrated in young adulthood, with the largest proportion (38.0%) in the 21–30-year age group, followed by ≤20 years (34.0%). Females constituted 64.0% of participants, yielding a female-to-male ratio of 1.8:1. More than half (56.0%) of the patients had completed secondary or higher secondary education, while over one-third (34%) had primary or informal education. Moreover, 68.0% of the patients resided in urban areas, with females constituting over two-thirds (67.65%) of the urban population. These socio-demographic factors were not significantly associated with sex (p > 0.05). Socio economically, 44.0%, 38.0%, and only 18.0% belonged to the poor, middle-income, and upper income group, respectively. Household cleaning products predominated, with Savlon accounting for 36.0% of ingestions, Harpic for 24.0%, bleach/Lysol for 16.0%, phenol for 10.0%, hydrochloric acid for 8.0%, and Sulphuric acid for 6.0%. Regarding healthcare utilization, nearly two-thirds (64.0%) sought treatment within 5 hours, while about one-third (32.0%) within 6-12 hours, and only 4.0% after 12 hours of ingestion. Overall, 58.0% presented directly to government hospitals, whereas 42.0% initially sought treatment elsewhere (private hospitals or clinics, private physicians, and quack practitioners) before referral. Familial disharmony was the most prevalent precipitating factor (48.0%), followed by romantic disappointment (28.0%), misunderstanding with parents (10.0%), educational stress (10.0%), and extramarital relationship problems (4.0%).

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Familial disharmony predominated among male participants, whereas romantic disappointment was substantially more frequent among females. However, the relationship between sex and the reported causal factors did not reach statistical significance ($p = 0.074$). Corrosive poisoning predominantly affected young urban females from socioeconomically disadvantaged households and was closely related to psychosocial stressors, particularly familial disharmony. Household cleaning agents were the principal corrosive substances, and most patients sought medical attention within five hours. Public health interventions should focus on psycho-social support, community awareness, and strengthening emergency referral systems to reduce the burden of corrosive poisoning in Bangladesh.

Keywords: Corrosive poisoning; sociodemographic factors; treatment-seeking behaviour; psychosocial factors; household cleaning agents.

INTRODUCTION

Poisoning remains a major public health problem worldwide and is responsible for substantial mortality, morbidity, and healthcare expenditure, particularly in low- and middle-income countries. Deliberate self-poisoning, especially among children and young adults, accounts for a considerable proportion of emergency medical admissions. In Bangladesh, poisoning represents an important cause of hospital admission. According to the Directorate General of Health Services (DGHS), poisoning and other external causes account for nearly one-third of adult hospital admissions, while injuries and poisoning together contribute substantially to hospital deaths, underscoring the continuing public health importance of this problem.^{1,2}

Among various toxic exposures, corrosive poisoning is particularly important because it causes immediate chemical injury to the upper gastrointestinal tract. Corrosive agents include strong acids and alkalis commonly found in household cleaning products, toilet cleaners, bleaching agents, disinfectants, rust removers, drain cleaners, and industrial chemicals. In Bangladesh, hydrochloric acid-containing toilet cleaners, phenolic disinfectants, sodium hypochlorite solutions, and other domestic cleansing agents are among the commonly implicated substances in corrosive poisoning.³⁻⁶ Household disinfectants, toilet cleaners, antiseptic solutions, and bleaching products have become increasingly common. Similar observations have

been reported from neighbouring countries.^{8,13,14} Availability of corrosive substances, and their widespread domestic use increases the likelihood of both accidental exposure and impulsive acts of self-harm.^{3,6,19}

In high-income nations, accidental ingestion predominantly affects young children and frequently involves alkaline household products. Conversely, in South Asian countries, including Bangladesh, India, and Pakistan, intentional ingestion among adolescents and young adults constitutes the majority of cases, with acidic household cleaning agents being more commonly implicated than alkalis.^{5,7,8} Several studies have demonstrated that females constitute a higher proportion of patients presenting with deliberate corrosive ingestion.^{9,10}

Young adults consistently represent the highest-risk population. Previous Bangladeshi studies have reported that approximately one-third to two-fifths of poisoning victims are between 21 and 30 years of age, while females comprise approximately two-thirds to three-quarters of deliberate poisoning cases.^{9,10} Furthermore, most patients belong to lower- or middle-income households and possess only secondary or higher secondary education.^{9,14,15}

Many patients initially seek treatment from private practitioners, local clinics, or informal healthcare providers before referral to tertiary hospitals, resulting in potentially preventable delays in definitive management. Understanding treatment-seeking behaviour is therefore essential for developing effective referral systems and public health interventions aimed at reducing morbidity associated with corrosive poisoning.¹⁵⁻¹⁷

Family conflict, relationship problems, poverty, academic failure, and psychological distress are frequent antecedents of deliberate self-poisoning; however, changing patterns of urbanization and increasing availability of household cleaning products may have altered the epidemiology of corrosive poisoning in Bangladesh.^{13,14,18} Familial disharmony, domestic violence, interpersonal conflict, romantic disappointment, financial hardship, educational stress, and social instability are common precipitating factors for deliberate self-poisoning.^{14,21,22}

Early hospital presentation facilitates prompt stabilization, airway protection, nutritional support, and appropriate diagnostic evaluation, thereby reducing the risk of complications. Understanding where patients first seek medical care, the time elapsed before hospital admission,

and the factors influencing healthcare utilization can provide valuable information for strengthening referral pathways and improving emergency care services.^{15,16,20}

Identifying high-risk age groups, sex distribution, educational attainment, socioeconomic status, and residential patterns enables policymakers to design targeted prevention strategies for vulnerable populations. Such information may also support the development of school-based mental health programmes, community education regarding safe storage of corrosive substances, and improved poison prevention initiatives.^{1,2,15,23}

Therefore, this study was undertaken to describe the sociodemographic characteristics of adults presenting with corrosive poisoning, identify the commonly ingested corrosive agents, evaluate treatment-seeking behaviour following ingestion, and explore the psycho-social factors associated with corrosive poisoning in a tertiary care hospital in Bangladesh.

MATERIALS AND METHODS

Study Design and Setting: This hospital-based cross-sectional observational study was conducted in the Department of Medicine, Dhaka Medical College Hospital (DMCH), Dhaka, Bangladesh, one of the largest tertiary referral hospitals in the country. The study was carried out over six months from 14 October 2013 to 13 April 2014. The study aimed to investigate the socio-demographic characteristics, treatment-seeking behaviour, and psycho-social factors associated with corrosive poisoning among adult patients admitted to the hospital.

Study Population: The study population comprised adult patients presenting with a definite history of corrosive substance ingestion who were admitted to the Department of Medicine during the study period. All eligible patients admitted consecutively during the study period were considered for inclusion. Patients were eligible if they were aged 18 years or older, had a definite history of ingestion of a corrosive substance, were admitted within 24 hours of ingestion, and provided informed written consent to participate. Patients who had poisoning due to non-corrosive substances, had a previous history of oesophageal or gastric surgery, had known oesophageal malignancy or chronic oesophageal disease, were haemodynamically unstable or medically unsuitable for study procedures, and declined to participate were excluded from the study.

Sample Size and Sampling Technique: The estimated minimum sample size was calculated using the standard formula for a single population proportion based on the expected prevalence of corrosive poisoning reported in previous literature. However, because corrosive poisoning is relatively uncommon and the study duration was limited to six months, all eligible patients during the data collection period were included (consecutive census), resulting in a final sample of 50 participants. Consecutive sampling minimized selection bias and reflected the actual hospital caseload during the study period.

Data Collection Procedure: Following initial clinical stabilization, eligible patients were interviewed using a pretested structured case record form developed for the study. Whenever patients were unable to provide reliable information immediately after admission, additional information was obtained from accompanying family members or caregivers and subsequently verified with the patient whenever possible. Data were collected through direct interviews, physical examination, review of hospital records, and relevant laboratory reports. Information was recorded prospectively by the investigators throughout hospitalization.

Primary Outcome Variables:

The principal variables evaluated in this manuscript included age; sex; place of residence; marital status; educational attainment; occupation; socioeconomic status; type of corrosive substance ingested; circumstances and underlying causes of poisoning; interval between ingestion and hospital presentation; first healthcare facility or healthcare provider consulted; and referral pathway before admission to the tertiary hospital. The principal exposure variables included demographic characteristics, socioeconomic status, accessibility of corrosive agents, psychosocial factors, and treatment-seeking behaviour following ingestion.

Operational Definitions

Corrosive poisoning: Ingestion of a strong acidic or alkaline chemical capable of causing chemical injury to the mucosa of the upper gastrointestinal tract.

Treatment-seeking behaviour: The sequence of actions undertaken by the patient after corrosive ingestion, including the first healthcare provider consulted, time elapsed before hospital presentation, referral pathway, and

treatment received before admission to Dhaka Medical College Hospital.

Socioeconomic status: Socioeconomic class was categorized according to monthly household income as poor (approximately BDT 5,000 or <5000), middle (between BDT 5,800 and BDT 19,000), and upper (BDT 19,000 or above) class. Socioeconomic status is classified by household income, in accordance with the Executive Summary and Statistical Pocketbook of Bangladesh-2013: Bangladesh Bureau of Statistics.

Psychosocial factors: Psychosocial factors were identified by the physician's report and patient's statement.

Ethical Considerations: Ethical approval was obtained from the institutional ethical review authority of Dhaka Medical College before commencement of the study. Written informed consent was obtained from every participant before enrolment. Confidentiality of patient information was maintained throughout the study, and all collected data were anonymized before analysis. Participation was voluntary, and patients retained the right to withdraw from the study at any stage without affecting their treatment.

Statistical Analysis: Data were checked for completeness, coded, and entered into a computerized database before analysis using Statistical Package for the Social Sciences (SPSS) software (version 16). Continuous variables were summarized as mean $\pm$ standard deviation and categorical

variables were expressed as frequencies and percentages. Associations between categorical variables were evaluated using the Chi-square test or Fisher's exact test whenever appropriate. All statistical tests were two-tailed, and a p -value <0.05 was considered statistically significant.

RESULTS

Participant Characteristics

Table I shows the baseline demographic and socioeconomic characteristics of the participants. A total of 50 adult patients with corrosive poisoning were enrolled in the study. The mean age $\pm$ standard deviation (Mean $\pm$ SD) of respondents was 26.4 ± 6.1 , whereas females constituted 64% of the study population, yielding a male-to-female ratio of about 1:1.8. Here, 38.0%, 34%, and 28% of patients were in the age group of 21 - 30, ≤ 20 , and 31 - >40 years, respectively. Regarding educational attainment, primary and informal education, secondary, higher secondary, and graduate and above levels of education were found in 17 (34%), 13 (26.0%), 15 (30.0%), and 5 (10.0%) of patients, respectively. In males, 53.8% and in females, 46.2% were found at the secondary level, whereas in females, 11 (73.3%) and in males, 26.7% of patients were found at the higher secondary level. Patients affected from urban areas were 68.0%, and from rural areas, 32.0%. The distributions of age group, educational level, and place of residence did not differ significantly between male and female patients (p -value significant at $< .05$).

Table I. Baseline Sociodemographic Characteristics of Participants (N = 50)

Characteristic	Category	Total n	M n (%)	F n (%)	p-value*
	Mean $\pm$ SD	26.4 $\pm$ 6.1			
Age (years)	≤ 20	17	3 (17.6)	14 (82.4)	0.147
	21–30	19	9 (47.4)	10 (52.6)	
	31– >40	14	6 (42.9)	8 (57.1)	
Educational level	Primary & informal education	17	6 (35.3)	11 (64.7)	0.404
	Secondary	13	7 (53.8)	6 (46.2)	
	Higher secondary	15	4 (26.7)	11 (73.3)	
	Graduate & above	5	1 (20.0)	4 (80.0)	
Residence	Rural	16	7 (43.8)	9 (56.2)	0.434
	Urban	34	11 (32.4)	23 (67.6)	

SD= Standard deviation; M= Male; F= Female; *Pearson's χ^2 test. Values are presented as number (%). Percentages for males and females are calculated within each category, whereas percentages in the Total column are based on the overall study population (N = 50).

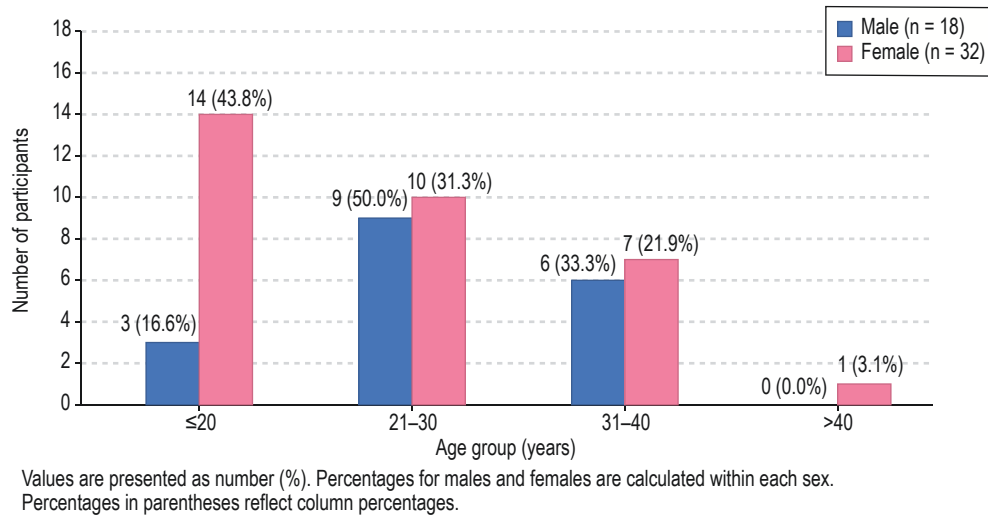
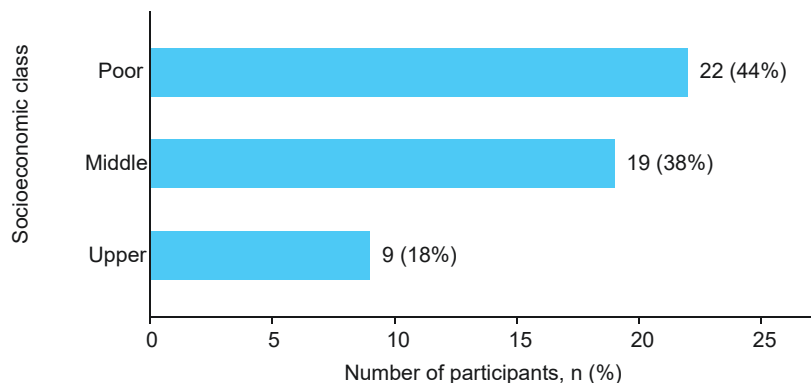


Figure 1: Age and Sex Distribution of Study Participants (N = 50)

Figure 1 illustrates the distribution of male and female participants across different age groups. In all age groups, females were higher than males; males versus females showed 9 (50.0%) vs 10 (31.25%), 3 (16.6%) vs 14 (43.75%), and 6 (33.3%) vs 7 (21.87%) in the age groups of 21 - 30, ≤20, and 31 - > 40 years, respectively. There was only one (01) female participant aged over 40 years.



The poor socioeconomic class comprised 22 (44%) participants, followed by the middle class 19 (38%) and the upper class 9 (18%).

Figure 2: Socioeconomic Status of Study Participants (N = 50)

Figure 2, the horizontal bar chart illustrating the socioeconomic distribution of study participants. The poor socioeconomic class represented 22 (44.0%) of patients, followed by the middle-income class 19 (38.0%), while the upper class accounted for 9 (18.0%).

Corrosive Exposure Profile

Table 2 presents the distribution of individual corrosive substances responsible for poisoning. Savlon (acid) was ingested by 36.0% of patients, followed by Harpic (neutral) (24.0%). Bleach/Lysol, phenol, hydrochloric acid, and Sulphuric acid were progressively less frequent exposures of corrosive poisoning.

Table II. Distribution of Corrosive Substances Ingested by Patients (N = 50)

Corrosive substance	Number of Patients	Percentage (%)
Savlon (acid)	18	36.0
Harpic (neutral)	12	24.0
Bleach/Lysol	8	16.0
Phenol	5	10.0
Hydrochloric acid	4	8.0
Sulphuric acid	3	6.0
Total	50	100.0

Treatment-Seeking Behaviour

Figure 3, the line chart, displays the distribution of patients according to the interval between corrosive ingestion and presentation for medical care. Patients who sought treatment at a health facility within 3-5 hours were 46.0%, followed by 32.0% within 6-12 hours. Only 18.0% presented within the first 2 hours, while delayed presentation beyond 12 hours occurred in 4.0% of patients. Overall, 96.0% of patients sought medical attention within the first 12 hours after ingestion.

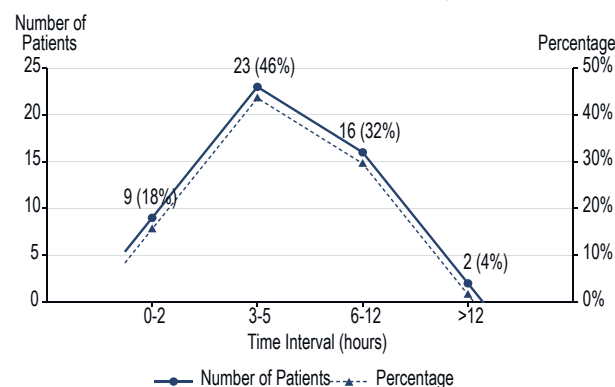


Figure 3: Time Interval between Corrosive Poisoning and Treatment Seeking (N = 50)

Figure 4: Flow diagram illustrating the treatment-seeking pathway after corrosive poisoning. Of the 50 participants, 29 (58.0%) presented directly to a government healthcare facility, whereas 21 (42.0%) initially sought treatment elsewhere before referral. Among these 21 patients, 14 (28.0% of the total cohort) first attended private hospitals or clinics, 5 (10.0%) consulted private physicians, and 2 (4.0%) received treatment from quack (unqualified) practitioners before admission to the government tertiary hospital.

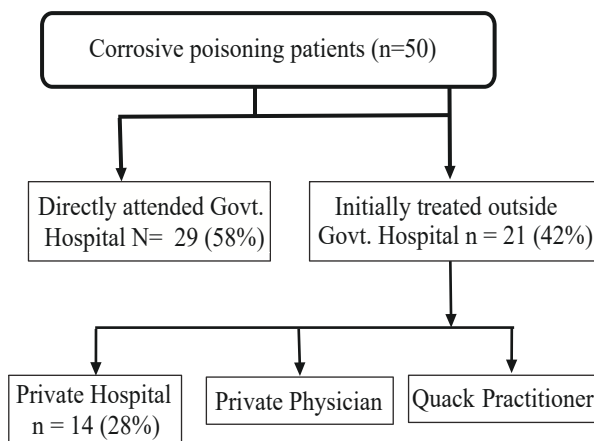


Figure 4: Flow Diagram of Initial Healthcare Facility Utilized Following Corrosive Poisoning (N = 50)

Psychosocial and Causal Factors

Table III states the psycho-social factors associated with corrosive poisoning according to sex. Here, 48.0% of respondents stated that familial disharmony was related to the ingestion of a corrosive substance, and was reported considerably more often among males (72.2%) than females (34.4%). In contrast, 28.0% of participants stated that romantic disappointment was the reason for corrosive poisoning, and was reported considerably more often among females (37.5%) than males (11.1%). Educational problems 5 (10.0%), misunderstanding with parents 5 (10.0%), and extramarital relationships 2 (4.0%) accounted for relatively few cases

Table III: Psychosocial Factors Associated with Corrosive Poisoning According to Sex (N = 50)

Psychosocial factor	M n (%)	F n (%)	Total n (%)	p- value
Familial disharmony	13 (72.2)	11 (34.4)	24 (48.0)	0.074
Romantic disappointment	2 (11.1)	12 (37.5)	14 (28.0)	
Educational-related problems	1 (5.6)	4 (12.5)	5 (10.0)	
Extramarital relationship	0 (0.0)	2 (6.3)	2 (4.0)	
Misunderstanding with parents	2 (11.1)	3 (9.4)	5 (10.0)	
Total (N)	18 (100.0)	32 (100.0)	50 (100.0)	

M= Male; F= Female; Values are presented as numbers (%). Percentages for males and females are calculated within each sex. Percentages in the Total column are calculated using the overall study population (N = 50). Pearson's χ^2 test: $p = 0.074$.

DISCUSSION

This study provides a comprehensive overview of the sociodemographic characteristics, treatment-seeking behaviour, and psychosocial determinants of corrosive poisoning among patients admitted to a tertiary care hospital in Bangladesh. The findings indicate that corrosive poisoning predominantly affected young adults, with females constituting nearly two-thirds (64.0%) of the study population and individuals aged 21-30 years accounting for the largest age group (38.0%). Most patients had attained secondary or higher secondary education (56.0%), belonged to poor or middle-income households (82.0%), and resided in urban areas (68.0%), while females constituted 67.65% of the urban residents. Savlon and Harpic together accounted for 60.0% of corrosive ingestions; nearly two-thirds (64.0%) sought treatment within 5 hours of ingestion, and familial disharmony emerged as the leading precipitating factor (48.0%), followed by romantic disappointment (28.0%).

The predominance of young adults is consistent with reports from Bangladesh and neighbouring South Asian countries, where corrosive poisoning disproportionately affects economically productive age groups.¹⁻⁵ Young adults frequently experience psychosocial stress, interpersonal conflicts, educational pressure, and financial uncertainty, all of which may increase vulnerability to intentional poisoning. Similar age distributions have been reported from Dhaka Medical College Hospital and other regional studies, where most patients were younger than 35 years.⁵⁻⁸ The concentration of cases within this age group underscores the substantial social and economic consequences of corrosive poisoning in low and middle-income countries.

Females represented almost two-thirds of the study population, a finding that differs from several earlier Bangladeshi and international studies reporting male predominance among poisoning cases.¹⁻⁷⁻⁸ However, this observation agrees with reports demonstrating a relatively higher frequency of intentional self-poisoning among women, particularly in South Asia, where interpersonal conflict, domestic violence, and psychosocial distress disproportionately affect young females.⁹⁻¹⁰ This difference may also reflect the specific pattern of corrosive ingestion, which is more commonly associated with deliberate self-harm than accidental occupational exposure in adults.

Educational attainment in this study was generally moderate, with more than half of the participants completing secondary or higher secondary education. Although education is often regarded as protective against

hazardous behaviour, previous studies suggest that educational achievement alone does not eliminate vulnerability to self-harm when emotional stress, family conflict, or socioeconomic adversity coexist.⁵⁻¹¹ The predominance of patients from poor and middle-income households further supports the influence of socioeconomic disadvantage on poisoning risk. Financial hardship may contribute to psychological distress while simultaneously increasing household availability of inexpensive corrosive cleaning agents.

Urban residents constituted more than two-thirds of the study population. This distribution probably reflects easier access to tertiary healthcare facilities in metropolitan areas and the widespread household availability of commercial cleaning products in urban settings. Similar urban predominance has been reported in Bangladeshi hospital-based studies, although rural populations remain underrepresented because of delayed referral and barriers to healthcare access.²⁻⁷

Commercial household cleaning products, particularly Savlon and Harpic, accounted for the majority of ingestions, whereas concentrated mineral acids such as hydrochloric and sulphuric acid were comparatively less common. This finding mirrors recent changes in poisoning epidemiology in Bangladesh, where readily available domestic cleaning agents have increasingly replaced industrial chemicals as the principal corrosive substances.¹⁻⁷⁻¹²

Treatment-seeking behaviour was relatively encouraging, with 64.0% of patients presenting within 5 hours of ingestion and only 4.0% presenting after twelve hours. Furthermore, 58.0% sought care directly at government hospitals, while the remainder initially consulted private facilities or informal healthcare providers before referral. Early hospital presentation is clinically important because prompt resuscitation, airway assessment, and timely upper gastrointestinal endoscopy improve diagnostic accuracy and facilitate appropriate management.¹³⁻¹⁶

Familial disharmony was identified in nearly half of all cases, followed by romantic disappointment and educational stress. Similar psychosocial determinants have been described in Bangladesh, Sri Lanka, and India, where deliberate self-poisoning frequently follows acute interpersonal conflict rather than longstanding psychiatric illness.⁹⁻¹⁰⁻¹⁷

Limitations of the Study

The study was conducted at a single tertiary care hospital with a relatively small sample size (n=50), which may limit the generalizability of the findings to the broader

Bangladeshi population. Cross-sectional design precludes causal inference between sociodemographic characteristics, psychosocial factors, and corrosive poisoning. Information on treatment-seeking behaviour and precipitating factors was largely based on patient or family reports and may therefore be subject to recall or reporting bias. Detailed psychiatric evaluation, long-term psychosocial follow-up, and assessment of environmental or household risk factors were beyond the scope of this study.

CONCLUSION

Corrosive poisoning in this study predominantly affected young adults, particularly females; furthermore, urban female residents, and was related to psychosocial stressors, especially familial disharmony and romantic disappointment. Household cleaning agents were the principal corrosive substances, and most patients sought medical care within 5 hours of ingestion, although a considerable proportion initially presented to non-specialized healthcare facilities. These findings underscore the need for integrated prevention strategies that combine public education, strengthened referral systems, and accessible mental health and psychosocial support services to reduce the burden of corrosive poisoning in Bangladesh.

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Original Article

Effectiveness and Safety of Pamidronate in Refractory Axial Spondyloarthritis: A Prospective Observational Study from a Tertiary Care Hospital in Bangladesh

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Abstract

Pamidronate has been evaluated in several clinical studies involving patients with active or refractory ankylosing spondylitis. Although biologic disease-modifying antirheumatic drugs are effective for refractory disease like spondyloarthritis (axSpA), their high cost and limited availability restrict their use in many low-resource settings. Intravenous pamidronate has emerged as a potential alternative because of its anti-inflammatory and immunomodulatory properties. This study evaluates the effectiveness and safety of intravenous pamidronate in patients with refractory radiographic axSpA (RR axSpA) treated at a tertiary care hospital in Bangladesh. This prospective observational study was conducted among 17 patients with RR axSpA, who received intravenous pamidronate and were followed for six months in the Department of Rheumatology, Bangladesh Medical University (BMU), Dhaka, from March 2022 to September 2024. Clinical outcomes were assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), and Bath

Ankylosing Spondylitis Global Score (BAS-G). Inflammatory activity was evaluated using erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Changes over time were analyzed using the Friedman test with Wilcoxon signed-rank post hoc comparisons, while correlations between clinical measures and inflammatory markers were assessed using Spearman's rank correlation. The mean age was 28.0 ± 6.09 years, with a male predominance (94.1%). Mean disease duration was 4.5 ± 1.17 years, and peripheral joint involvement was present in 11.8%. The mean age of the participants was 28.0 ± 6.09 years, and 94.1% were male. Significant improvements were observed in all clinical outcome measures over six months. Mean BASDAI decreased from 6.87 ± 1.38 at baseline to 3.16 ± 1.27 at six months (Friedman $\chi^2 = 27.4$, $p < 0.001$), BASFI from 6.31 ± 1.77 to 3.45 ± 1.41 ($\chi^2 = 24.8$, $p < 0.001$), BASMI from 0.87 ± 0.60 to 0.58 ± 0.50 ($\chi^2 = 8.9$, $p = 0.012$), and BAS-G from 8.03 ± 1.50 to 4.21 ± 1.63 ($\chi^2 = 26.1$, $p < 0.001$). ESR declined from 60.5 ± 34.2 to 28.5 ± 22.4 mm/hour, while CRP decreased from 23.9 ± 25.0 to 10.6 ± 12.3 mg/L (both $p < 0.001$). Pamidronate therapy was significantly associated with clinical outcome and inflammatory markers, i.e., progressive improvement in disease activity, function, spinal mobility, and patient global assessment. By six months, 94.0% of patients achieved at least a 20% reduction in BASDAI, 52.9% achieved a 50% reduction, and 29.4% achieved a 70% reduction. Baseline correlation analysis demonstrated strong positive associations between BASFI and BASMI ($r_s = 0.64$), BASFI and BAS-G ($r_s = 0.60$), and BASMI and BAS-G ($r_s = 0.63$), indicating close relationships among functional impairment, spinal mobility, and patient-reported disease status. Pamidronate was well tolerated, with only mild transient infusion-related adverse events and no serious treatment-related complications.

Keywords: Axial spondyloarthritis; ankylosing spondylitis; pamidronate; bisphosphonate; disease activity; BASDAI.

INTRODUCTION

Axial spondyloarthritis (axSpA) is a chronic immune-mediated inflammatory rheumatic disease primarily

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affecting the sacroiliac joints and spine, resulting in inflammatory back pain, progressive spinal stiffness, impaired physical function, and reduced quality of life. The disease spectrum includes both non-radiographic and radiographic axSpA, the latter traditionally known as ankylosing spondylitis (AS).^{1, 4-6, 28, 30} Besides axial skeletal involvement, patients may present with peripheral arthritis, enthesitis, dactylitis, and extra-articular manifestations such as acute anterior uveitis, inflammatory bowel disease, and psoriasis, reflecting the systemic nature of the disease.^{4, 5, 24, 25, 30} Persistent inflammation may ultimately lead to structural damage, spinal ankylosis, disability, reduced work productivity, and considerable socioeconomic burden if timely diagnosis and effective treatment are not achieved.^{5, 24, 25, 30}

The management of axSpA has evolved considerably over the past two decades with the introduction of evidence-based treatment strategies and biologic therapies. Current international recommendations from the Assessment of Spondyloarthritis International Society (ASAS), the European Alliance of Associations for Rheumatology (EULAR), the British Society for Rheumatology (BSR), and the American College of Rheumatology (ACR) advocate a treat-to-target approach that combines patient education, regular exercise, physiotherapy, non-steroidal anti-inflammatory drugs (NSAIDs), and biologic or targeted synthetic disease-modifying antirheumatic drugs (bDMARDs/tsDMARDs) for patients with persistently active disease.^{1-3, 26, 29} Tumour necrosis factor (TNF)- α inhibitors and interleukin (IL)-17 inhibitors have demonstrated substantial efficacy in reducing disease activity, improving physical function, suppressing inflammation, and slowing radiographic progression in appropriately selected patients.^{2, 3, 12, 26, 29}

Despite these therapeutic advances, a considerable proportion of patients continue to experience active disease because of inadequate response, intolerance, contraindications, or limited access to biologic agents. This challenge is particularly evident in low- and middle-income countries, including Bangladesh, where the high cost of biologic therapies, limited availability, and financial constraints frequently restrict their use.^{2,3,17,18} Consequently, identifying affordable and effective alternative treatment options for patients with refractory axSpA remains an important clinical priority in resource-constrained healthcare settings.

Bisphosphonates are synthetic analogues of pyrophosphate primarily used for the prevention and treatment of

metabolic bone diseases through inhibition of osteoclast-mediated bone resorption. However, accumulating experimental and clinical evidence indicates that nitrogen-containing bisphosphonates, including pamidronate, possess immunomodulatory and anti-inflammatory properties beyond their skeletal effects. These agents have been shown to influence monocyte and macrophage function, inhibit osteoclast activation, suppress the production of pro-inflammatory cytokines including TNF- α and interleukin-1, and interfere with inflammatory pathways involved in the pathogenesis of spondyloarthritis.^{12, 13, 20, 23} These biological effects provide a plausible rationale for investigating pamidronate as a potential therapeutic option in patients with refractory axSpA.

Open-label studies, randomized clinical trials, and subsequent observational reports have demonstrated improvements in disease activity, functional capacity, spinal mobility, patient global assessment, and inflammatory markers following repeated intravenous pamidronate infusions, although the magnitude of benefit has varied among studies.¹³⁻²⁰ A recent meta-analysis further suggested that bisphosphonate therapy may provide clinically meaningful improvement in disease activity and functional outcomes in selected patients with ankylosing spondylitis, while maintaining an acceptable safety profile.¹³

Evidence regarding pamidronate therapy in South Asian populations is particularly limited. A few studies conducted in Bangladesh have reported encouraging results with pamidronate and thalidomide in patients with refractory axial spondyloarthritis, suggesting that these relatively inexpensive therapeutic options may have an important role where access to biologic therapy is restricted.¹⁶⁻¹⁸ Generating local evidence is especially important because disease characteristics, healthcare accessibility, treatment affordability, and patient adherence may differ substantially from those reported in high-income countries.

Against this background, this study was undertaken to evaluate the effectiveness and safety of intravenous pamidronate in patients with refractory axial spondyloarthritis attending a tertiary care rheumatology centre in Bangladesh. The study assessed changes in disease activity, functional status, spinal mobility, patient global assessment, and inflammatory markers using validated outcome measures, including the BASDAI, BASFI,

BASMI, BAS-G, ESR, and CRP, while simultaneously evaluating the tolerability and safety of pamidronate therapy during six months of follow-up.^{7–11, 20}

MATERIALS AND METHODS

Study Design and Setting: This prospective observational study was conducted in the Department of Rheumatology, BMU [formerly Bangabandhu Sheikh Mujib Medical University], Dhaka, Bangladesh, between March 2022 and September 2024. The study was designed to evaluate the effectiveness and safety of intravenous pamidronate in patients with RR axSpA.

Ethical Considerations: The study protocol was reviewed and approved by the Institutional Ethics Committee of BMU. Written informed consent was obtained from all participants before enrolment. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki for research involving human participants.

Study Participants: A total of 17 consecutive adult patients were enrolled during the study period. Eligible participants were aged >18 years and fulfilled the modified New York classification criteria for ankylosing spondylitis.⁶ Since all patients had radiographic disease, they were considered to represent the radiographic form of axSpA.

Refractory disease was defined as persistently active disease despite receiving optimal conventional treatment, as demonstrated by a BASDAI score of ≥ 4 after at least 3 months of non-steroidal anti-inflammatory drug (NSAID) therapy, or inability to receive biologic therapy due to intolerance, contraindications, or financial constraints.^{2,3,7}

Inclusion and Exclusion Criteria: Patients were eligible if they were adults (≥ 18 years) with confirmed ankylosing spondylitis, had active disease (BASDAI ≥ 4), and presented with either isolated axial involvement or combined axial and peripheral joint involvement.

Patients were excluded if they had severe renal impairment, uncontrolled hypertension, active infection, pregnancy or lactation, previous intravenous bisphosphonate therapy within the preceding 12 months, known hypersensitivity to bisphosphonates, or any medical condition considered by the investigators to interfere with safe administration of pamidronate or study follow-up.

Treatment Protocol: All eligible patients received intravenous pamidronate at a dose of 60 mg once monthly for 3 consecutive months according to the departmental treatment protocol. Patients continued their stable background medications, including NSAIDs and low-dose

corticosteroids when clinically indicated, throughout the study period. No additional disease-modifying therapy was initiated during follow-up unless medically necessary.

Patients were observed during and after each infusion for immediate adverse reactions. Routine laboratory investigations were performed before treatment and during follow-up to monitor treatment safety.

Outcome Measures: Clinical and laboratory assessments were performed at baseline, 3 months, and 6 months after initiation of pamidronate therapy.

Disease activity was assessed using the BASDAI,⁸ BASFI,⁹ Spinal mobility was assessed using the BASMI.¹⁰ Patient-perceived overall disease status was measured using the BAS-G.¹¹

Inflammatory activity was evaluated by measuring ESR and serum CRP concentrations at each assessment visit.

Safety Assessment: Safety was evaluated throughout the study by recording all adverse events occurring during treatment and follow-up. Particular attention was given to infusion-related reactions, flu-like symptoms, hypocalcaemia, renal dysfunction, and other clinically significant adverse events. The severity and possible relationship of each adverse event to pamidronate therapy were assessed according to established clinical recommendations.²⁰

Data Collection: Baseline demographic and clinical characteristics, including age, sex, disease duration, and peripheral involvement, were recorded at enrolment. Clinical outcome measures and laboratory investigations were repeated at 3 and 6 months using standardized assessment procedures.

Statistical Analysis: Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 25.0. Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR), as appropriate according to data distribution, while categorical variables were summarized as frequencies and percentages.

Changes in continuous outcome measures over time were evaluated using the Friedman test for repeated measurements. Where significant overall differences were identified, pairwise comparisons between baseline and follow-up assessments were performed using the Wilcoxon signed-rank test with appropriate adjustment for multiple comparisons. Correlations between clinical indices and inflammatory markers were analyzed using Spearman's

rank correlation coefficient. All statistical tests were two-tailed, and a p-value of <0.05 was considered statistically significant.

RESULTS

A total of 17 patients with refractory radiographic axial spondyloarthritis completed the study and were evaluated at baseline, 3 months, and 6 months following intravenous pamidronate therapy. All enrolled participants completed the scheduled follow-up assessments, and no patient was lost to follow-up.

Baseline Demographic and Clinical Characteristics

Table I summarizes the baseline demographic and clinical characteristics of the study participants. The mean age was 28.0 ± 6.09 years, with a male predominance (94.1%). Mean disease duration was 4.5 ± 1.17 years, and peripheral joint involvement was present in 11.8%. Baseline disease activity was high, with mean BASDAI 6.87 ± 1.38 , BASFI 6.31 ± 1.77 , BASMI 0.87 ± 0.60 , BAS-G 8.03 ± 1.50 , ESR 60.5 ± 34.2 mm/hour, and CRP 23.9 ± 25.0 mg/L.

Table I. Baseline Demographic and Clinical Characteristics of Patients with Refractory Radiographic Axial Spondyloarthritis (N = 17)

Variable	Value
Age (years), mean $\pm$ standard deviation (SD)	28.0 ± 6.09
Male sex, n (%)	16 (94.1)
Disease duration (years), mean $\pm$ SD	4.5 ± 1.17
Peripheral joint involvement, n (%)	2 (11.8)
ESR (mm/hour), mean $\pm$ SD	60.5 ± 34.2
CRP (mg/L), mean $\pm$ SD	23.9 ± 25.0
BASDAI, mean $\pm$ SD	6.87 ± 1.38
BASFI, mean $\pm$ SD	6.31 ± 1.77
BASMI, mean $\pm$ SD	0.87 ± 0.60
BAS-G, mean $\pm$ SD	8.03 ± 1.50

Changes in Clinical Outcome Measures and Inflammatory Markers Following Pamidronate Therapy

Table II displays a series of clinical evaluations that reflect progressive improvement in clinical outcome measures and inflammatory markers following pamidronate therapy. The mean $\pm$ SD of BASDAI decreased from 6.87 ± 1.38 at baseline to 4.12 ± 1.46 at 3 months and 3.16 ± 1.27 at 6 months ($\chi^2=27.4$, $p<0.001$). BASFI declined from 6.31 ± 1.77 to 3.45 ± 1.41 at 6 months ($\chi^2=24.8$, $p<0.001$). BASMI showed modest but significant improvement (0.87 ± 0.60 to 0.58 ± 0.50 , $\chi^2=8.9$, $p=0.012$). BAS-G decreased from 8.03 ± 1.50 to 4.21 ± 1.63 ($\chi^2=26.1$, $p<0.001$). ESR and CRP both declined significantly ($p<0.001$).

Table II: The Temporal Trends in Clinical Outcome Measures and Inflammatory Markers Following Intravenous Pamidronate Therapy (N=17)

Outcome measure	Baseline	3 months	6 months	Friedman χ^2	p-value
BASDAI	6.87 ± 1.38	4.12 ± 1.46	3.16 ± 1.27	27.4	<0.001
BASFI	6.31 ± 1.77	4.55 ± 1.63	3.45 ± 1.41	24.8	<0.001
BASMI	0.87 ± 0.60	0.71 ± 0.55	0.58 ± 0.50	8.9	0.012
BAS-G	8.03 ± 1.50	5.42 ± 1.72	4.21 ± 1.63	26.1	<0.001
ESR (mm/hour)	60.5 ± 34.2	39.2 ± 26.8	28.5 ± 22.4	18.6	<0.001
CRP (mg/L)	23.9 ± 25.0	15.8 ± 18.6	10.6 ± 12.3	16.9	<0.001

Values are presented as mean $\pm$ standard deviation.

Overall comparisons across baseline, 3 months, and 6 months were performed using the Friedman test. Pairwise comparisons were performed using the Wilcoxon signed-rank test with Bonferroni adjustment

Figure 1 line graph showing consistent downward trends in disease activity, function, spinal mobility, and patient global assessment (BASDAI, BASFI, BASMI, and BAS-G). The steepest decline occurred within the first 3 months and was sustained at 6 months.

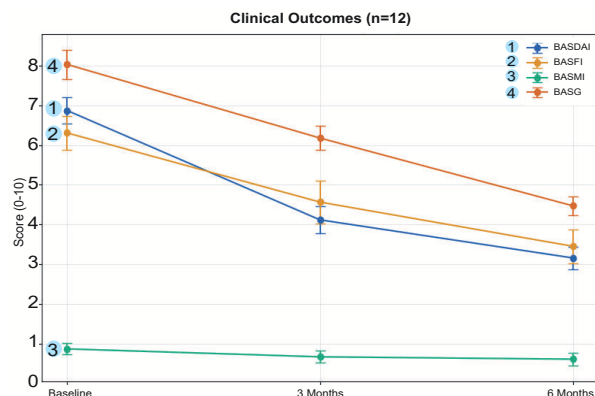


Figure 1. Trends in BASDAI, BASFI, BASMI, and BAS-G During Six Months of Intravenous Pamidronate Therapy

Clinical Response According to BASDAI Scores

Table III presents the proportion of responders achieving specific thresholds of decrease in BASDAI scores during the follow-up period from baseline. Responder analysis confirmed progressive improvement. At 3 months, 76.5% achieved $\geq 20\%$ reduction in BASDAI, 23.5% achieved $\geq 50\%$, and 5.9% achieved $\geq 70\%$. By 6 months, 94.0% achieved $\geq 20\%$, 52.9% achieved $\geq 50\%$, and 29.4% achieved $\geq 70\%$ reduction in BASDAI.

Table III. Proportion of Responders Achieving Predefined BASDAI Response Thresholds During Follow-up (N = 17)

Time point	Response Threshold	No. of Patients	Percentage (%)
3 Months	20% decrease in BASDAI scores	13	76.5%
	50% decrease in BASDAI scores	4	23.5%
	70% decrease in BASDAI scores	1	5.9%
6 Months	20% decrease in BASDAI scores	16	94.0%
	50% decrease in BASDAI scores	9	52.9%
	70% decrease in BASDAI scores	5	29.4%

Values represent the number and percentage of patients achieving $\geq 20\%$, $\geq 50\%$, and $\geq 70\%$ reductions in BASDAI scores compared with baseline.

Correlation Between Clinical Outcomes and Inflammatory Markers

Table IV presents Spearman's rank correlation coefficients (r_s) describing relationships between clinical outcome measures and inflammatory markers at baseline, 3 months, and 6 months after intravenous pamidronate therapy. BASFI showed a strong positive correlation with BASMI ($r_s = 0.64$) and BAS-G ($r_s = 0.60$), indicating the association of reduced spinal mobility with greater functional impairment and close alignment between functional disability and patient-reported well-being, respectively.

Figure 2 the line graph demonstrating progressive reductions in ESR and CRP, both more than halved by 6 months, reflecting systemic anti-inflammatory effects.

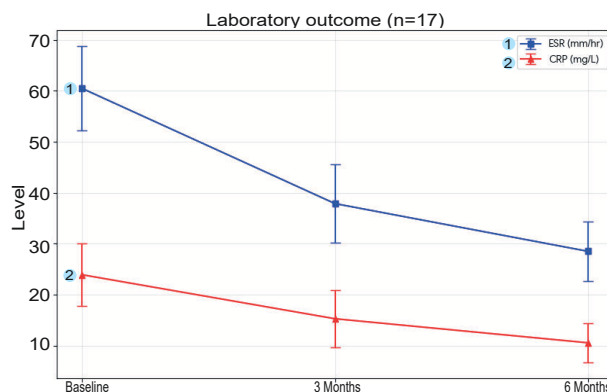


Figure 2: Trends in ESR and CRP during Six Months of Intravenous Pamidronate Therapy (N=17)

BASDAI showed a moderate positive correlation with BASMI and a weak positive correlation with BASFI and BAS-G. BASMI showed a strong positive correlation with BASG. Remarkably, BASDAI showed weak correlations with ESR and no correlations with CRP ($r_s = 0.20$, $r_s = -0.02$), suggesting that patient-reported symptoms and objective inflammatory markers may capture different aspects of the disease burden in this cohort.

[Correlation strength was interpreted as negligible (<0.20), weak ($0.20-0.39$), moderate ($0.40-0.59$), strong ($0.60-0.79$), or very strong (≥ 0.80)].

Table IV: Spearman's Rank Correlation Coefficients (R_s) between Clinical Outcome Measures And Inflammatory Markers at Baseline and During Follow-Up Among Patients (N = 17)

Variable Pair	r_s Value	Interpretation
BASDAI ↔ BASFI	0.25	Weak positive association
BASDAI ↔ BASMI	0.40	Moderate positive association
BASDAI ↔ BASG	0.19	Weak positive association
BASDAI ↔ ESR	0.20	Weak positive association
BASDAI ↔ CRP	-0.02	No correlation
BASFI ↔ BASMI	0.64	Strong positive association
BASFI ↔ BASG	0.60	Strong positive association
BASMI ↔ BASG	0.63	Strong positive association

Spearman's rank correlation was selected because of the small sample size and the non-parametric distribution of the clinical and laboratory variables. r_s range from -1.00 to +1.00.

Figure 3, the scatter plot showing a positive association between reductions in CRP and improvements in BASDAI, supports a link between suppression of systemic inflammation and clinical symptom relief.

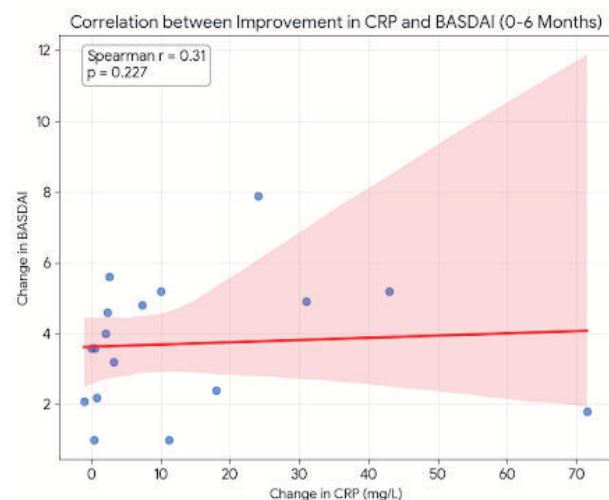


Figure 3: Association between Changes in CRP and BASDAI from Baseline to Six Months

INDIVIDUAL PATIENT RESPONSES

Individual patient responses varied in degree of improvement following pamidronate therapy. Most participants showed progressive reductions in BASDAI scores over successive follow-up visits, although the

magnitude of improvement varied among individuals. A small proportion of patients experienced marked clinical improvement, whereas others achieved more modest reductions in disease activity.

SAFETY OUTCOMES

Pamidronate therapy was generally well tolerated throughout the study period. Adverse events were predominantly mild and transient, consisting mainly of self-limiting infusion-related reactions and flu-like symptoms that resolved with conservative management. No patient discontinued treatment because of adverse events.

No serious infusion reactions, clinically significant renal impairment, symptomatic hypocalcaemia, opportunistic infections, or treatment-related hospitalizations or deaths were observed during follow-up.

DISCUSSION

This study evaluated the effectiveness and safety of monthly intravenous pamidronate in patients with refractory axSpA treated at a tertiary care hospital in Bangladesh. The study demonstrated significant improvements in disease activity, functional status, spinal mobility, patient global assessment, and inflammatory markers over six months, while treatment was generally well tolerated without serious adverse events.

The demographic characteristics of the study population were consistent with the recognized epidemiology of axSpA. Most participants were young males (94.1%) with a mean age of 28.0 ± 6.09 years and a mean disease duration of 4.5 ± 1.17 years, reflecting the typical onset of the disease during early adulthood and its male predominance.¹⁻⁴ Persistent high baseline BASDAI (6.87 ± 1.38), BASFI (6.31 ± 1.77), BAS-G (8.03 ± 1.50), ESR (60.5 ± 34.2 mm/hour), and CRP (23.9 ± 25.0 mg/L) confirmed that the cohort had active disease despite conventional treatment, fulfilling the definition of refractory disease described in previous studies.⁵⁻⁸

The most important finding was the significant and sustained reduction in disease activity following pamidronate therapy. BASDAI decreased by 4.12 ± 1.46 after 3 months and by 3.16 ± 1.27 after six months from a baseline of 6.87 ± 1.38 , with statistically significant improvements demonstrated by Wilcoxon signed-rank testing ($p < 0.001$). These findings agree with earlier open-label studies and randomized clinical trials that

reported clinically meaningful reductions in disease activity following repeated intravenous pamidronate infusions.¹²⁻¹⁸ Although biologic disease-modifying agents remain the standard treatment for refractory axSpA, several studies have suggested that nitrogen-containing bisphosphonates can reduce pain and disease activity through anti-inflammatory and immunomodulatory effects, particularly when biologic therapy is unavailable or contraindicated.¹³⁻¹⁶

Substantial improvement in functional status was also observed, with BASFI decreasing by 3.45 ± 1.41 at six months from baseline 6.31 ± 1.77 . Functional recovery is clinically important because impaired physical function is a major determinant of disability, work productivity, and quality of life in axSpA.^{3, 9, 19} Similar improvements in BASFI following pamidronate therapy have been reported previously, supporting the concept that effective suppression of inflammation may translate into meaningful improvements in daily physical activities.¹⁴⁻¹⁸ In contrast, improvement in spinal mobility (BASMI) was more modest (29.7%), although statistically significant. This finding is expected because spinal mobility is influenced not only by active inflammation but also by irreversible structural damage, which generally responds more slowly to treatment.^{2, 4, 19}

Patient-reported global health status improved considerably during follow-up, with BAS-G decreasing by 4.21 ± 1.63 after 6 months from baseline 8.03 ± 1.50 . The parallel improvement in BASDAI, BASFI, and BAS-G indicates that reductions in inflammatory symptoms were accompanied by better physical functioning and overall patient-perceived health. These observations support the continued use of validated composite indices such as BASDAI, BASFI, BASMI, and BAS-G for comprehensive assessment of treatment response, as recommended by ASAS-EULAR management guidelines.^{1, 2, 10, 11}

The significant reductions in ESR from 60.5 ± 34.2 at baseline to 28.5 ± 22.4 after 6 months and CRP 23.9 ± 25.0 at baseline to 10.6 ± 12.3 after 6 months further support the anti-inflammatory effect of pamidronate. Nitrogen-containing bisphosphonates inhibit osteoclast activity and have immunomodulatory properties through suppression of macrophage activation, $\gamma\delta$ T-cell proliferation, and pro-inflammatory cytokines, including tumour necrosis factor- α and interleukin-1.^{12, 13, 20} These mechanisms provide a plausible biological explanation for the parallel improvements observed in both laboratory and clinical outcomes.

Baseline Spearman correlation analysis demonstrated strong positive associations among BASFI, BASMI, and BAS-G, indicating that functional disability, impaired spinal mobility, and patients' perception of disease burden were closely related. Conversely, BASDAI showed only weak correlations with ESR and CRP, suggesting that patient-reported disease activity and laboratory inflammatory markers reflect complementary rather than identical dimensions of disease severity. Similar findings have been reported previously, where acute-phase reactants correlated only modestly with subjective measures because pain, stiffness, fatigue, and structural damage also contribute to patients' overall disease experience.^{9-12, 21, 22}

Responder analysis further strengthened the clinical significance of the findings. By six months, 94.0% of patients achieved at least a 20% improvement in BASDAI, 52.9% achieved a 50% improvement, and 29.4% achieved a 70% improvement, indicating progressive and sustained therapeutic benefit. Individual response analysis also demonstrated variability in treatment outcomes, consistent with previous reports showing that disease duration, structural damage, comorbidities, and socioeconomic factors influence therapeutic response.^{4, 15, 23-26}

This study provides contemporary evidence from Bangladesh, where published data regarding pamidronate therapy remain limited.²⁷⁻³⁰

LIMITATIONS OF THE STUDY

The relatively small sample size (N=17) and single-centre design may limit the generalizability of the findings. As a prospective observational study without a control group or randomization, causal inferences regarding the effectiveness of pamidronate should be interpreted cautiously. Furthermore, magnetic resonance imaging was not used to assess objective inflammatory changes.

CONCLUSION

Monthly intravenous pamidronate therapy was associated with significant improvements in disease activity, functional status, spinal mobility, patient global assessment, and inflammatory markers over six months in patients with refractory radiographic axial spondyloarthritis. Significant reductions in BASDAI, BASFI, BASMI, BAS-G, ESR, and CRP, together with high BASDAI responder rates and an acceptable short-term safety profile, suggest that pamidronate may provide clinically meaningful benefit in carefully selected patients who have persistent active disease. Larger

multicentre randomized controlled trials with longer follow-up are required to confirm its long-term efficacy, safety, and place in the management of axial spondyloarthritis.

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Original Article

Risk Factors Associated with Stroke in Young Adults: A Cross-Sectional Study at a Tertiary Care Hospital in Bangladesh

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Abstract

Stroke in young adults represents an important emerging health challenge, particularly in low and middle income countries where modifiable vascular risk factors are increasingly prevalent. Identification of associated risk factors among young stroke patients is essential for developing effective prevention strategies. This study aimed to determine the risk factors associated with stroke among young adults admitted to a tertiary care hospital in Bangladesh. This hospital-based cross-sectional study was conducted among 100 consecutive stroke patients aged 18-50 years admitted to the Department of Medicine, Jahurul Islam Medical College Hospital, Bangladesh, from September 2020 to February 2021. Stroke diagnosis was confirmed by computed tomography or magnetic resonance imaging. Socio-demographic characteristics, clinical profiles, vascular risk factors, and lifestyle related factors were assessed using a structured questionnaire and clinical evaluation. Data were analyzed using SPSS version 23.0. Associations between stroke subtype and risk factors were evaluated using Pearson's χ^2 test, and logistic regression analysis was performed to identify predictors of ischemic and hemorrhagic stroke. The mean age of participants was 42.09 ± 7.14 years. Most patients belonged to the 36-50-year age group (88%), and males predominated (74%; male to female ratio 2.85:1). Most participants were married (96%), had low educational attainment (68% had no formal education or education below secondary level), and belonged to lower-income groups (74% had monthly family income $\leq 20,000$ BDT). Ischemic stroke accounted for 81% of cases, while hemorrhagic stroke accounted for 19%. The most prevalent risk factor was hypertension (64%), followed by diabetes mellitus (45%), current smoking (39%), and dyslipidemia (38%). Multiple

risk-factor clustering (≥ 2 risk factors) was observed in 92% of patients and was significantly associated with stroke subtype ($p=0.001$). Hypertension ($p=0.041$), dyslipidemia ($p=0.027$), and current smoking ($p=0.014$) were significantly associated with stroke subtype. Logistic regression demonstrated that smoking (OR 7.15, $p=0.012$) and dyslipidemia (OR 4.06, $p=0.034$) were significant predictors of ischemic stroke, whereas hypertension showed a tendency toward association with hemorrhagic stroke (OR 3.68, $p=0.052$). Young adult stroke in this study was strongly associated with modifiable vascular risk factors, particularly hypertension, smoking, dyslipidemia, and clustering of multiple risk factors. Early identification and management of these factors are essential for reducing stroke burden among young adults in Bangladesh.

Keywords: Young stroke; risk factors of stroke; hypertension; dyslipidemia; smoking; ischemic stroke; hemorrhagic stroke.

INTRODUCTION

Stroke remains one of the leading causes of mortality and long-term disability worldwide, creating a substantial public health burden. The global burden of stroke has increased considerably, with low- and middle-income countries experiencing a disproportionate share of stroke related morbidity and mortality.¹ Despite being traditionally considered a disease of older populations, stroke among young adults has gained increasing attention due to its significant social and economic consequences, affecting individuals during their productive years.^{2,3}

Young adult stroke is generally defined as stroke occurring between 18 and 50 years of age. Compared with older populations, stroke in young adults demonstrates distinct epidemiological and etiological characteristics, including a higher contribution of modifiable vascular, metabolic, lifestyle-related, and cardiac risk factors.^{3,4} Previous studies have reported that ischemic stroke accounts for approximately 70–85% of young stroke cases globally, whereas hemorrhagic stroke represents a smaller but clinically important proportion.^{19,20}

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The increasing prevalence of conventional vascular risk factors among young adults has become a major concern. Hypertension remains the most important modifiable risk factor for stroke worldwide and contributes to both ischemic and intracerebral hemorrhagic stroke. The INTERSTROKE study identified hypertension as the strongest population-attributable risk factor for stroke, emphasizing its critical role in prevention.¹¹ In Bangladesh, hypertension affects approximately one-quarter of adults, while awareness and treatment rates remain suboptimal, contributing to persistent cerebrovascular risk.⁸

Diabetes mellitus is another important contributor to cerebrovascular disease through mechanisms involving endothelial dysfunction, accelerated atherosclerosis, and thrombosis.¹³ Dyslipidemia, particularly elevated low-density lipoprotein cholesterol and triglycerides, promotes atherosclerotic vascular changes and has been increasingly associated with ischemic stroke among younger populations.^{13,14}

Lifestyle-related risk factors, especially tobacco use, have a substantial influence on stroke risk among young adults. Smoking contributes to vascular inflammation, endothelial injury, and increased thrombotic tendency. Studies from South Asia have reported smoking prevalence among young stroke patients ranging from approximately 30% to 40%, consistent with the increasing burden of tobacco exposure in this population.^{15,16}

The coexistence of multiple risk factors is common among young stroke patients. Hypertension, diabetes, dyslipidemia, smoking, and sedentary lifestyle frequently cluster together, resulting in synergistic vascular damage and increased stroke susceptibility.¹⁷ Comprehensive risk assessment is therefore essential because isolated identification of single risk factors may underestimate the cumulative vascular burden.

Bangladesh has experienced an epidemiological transition with increasing urbanization, lifestyle changes, dietary modification, and rising prevalence of metabolic disorders.^{17,18} However, data regarding risk factors associated with stroke among young adults remain limited. Previous Bangladeshi studies have identified hypertension, lifestyle-related factors, and metabolic abnormalities as important contributors, but

comprehensive evaluation of multiple vascular risk factors remains insufficient.^{4,9,10}

Understanding the distribution and association of risk factors among young stroke patients is essential for developing targeted preventive strategies. Early detection and management of hypertension, diabetes, dyslipidemia, and smoking may significantly reduce stroke incidence, recurrence, and disability.²²⁻²⁵

Therefore, this study aimed to determine the risk factors associated with stroke among young adults admitted to a tertiary care hospital in Bangladesh, with particular emphasis on conventional vascular risk factors, lifestyle-related factors, and their relationship with ischemic and hemorrhagic stroke subtypes.

MATERIALS AND METHODS

Study Design and Setting: This hospital-based cross-sectional study was conducted in the Department of Medicine, Jahurul Islam Medical College Hospital, Kishoreganj, Bangladesh, from September 2020 to February 2021. The hospital functions as a tertiary referral center serving both urban and rural populations.

Study Population: A total of 100 consecutive patients aged 18-50 years with confirmed stroke were enrolled. Stroke diagnosis was established clinically and confirmed by neuroimaging (CT/MRI). Patients with traumatic brain injury, transient ischemic attack, or incomplete clinical records were excluded.

Variables: The primary outcome variable was stroke subtype, classified as ischemic or hemorrhagic stroke based on neuroimaging findings. Explanatory variables included hypertension, diabetes mellitus, dyslipidemia, smoking, sedentary lifestyle, previous stroke, atrial fibrillation, alcohol consumption, and oral contraceptive pill use. Sociodemographic and economic variables included age, sex, marital status, education, occupation, residence, and income.

Operational Definitions: Hypertension was defined as blood pressure $\geq 140/90$ mmHg or current antihypertensive medication use. Diabetes mellitus was defined as fasting plasma glucose ≥ 7.0 mmol/L or use of antidiabetic medication. Dyslipidemia was defined according to lipid parameters or use of lipid-lowering therapy. Smoking included current or previous tobacco use.

Statistical Analysis: Data were systematically entered and analyzed utilizing IBM Statistical Package for Social Sciences (SPSS) version 23.0. Continuous variables were expressed as mean $\pm$ SD and categorical variables as frequency and percentage. Pearson's χ^2 test was used to assess associations between categorical variables. Logistic regression analysis was performed to identify predictors of stroke subtype, with odds ratios (OR) and 95% confidence intervals (CI). A p-value <0.05 was considered statistically significant.

Ethical Considerations: The study protocol was reviewed and approved by the Ethical Review Committee of Jahurul Islam Medical College and Hospital. All procedures adhered to the Declaration of Helsinki. Confidentiality of patient data was strictly maintained. Written informed consent was obtained from all participants or, when applicable, their legal representatives.

RESULTS

A total of 100 young adult stroke patients were included in the study. The demographic characteristics, socioeconomic

profile, clinical presentation, stroke subtypes, and associated vascular risk factors were analyzed. The distribution of ischemic and hemorrhagic stroke was evaluated, and associations between stroke subtype and potential risk factors were assessed using appropriate statistical tests.

Table I shows the socioeconomic characteristics of the study participants. Most patients were married (96%). Educational attainment was generally low: 35% had no formal education, 33% had less than a secondary education, 10% had completed secondary school, 16% had completed higher secondary education, and 6% were graduates or above. Occupationally, 37% were grouped as others, including day laborers, drivers, or small-scale workers, followed by businesspersons (22%), housewives (16%), non-government employees (12%), government employees (9%), unemployed individuals (2%), and students (2%). Urban residents constituted 79% of the cohort, and 21% were from rural areas. Monthly income was below 10,000 BDT in 35% and 10,001-20,000 BDT in 39%, whereas only 6% reported income above 40,000 BDT.

Table I: Sociodemographic and Economic Characteristics of Young Stroke Patients

Characteristic	Category	Frequency (n)	Percentage (%)
Mean age $\pm$ Standard deviation (years)	42.09 $\pm$ (7.14)	42.09 $\pm$ (7.14)	
Age Group (years)	18-35	12	12%
	36-50	88	88%
Sex	Male	74	74%
	Female	26	26%
Male to Female Ratio	2.85:1		
Marital status	Single	4	4%
	Married	96	96%
Education	No education	35	35%
	Below secondary	33	33%
	Secondary passed	10	10%
	Higher secondary and above	22	22%
Occupation	Service holders	21	21%
	Business	22	22%
	Housewife	16	16%
	Others	41	41%
Residence	Rural	21	21%
	Urban	79	79%
Monthly Family Income (Taka)	<10,000	35	35%
	>10,000-20,000	39	39%
	>20,001-40,000	20	20%
	>40,000	6	6%

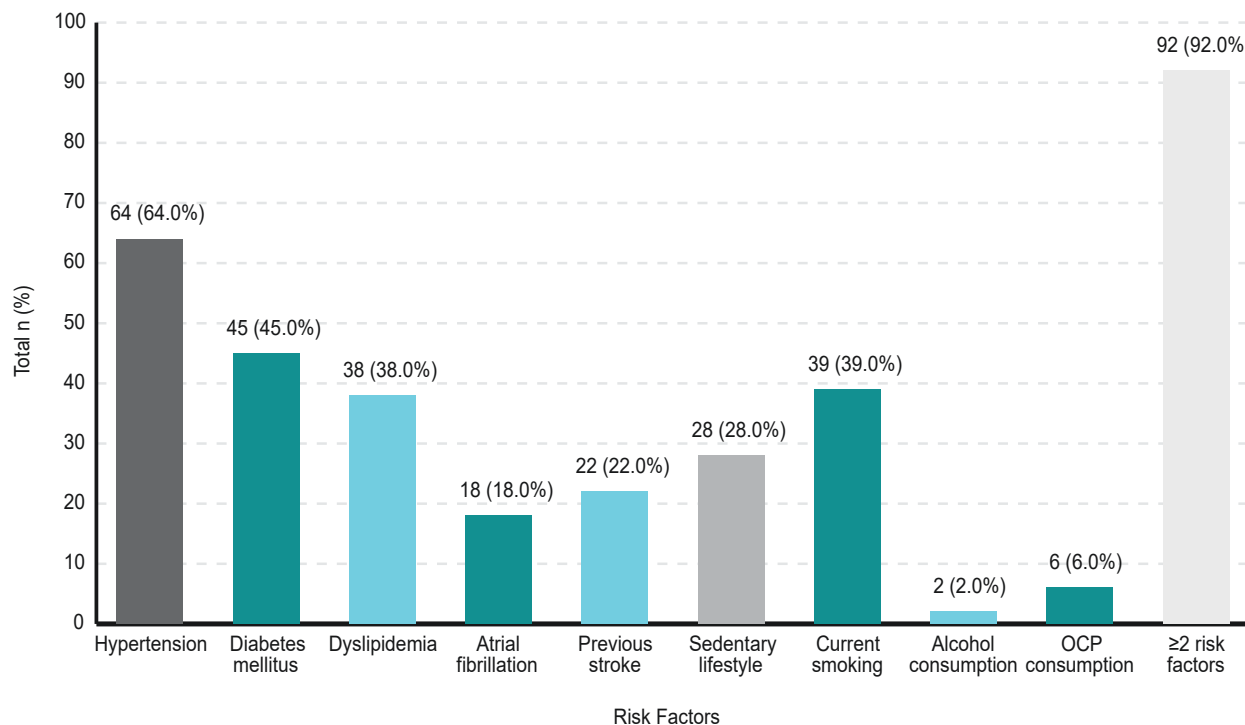


Figure 1: Distribution of Associated Risk Factors among Young Stroke Patients (n=100).

Figure 1 illustrates the distribution of associated risk factors among young adult stroke patients. The presence of two or more risk factors was identified in 92.0% of patients. Among individual risk factors, hypertension was affecting 64.0% of patients, followed by diabetes mellitus (45.0%), current smoking (39.0%), and dyslipidemia (38.0%). Other associated factors included a sedentary lifestyle in 28.0%, a previous history of stroke in 22.0%, and atrial fibrillation in 18.0% of patients. Less frequent risk factors were oral contraceptive pill (OCP) consumption and alcohol consumption, observed in 6.0% and 2.0% of patients, respectively.

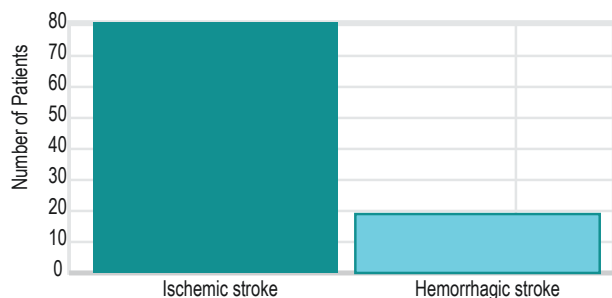


Figure 2: Distribution of Stroke Subtypes

Figure 2 illustrates the distribution of stroke subtypes. The ischemic stroke occurred in 81% of the participants, whereas the hemorrhagic stroke represented 19%.

Table II demonstrates the distribution and association of risk factors among young adult stroke patients according to stroke subtype (ischemic and hemorrhagic stroke). Overall, ≥2 risk factors were present in 92 (92.0%) patients. This clustering of risk factors was significantly associated with stroke subtype ($p=0.001$). Among individual risk factors, hypertension was affecting 64 (64.0%) patients. It was more frequently observed among patients with hemorrhagic stroke (84.2%) compared with ischemic stroke (59.3%), showing a statistically significant association ($p=0.041$). Diabetes mellitus was present in 45 (45.0%) patients and was more common among ischemic stroke patients (48.1%) than hemorrhagic stroke patients (31.6%); however, the association was not statistically significant ($p=0.191$). Dyslipidemia was identified in 38 (38.0%) patients and showed a higher frequency among ischemic stroke patients (43.2%) compared with hemorrhagic stroke patients (15.8%). This association was statistically significant ($p=0.027$). Regarding lifestyle-related factors, current smoking was reported in 39 (39.0%) patients and was significantly associated with stroke subtype ($p=0.014$). Smoking was substantially more frequent among ischemic stroke patients (45.7%) compared with hemorrhagic stroke patients (10.5%).

Table II: Distribution and Association of Risk Factors According to Stroke Type Among Young Adult Stroke Patients (n=100)

Risk factor	IS n (%)	HS n (%)	Total n (%)	p value
Vascular Risk Factors				
Hypertension	48 (59.3)	16 (84.2)	64 (64.0)	0.041
Diabetes mellitus	39 (48.1)	6 (31.6)	45 (45.0)	0.191
Dyslipidemia	35 (43.2)	3 (15.8)	38 (38.0)	0.027
Current smoking	37 (45.7)	2 (10.5)	39 (39.0)	0.014
Other Associated Risk Factors				
Atrial fibrillation	17 (23.3)	1 (5.3)	18 (18.0)	0.108
Previous stroke	21 (25.9)	1 (5.3)	22 (22.0)	0.050
Sedentary lifestyle	25 (30.9)	3 (15.8)	28 (28.0)	0.188
Alcohol consumption	2 (2.7)	0	2 (2.0)	0.489
OCP consumption	6 (7.4)	0	6 (6.0)	0.221
≥2 risk factors	78 (96.3)	14 (73.7)	92 (92.0)	0.001

Data are presented as frequency and percentage [n (%)]. The association between individual risk factors and stroke type (ischemic versus hemorrhagic stroke) was assessed using the Pearson χ^2 test. A p-value <0.05 was considered statistically significant. OCP: oral contraceptive pill. IS = ischemic stroke; HS = hemorrhagic stroke.

Other associated factors included sedentary lifestyle (IS: 30.9% vs HS:15.8%), previous stroke history (IS: 25.9% and HS:5.3%), and atrial fibrillation (IS: 23.3% vs HS: 5.3%). Previous stroke showed a borderline association with stroke subtype (p=0.050), while atrial fibrillation and sedentary lifestyle were not statistically significant.

Less common risk factors included oral contraceptive pill (OCP) use (IS: 7.4% vs HS: 0%) and alcohol use (IS: 2.7% vs HS: 0%), with no significant association observed.

A logistic regression analysis was performed to identify vascular risk factors associated with ischemic stroke compared with hemorrhagic stroke. Logistic regression analysis demonstrated differential vascular risk profiles between ischemic and hemorrhagic stroke.

Table IIIA shows smoking was the strongest predictor of ischemic stroke (OR 7.15; p=0.012), followed by dyslipidemia (OR 4.06; p=0.034).

In contrast, Table IIIB demonstrates that hypertension showed a tendency toward association with hemorrhagic stroke (OR 3.68; p=0.052).

Table III: Logistic Regression Analysis of Vascular Risk Factors Associated with Ischemic and Hemorrhagic Stroke Among Young Adults**A: Predictors of ischemic stroke**

Vascular risk factor	IS n/N (%)	HS n/N (%)	OR (95% CI)	p value
Hypertension	48/81 (59.3)	16/19 (84.2)	0.27 (0.07–1.01)	0.052
Diabetes mellitus	39/81 (48.1)	6/19 (31.6)	2.01 (0.70–5.81)	0.200
Dyslipidemia	35/81 (43.2)	3/19 (15.8)	4.06 (1.10–15.03)	0.034*
Current smoking	37/81 (45.7)	2/19 (10.5)	7.15 (1.55–32.98)	0.012*

B: Predictors of hemorrhagic stroke

Vascular risk factor	HS n/N (%)	IS n/N (%)	OR (95% CI)	p value
Hypertension	16/19 (84.2)	48/81 (59.3)	3.68 (0.99–13.60)	0.052
Diabetes mellitus	6/19 (31.6)	39/81 (48.1)	0.50 (0.17–1.43)	0.200
Dyslipidemia	3/19 (15.8)	35/81 (43.2)	0.25 (0.07–0.91)	0.034*
Current smoking	2/19 (10.5)	37/81 (45.7)	0.14 (0.03–0.64)	0.012

*IS = ischemic stroke; HS = hemorrhagic stroke.

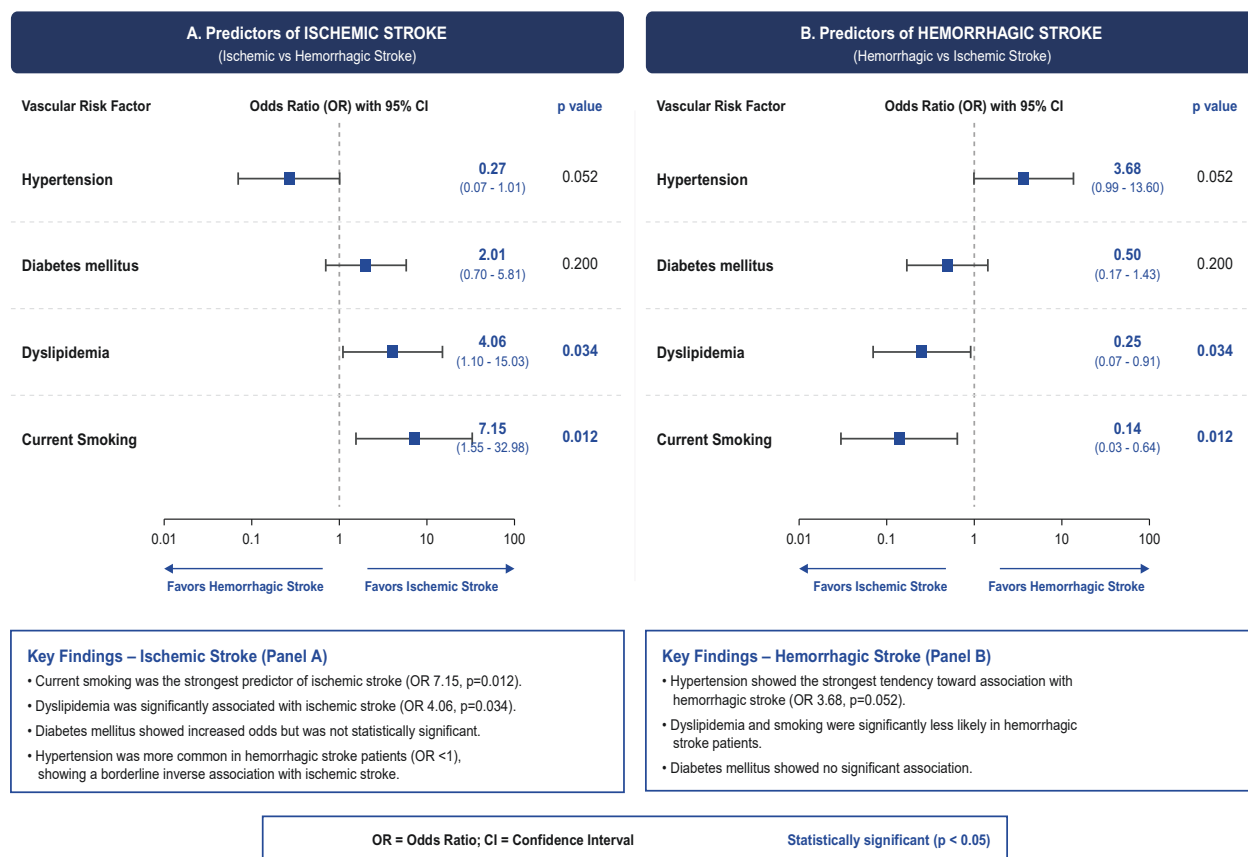


Figure 3: Vascular Risk Factors Associated with Stroke Subtypes
(Crude Logistic Regression Analysis)

Figure 3, the graphical presentation, illustrates the association between major vascular risk factors and stroke subtypes using crude logistic regression analysis. The figure compares the effects of hypertension, diabetes mellitus, dyslipidemia, and current smoking on the likelihood of ischemic stroke versus hemorrhagic stroke.

In the ischemic stroke model, current smoking demonstrated the strongest positive association with ischemic stroke, followed by dyslipidemia. Diabetes mellitus showed increased odds of ischemic stroke but without statistical significance. Hypertension showed a lower odds estimate, indicating that it was relatively more frequent among hemorrhagic stroke patients.

In the hemorrhagic stroke model, hypertension showed the strongest tendency toward association with hemorrhagic stroke. Conversely, dyslipidemia and smoking were less likely to be associated with hemorrhagic stroke, reflecting their stronger relationship with ischemic stroke.

DISCUSSION

This hospital-based cross-sectional study evaluated the distribution and association of risk factors among young adults with stroke in a tertiary care hospital in Bangladesh. The study also highlights important socio-demographic and economic characteristics of young stroke patients, providing insight into the population vulnerable to premature cerebrovascular disease.

In this study, the mean age of participants was 42.09 ± 7.14 years, and most of them (88%) belonged to the 36–50 years age group, indicating that stroke occurred predominantly among older young adults. This pattern is consistent with previous studies showing that although stroke may occur in early adulthood, incidence increases progressively toward the upper limit of the young adult age range.¹⁻³ Similar observations have been reported from Bangladesh, where young stroke patients were commonly identified in the fourth and fifth decades of life.^{4,20}

The study showed male predominance (74%), and the male-to-female ratio was 2.85:1. Similar male predominance has been reported from South Asia and other regions.^{3,4} This gender difference may be explained by greater exposure of males to vascular risk factors such as smoking, occupational stress, sedentary lifestyle, and metabolic risk factors. However, sex alone was not significantly associated with stroke subtype in this study ($\chi^2=1.267$, $p=0.260$), suggesting that once stroke occurs, the distribution of ischemic and hemorrhagic stroke may not differ significantly between males and females.

The socio-demographic findings provide important contextual information. Almost all participants were married (96%); a substantial proportion had limited educational attainment, with 68% having no formal education or education below secondary level, and 74% belonged to lower-income groups (monthly family income $\leq 20,000$ BDT). These findings suggest that socioeconomic disadvantage may contribute to increased exposure to untreated or poorly controlled vascular risk factors. Previous studies from Bangladesh have emphasized the relationship between socioeconomic transition, education, lifestyle modification, and cardiovascular disease risk.^{6,17,18}

Regarding stroke subtype, ischemic stroke was the predominant presentation, accounting for 81% of cases, whereas hemorrhagic stroke represented 19%. This distribution is consistent with global and regional evidence indicating that ischemic stroke constitutes approximately 70–85% of young adult stroke cases.^{1,19,20}

Hypertension was the most common risk factor identified in this study, affecting 64% of patients. Hypertension showed a statistically significant association with stroke subtype ($p=0.041$), with a higher prevalence among hemorrhagic stroke patients (84.2%) compared with ischemic stroke patients (59.3%). Logistic regression analysis demonstrated that hypertension increased the likelihood of hemorrhagic stroke (OR 3.68), although the association was borderline ($p=0.052$). These findings are consistent with evidence from the INTERSTROKE study, which identified hypertension as the strongest modifiable risk factor for stroke globally and particularly important for intracerebral hemorrhage.¹¹ Similar findings have been reported in Bangladesh, where hypertension remains highly prevalent and inadequately controlled.⁸

Diabetes mellitus was present in 45% of participants, with a higher proportion among ischemic stroke patients (48.1%) compared with hemorrhagic stroke patients

(31.6%), although this difference was not statistically significant ($p=0.191$). Diabetes contributes to stroke risk through endothelial dysfunction, inflammation, accelerated atherosclerosis, and increased thrombotic tendency.¹³ The relatively high prevalence of diabetes in this young stroke population reflects the growing burden of metabolic disorders associated with epidemiological transition in Bangladesh.^{17,18}

Dyslipidemia was identified in 38% of patients and demonstrated a significant association with stroke subtype ($p=0.027$). It was more frequent among ischemic stroke patients (43.2%) than hemorrhagic stroke patients (15.8%). Furthermore, logistic regression showed dyslipidemia as an independent predictor of ischemic stroke (OR 4.06, $p=0.034$). This finding supports previous evidence linking abnormal lipid profiles with premature atherosclerosis and ischemic cerebrovascular events.^{13,14}

Smoking was reported among 39% of participants and showed a significant relationship with stroke subtype ($p=0.014$). Current smoking was substantially more common among ischemic stroke patients (45.7%) compared with hemorrhagic stroke patients (10.5%). In regression analysis, smoking showed the strongest association with ischemic stroke (OR 7.15, $p=0.012$). These findings are consistent with previous studies demonstrating tobacco exposure as a major contributor to early vascular disease through endothelial injury, inflammation, and thrombosis.^{15,16}

A major finding of this study was the high burden of multiple risk factors. At least one risk factor was present in the majority of patients, while ≥ 2 risk factors were identified in 92%, showing a significant association with stroke subtype ($p=0.001$). Previous studies have emphasized that combined vascular risk factors produce a synergistic effect greater than individual risk factors alone.^{22,25}

Other evaluated factors included atrial fibrillation (18%), previous stroke (22%), sedentary lifestyle (28%), alcohol consumption (2%), and oral contraceptive pill use (6%). Although these factors were less frequent and did not demonstrate significant associations with stroke subtype, they remain clinically relevant contributors to stroke risk, particularly in selected young populations.^{2,3}

Overall, this study demonstrates that young adult stroke in Bangladesh is strongly associated with preventable vascular and lifestyle-related risk factors. Preventive strategies targeting young adults may reduce premature stroke incidence and its socioeconomic consequences in Bangladesh.²⁶⁻³⁰

LIMITATIONS OF THE STUDY

The hospital-based cross-sectional design and relatively small sample size (n=100) may limit generalizability to the broader young adult population of Bangladesh. The cross-sectional nature prevents establishing causal relationships between risk factors and stroke occurrence. Some lifestyle and socioeconomic variables were collected through patient interviews and may be affected by recall bias. Residual confounding from unmeasured factors such as diet, physical activity, genetic predisposition, and environmental exposures could not be completely excluded.

CONCLUSION

Stroke among young adults in this study was predominantly ischemic and strongly associated with modifiable vascular risk factors. Hypertension, dyslipidemia, smoking, and multiple risk-factor clustering were the major contributors. Early identification, lifestyle modification, and aggressive management of vascular risk factors are essential strategies for reducing the increasing burden of young adult stroke in Bangladesh.

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Original Article

Pattern of Infectious Morbidity During Post-Remission High-Dose Cytarabine Consolidation in Acute Myeloid Leukemia

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Abstract

High-dose cytarabine (HiDAC) is an established post-remission consolidation therapy for acute myeloid leukemia (AML), but infectious morbidity remains an important treatment-related concern. Data describing infectious complications during HiDAC consolidation in the Bangladeshi setting are limited. This study evaluated the pattern of infectious morbidity and microbiologically documented bacterial infections following HiDAC consolidation in adults with AML. This hospital-based cross-sectional observational study was conducted in the Department of Hematology, Chittagong Medical College Hospital, from January to December 2018. A total of 50 adults with AML who achieved remission following standard 3+7 induction therapy and subsequently received HiDAC consolidation were included by purposive sampling. HiDAC was administered at 3 g/m² twice daily on days 1, 3 and 5 for three planned cycles. Clinical manifestations of infection and microbiological findings were recorded during follow-up. Data were analysed using SPSS version 23. Results: Among 50 patients, 56.0% were male; male-to-female ratio, 1.27:1; Mean age $\pm$ standard deviation (SD) was 29.18 $\pm$ 8.583 years; 52.0% were aged 18-30 years and 76.0% were from rural areas. Pallor was present in 98.0% of patients. The most frequent infectious manifestations were unexplained fever (32.0%), mucositis in 28.0%, sore throat in 26.0%, diarrhoea in 18.0%, and pneumonia in 16.0%. Across successive cycles, the frequency of sore throat declined from 40.9% (9/22) in cycle 1 to 18.8% (3/16) and 8.3% (1/12) in cycles 2 and 3,

respectively; unexplained fever declined from 40.9% (9/22) to 25.0% (4/16) and remained 25.0% (3/12). Mucositis decreased from 36.4% (8/22) to 18.8% (3/16) before increasing to 25.0% (3/12). Bacteremia occurred in 9/50 (18.0%) patients, with Gram-positive organisms accounting for 7/9 (77.8%) isolates; *Staphylococcus epidermidis* was the most frequent bloodstream isolate. Non-bacteremic microbiologically documented infection occurred in 10/50 (20.0%), predominantly due to Gram-negative organisms (6/10, 60.0%), with *Escherichia coli* being the most frequent isolate. Infectious morbidity was common during HiDAC consolidation, with mucosal, respiratory, gastrointestinal, and febrile manifestations predominating. Bacteremia and other microbiologically documented infections occurred in a substantial proportion of patients, supporting close clinical monitoring and timely microbiological evaluation throughout consolidation therapy.

Keyword: Acute myeloid leukemia; high-dose cytarabine; HiDAC consolidation; cytarabine; infectious morbidity; bacterial infection.

INTRODUCTION

AML is an aggressive hematological malignancy in which achievement of complete remission with induction chemotherapy is generally followed by post-remission therapy to reduce the risk of relapse. High-dose cytarabine (HiDAC) is an established consolidation strategy, particularly in younger adults with favorable-risk AML, and has demonstrated substantial benefit in reducing relapse and improving survival.¹ The value of intensive cytarabine consolidation, however, must be balanced against treatment-related myelosuppression and infectious morbidity.²

Evidence from cooperative-group studies indicates that repeated courses of HiDAC can provide sustained antileukemic benefit, with three or more courses associated with improved disease control in selected patients, particularly those with core-binding-factor AML.³ A randomized study by the Japan Adult Leukemia Study Group found that three courses of HiDAC alone provided effective post-remission therapy compared with four courses of standard-dose multiagent chemotherapy, while the ALFA-9802 study similarly demonstrated the efficacy of HiDAC-based consolidation in younger adults.^{6,7} However, increasing treatment intensity raises concern about cumulative toxicity, particularly prolonged cytopenia and infection.²

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Infectious complications are among the most important adverse events during intensive AML chemotherapy. In a study from Manitoba evaluating standard induction followed by HiDAC consolidation, infectious morbidity occurred during the post-remission treatment period, including pneumonia, mucositis, soft-tissue infection and intra-abdominal infection.⁸ Importantly, the infectious burden associated with HiDAC may vary according to the intensity and duration of neutropenia, patient characteristics, disease status and supportive care. Neutrophil function may also persist despite a marked reduction in circulating neutrophil counts; Krauth et al. reported persistence of functionally active granulocytes until approximately day 10-12 following pulse cytarabine consolidation, suggesting that the relationship between numerical neutropenia and infection may not be straightforward.⁹

Microbiological characteristics of infection in AML are also clinically important because the causative organisms influence antimicrobial selection and infection-control strategies. De Rosa et al., in 81 patients with AML, documented 291 neutropenic episodes, of which 210 (72.2%) occurred during consolidation; fever occurred in 112 (53.4%) of these consolidation-related episodes. The mean duration of neutropenia decreased from 7 days during the first consolidation cycle to 5 days during the second and third cycles.¹⁰

The microbiological spectrum of infection is similarly heterogeneous. In a study of 163 admissions involving patients with AML and myelodysplastic syndromes, Ali et al. reported microbiologically documented infection in 44.8%; 19.6% involved Gram-positive organisms and 12.3% Gram-negative organisms, while 7.4% had mixed infections. Among 91 recovered pathogens, Gram-positive organisms accounted for 56%, with coagulase-negative staphylococci, including *Staphylococcus epidermidis*, being the most frequent Gram-positive group (25.3%); *Pseudomonas* species and *Escherichia coli* were the leading Gram-negative pathogens.¹³ Similarly, Kato et al. reported febrile neutropenia in 80.2% of patients receiving intensive AML chemotherapy, with bacteremia/fungemia and pulmonary infection occurring in 8.3% and 10.3%, respectively.¹⁴ Other studies have documented substantial variation in infection frequency and microbiological patterns during intensive AML treatment.^{15,16}

These observations are particularly relevant in Bangladesh, where access to allogeneic hematopoietic stem-cell transplantation remains limited, and HiDAC is an important post-remission treatment option for patients who achieve remission.

Despite extensive international experience with AML consolidation, there is limited published information from

Bangladesh describing the frequency and clinical spectrum of infectious morbidity specifically following post-remission HiDAC, the pattern of infection across successive consolidation cycles, and the microorganisms responsible for microbiologically documented bacterial infections. The present study was therefore undertaken to characterize infectious morbidity among adults with AML receiving HiDAC consolidation after standard 3+7 induction therapy. The study specifically assessed the prevalence and types of infectious morbidity and examined the occurrence of infectious manifestations across successive HiDAC cycles. This information may help provide locally relevant evidence for monitoring infection risk and optimizing supportive care during HiDAC consolidation.

MATERIALS AND METHODS

Study Design and Setting: This was a hospital-based observational study conducted in the Department of Hematology, Chittagong Medical College Hospital (CMCH), Chittagong, Bangladesh, from January to December 2018. The study included adult patients with AML who achieved remission following standard 3+7 induction chemotherapy and subsequently received HiDAC as post-remission consolidation.

Study Population and Sample Size: The study population comprised patients with newly diagnosed AML who achieved remission following standard 3+7 induction therapy and were admitted to the Department of Hematology for post-remission consolidation. The sample size was initially estimated using the single-proportion formula. The calculated sample size was 61. Because of time and resource constraints, 50 eligible patients were ultimately enrolled. Newly diagnosed AML treated with standard 3+7 induction chemotherapy; aged 18 years and above, and provided written informed consent were included in this study. Patients with refractory AML, secondary AML, or failure to achieve remission after induction therapy; or who declined written informed consent were excluded from the study.

HiDAC Consolidation and Follow-up: Following achievement of complete remission after induction therapy, patients received HiDAC consolidation at a dose of 3 g/m² administered twice daily at 12-hour intervals on days 1, 3 and 5. Patients were followed during consolidation for clinical evidence of infection, febrile episodes, and other relevant clinical and laboratory findings. The number of patients available for assessment decreased across successive consolidation cycles; therefore, infectious morbidity was analyzed using the cycle-specific denominators of 22 patients for cycle 1, 16 for cycle 2 and 12 for cycle 3 rather than treating the cycles as three independent groups.

Variables and Data Collection: Data were collected using a pretested structured case-record form. The recorded variables included demographic characteristics, clinical findings, site and type of infection, duration of treatment, and microbiological findings. The principal outcome variable was infectious morbidity during HiDAC consolidation. Infectious morbidity was characterized according to the clinical manifestation and, where available, microbiological documentation. Recorded clinical manifestations included unexplained fever, mucositis, sore throat, diarrhoea, pneumonia, dysuria, proctitis, soft-tissue infection and intra-abdominal infection. Patients could experience more than one infectious manifestation; therefore, the frequencies of individual infection types were not considered mutually exclusive.

Assessment of Neutropenia and Infection: Particular attention was given to patients with fever. For these episodes, clinical characteristics were recorded, together with investigations directed toward identifying an infectious focus.

Microbiological Investigations: For febrile neutropenic episodes, diagnostic investigations included chest radiography, urine routine examination, blood culture, sputum and urine cultures, rectal and throat swab cultures, and cultures of specimens obtained from skin or soft-tissue infections, as clinically indicated. Blood was collected aseptically following preparation of the venipuncture site with 70% isopropyl alcohol; a minimum of 10 mL of blood was inoculated into two culture bottles. Thioglycolate broth was used for anaerobic organisms, while MacConkey agar was used for urine culture of Gram-negative organisms. The site of infection, specimen type, and isolated microorganism were recorded. Microbiologically documented infections were categorized as bacteremic when organisms were isolated from blood culture and nonbacteremic microbiologically documented infections when a pathogen was identified from another relevant clinical specimen without documented bloodstream infection.

Statistical Analysis: Data were checked, verified, edited, and coded before analysis. Each participant was assigned an individual data record. Statistical analysis was performed using SPSS version 23.0. Categorical variables were summarized as frequencies and percentages, while continuous variables were summarized using appropriate descriptive statistics, including mean, standard deviation, and range. Because the number of patients decreased from 22 in the first HiDAC cycle to 16 in the second and 12 in the third, cycle-specific percentages were calculated using the corresponding denominator for each cycle. The

cycle-wise findings were interpreted descriptively, and no assumption was made that the three cycle populations represented independent groups.

Ethical Clearance: Written informed consent was obtained from all participants after explanation of the study objectives, procedures, potential implications, and voluntary nature of participation. Participants were informed that they could decline participation or withdraw at any time. Confidentiality of participant information was maintained throughout data collection and analysis.

RESULTS

Baseline Demographic Characteristics

The study included 50 patients with acute myeloid leukemia who received post-remission high-dose cytarabine consolidation therapy. Of these, 26 (52.0%) were aged 18–30 years, 13 (26.0%) were aged 31–40 years, 7 (14.0%) were aged 41–50 years, and 4 (8.0%) were aged >50 years. There were 28 (56.0%) males and 22 (44.0%) females, giving a male-to-female ratio of 1.27:1. Most patients were from rural areas (38, 76.0%), while 12 (24.0%) were from urban areas.

Table I: Baseline Demographic Characteristics of Patients (n=50)

Characteristics	Frequency, n	Percentage, %
Age (Mean $\pm$ SD years)	29.18 $\pm$ 8.583	
Age group (years)		
18–30	26	52.0
31–40	13	26.0
41–50	7	14.0
>50	4	8.0
Sex		
Male	28	56.0
Female	22	44.0
Locality		
Rural	38	76.0
Urban	12	24.0

Figure 1 demonstrates the frequency of selected clinical findings among the 50 patients with acute myeloid leukemia. Pallor was present in 49 (98.0%) patients, followed by abdominal findings in 12 (24.0%), skin abnormalities in 10 (20.0%), and chest findings in 8 (16.0%).

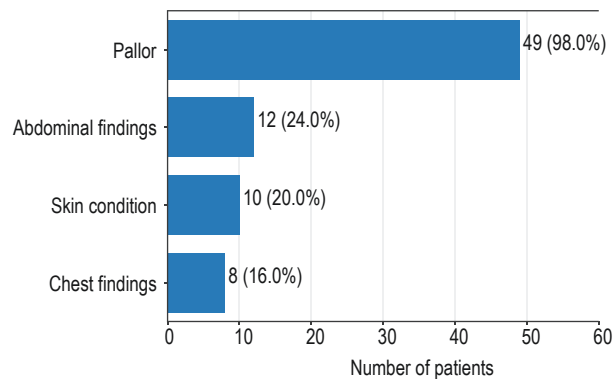


Figure 1: Baseline Clinical Findings in the Overall Study Population (n=50).

Table II displays the cycle-wise trends in infectious morbidity of patients with acute myeloid leukemia. Unexplained fever was 40.9% of patients during the first cycle, decreased to 25.0% during the second cycle, and remained stable during the third cycle. Sore throat occurred in 40.9% of patients during cycle 1, fell to 18.8% in cycle 2, and further declined to 8.3% in cycle 3. Mucositis occurred in 36.4% of patients during cycle 1 and declined to 18.8% during cycle 2, and subsequently increased to 25.0% during cycle 3. Diarrhoea showed 18.2% in cycle 1, 18.8% in cycle 2, and 16.7% in cycle 3. Pneumonia was recorded in 18.2% of patients during cycle 1, decreased to 12.5% during cycle 2, and subsequently increased to 16.7% during cycle 3. Dysuria occurred in 9.1% of patients during the first cycle, increased to 12.5%

Table II: Cycle-Wise Trends in Infectious Morbidity According to Successive Hidac Consolidation Cycles Using Cycle-Specific Denominators

Infectious morbidity	Cycle 1 (n=22)	Cycle 2 (n=16)	Cycle 3 (n=12)	Overall trend
Unexplained fever	40.9% (9)	25.0% (4)	25.0% (3)	↓ then stable
Sore throat	40.9% (9)	18.8% (3)	8.3% (1)	Consistent ↓
Mucositis	36.4% (8)	18.8% (3)	25.0% (3)	↓ then ↑
Diarrhoea	18.2% (4)	18.8% (3)	16.7% (2)	Essentially stable, slight ↓
Pneumonia	18.2% (4)	12.5% (2)	16.7% (2)	↓ then ↑
Dysuria	9.1% (2)	12.5% (2)	8.3% (1)	↑ then ↓
Proctitis	13.6% (3)	6.3% (1)	0% (0)	Consistent ↓
Soft-tissue infection	4.5% (1)	6.3% (1)	16.7% (2)	Progressive ↑
Intra-abdominal infection	4.5% (1)	6.3% (1)	8.3% (1)	Gradual ↑
Other	4.5% (1)	0% (0)	0% (0)	↓ to absent

during the second, and then decreased to 8.3% during the third. Proctitis decreased from 13.6% in cycle 1 to 6.3% in cycle 2 and to 0% in cycle 3. Soft-tissue infection increased from 4.5% in cycle 1 to 6.3% in cycle 2 and then to 16.7% in cycle 3. Intra-abdominal infection increased gradually from 4.5% in cycle 1 to 6.3% in cycle 2 and 8.3% in cycle 3. One additional/other infectious manifestation was recorded during the first cycle (4.5%), whereas none was recorded during the second or third cycles.

The most notable declining trends were observed for sore throat and proctitis, while unexplained fever declined after the first cycle and then remained stable. Mucositis and pneumonia showed a decline followed by a partial increase in the third cycle. Diarrhoea remained relatively stable, whereas dysuria fluctuated modestly. In contrast, soft-tissue infection and intra-abdominal infection

showed increasing percentages, although their absolute frequencies were very small.

Figure 2, the line graph, demonstrates cycle-specific frequencies of infectious manifestations during the first (n=22), second (n=16), and third (n=12) HiDAC consolidation cycles. Unexplained fever remained prominent across all three cycles; sore throat was prominent in the first cycle but became less frequent thereafter; mucositis remained consistently common and became the leading manifestation alongside unexplained fever in the third cycle; while pneumonia and diarrhoea persisted across all cycles at relatively lower frequencies. The decreasing numbers of patients across cycles (22 → 16 → 12) must be considered when interpreting these patterns.

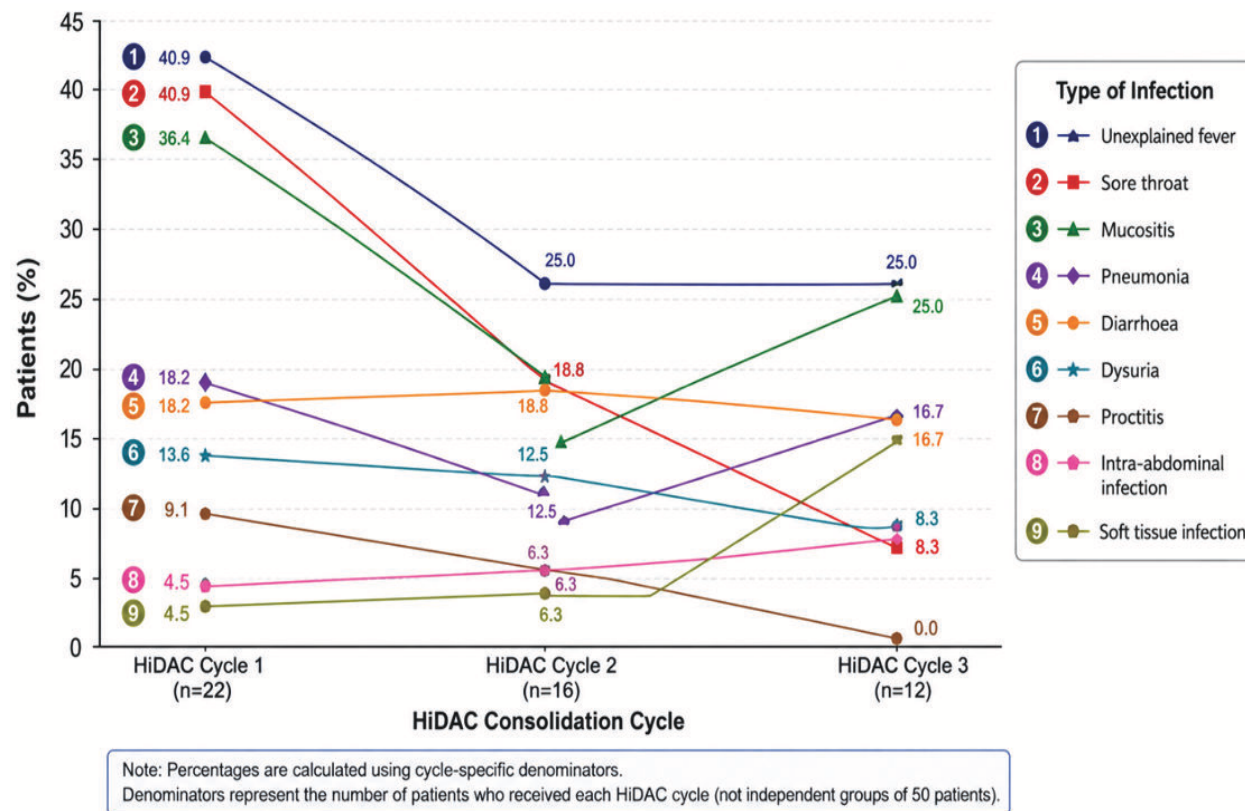
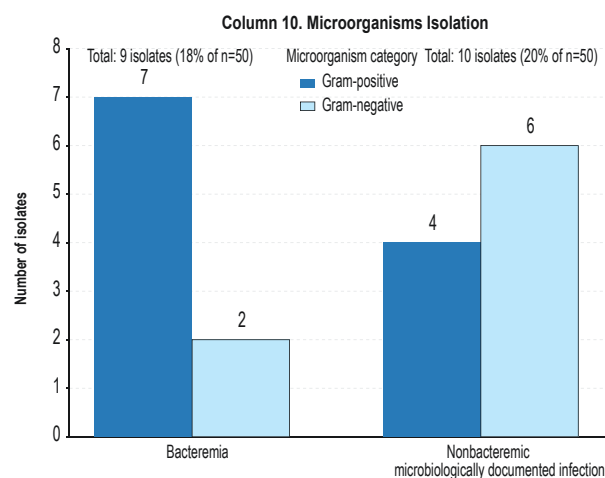


Figure 2: Pattern of Infectious Morbidity Across Successive HiDAC Consolidation Cycles.

Figure 3 demonstrates the distribution of isolated microorganisms according to the type of microbiologically documented infection. Among bacteremic episodes, 7 Gram-positive organisms were isolated compared with 2 Gram-



Source: Column 10 of the submitted manuscript: Bacteremia - 7 Gram-positive and 2 Gram-negative isolates; Nonbacteremic microbiologically documented infections - 4 Gram-positive and 6 Gram-negative isolates. Percentages refer to the total study population (n=50).

Figure 3: Microorganism Isolation Among Bacteremic and Nonbacteremic Microbiologically Documented Infections

negative isolates. Among nonbacteremic microbiologically documented infections, 6 Gram-negative organisms were isolated compared with 4 Gram-positive organisms. Overall, 19 isolates were documented across these two categories: streptococci (2), while urine cultures yielded *Escherichia coli* (3), *K. pneumoniae* (2), and *Proteus mirabilis* (1).

Figure 4, the bar chart, illustrates the distribution of specific microorganisms isolated from bacteremic and nonbacteremic microbiologically documented infections among the study patients. Among the 9 bloodstream isolates, 4 were *Staphylococcus epidermidis*, followed by 2 viridans streptococci, while *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* were each isolated in 1 case. Among the 10 nonbacteremic microbiologically documented infections, throat cultures yielded *Staphylococcus aureus* (2 isolates) and group-A streptococci (2 isolates), whereas urine cultures yielded *Escherichia coli* (3 isolates), *Klebsiella pneumoniae* (2 isolates), and *Proteus mirabilis* (1 isolate).

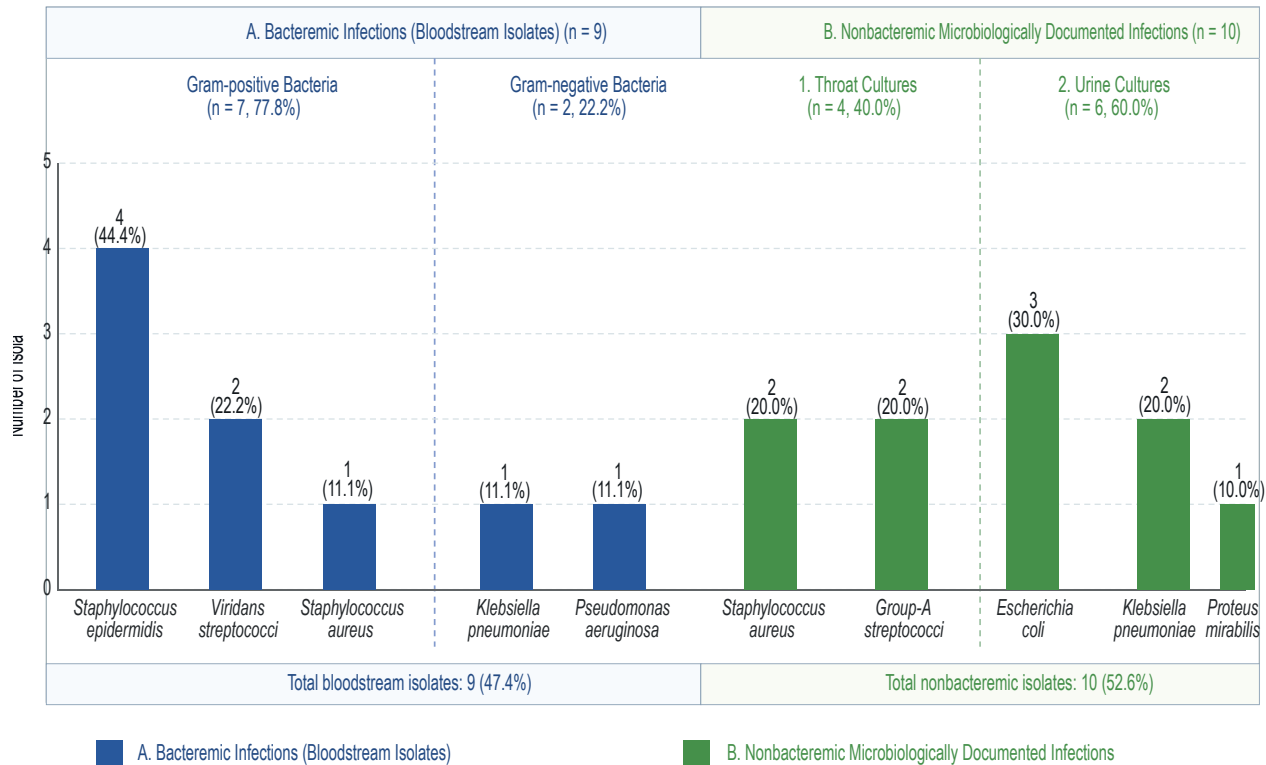


Figure 4: Microorganisms Isolated from Bacteremic and Nonbacteremic Microbiologically Documented Infections

DISCUSSION

This study evaluated infectious morbidity among 50 adults with AML receiving post-remission HiDAC consolidation after standard 3+7 induction therapy. The principal findings were that infectious morbidity was common and clinically heterogeneous, with unexplained fever (32%), mucositis (28%), sore throat (26%), diarrhoea (18%) and pneumonia (16%) being the most frequently recorded manifestations. Microbiological documentation identified 19 isolates, comprising 9 bloodstream isolates and 10 nonbacteremic isolates. These findings indicate that infectious morbidity remains an important component of supportive care during HiDAC consolidation, although the spectrum of manifestations extends beyond microbiologically confirmed infection.

The predominance of mucosal and upper respiratory manifestations in the present study is clinically plausible in the setting of intensive cytarabine therapy. Mucositis occurred in 14/50 (28%) patients and sore throat in 13/50 (26%), while pneumonia occurred in 8/50 (16%). Bow et al., in an earlier study of AML patients receiving post-remission therapy, reported mucositis in approximately 16%, pneumonia in 15%, soft-tissue infection in 5% and

intra-abdominal infection in 3%, broadly supporting the occurrence of these complications during intensive consolidation.⁸ The somewhat higher frequency of mucositis in the present series may reflect differences in patient characteristics, supportive care, diagnostic thresholds and study design.

The cycle-wise findings require cautious interpretation because the number of patients decreased from 22 in the first cycle to 16 in the second and 12 in the third. Thus, the percentages represent the experience of the patients actually receiving each cycle and should not be interpreted as longitudinal changes in a fixed cohort of 50 patients. Unexplained fever declined from 40.9% (9/22) in cycle 1 to 25.0% (4/16) in cycle 2 and remained 25.0% (3/12) in cycle 3. Sore throat showed the clearest reduction, from 40.9% to 18.8% and 8.3%, while proctitis decreased from 13.6% to 6.3% and 0%. In contrast, soft-tissue infection increased from 4.5% to 6.3% and 16.7%, and intra-abdominal infection increased modestly from 4.5% to 6.3% and 8.3%. Mucositis and pneumonia decreased during the second cycle but partially increased during the third. These fluctuations are more appropriately regarded as descriptive patterns than evidence of progressive cumulative toxicity.

The relatively stable or fluctuating pattern across cycles is consistent with previous observations that infectious complications do not necessarily increase progressively with each HiDAC course. De Rosa et al. reported 291 neutropenic episodes, 72.2% of which occurred during consolidation, with fever documented in 53.4% of consolidation-related episodes. Interestingly, the mean duration of neutropenia decreased from 7 days during the first consolidation cycle to 5 days during subsequent cycles.¹⁰ Previous studies have also reported broadly comparable infectious and antifungal outcomes across successive HiDAC courses.^{5,7,12} The present findings therefore do not support the assumption that every successive HiDAC cycle inevitably produces greater infectious morbidity.

Cytarabine-induced marrow suppression compromises host defense, while persistence of functionally active granulocytes for approximately 10-12 days after pulse cytarabine has also been described.⁹ This may partly explain why the frequency of infectious manifestations does not show a simple linear relationship with the number of consolidation cycles. Accordingly, the observed cycle-wise variation probably reflects the combined influence of neutropenia, mucosal injury, individual susceptibility and clinical exposure rather than cycle number alone.

Microbiologically, bacteremia occurred in 9/50 patients (18%). Gram-positive organisms accounted for 7/9 (77.8%) bloodstream isolates, whereas Gram-negative organisms accounted for 2/9 (22.2%). *Staphylococcus epidermidis* was the predominant bloodstream isolate (4/9), followed by viridans streptococci (2/9); *S. aureus*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* each accounted for one isolate. Among the 10 nonbacteremic microbiologically documented infections, Gram-negative organisms predominated (6/10, 60%) over Gram-positive organisms (4/10, 40%). *E. coli* was the most frequent nonbacteremic isolate (3/10), followed by *K. pneumoniae* (2/10).

The predominance of Gram-positive bloodstream isolates agrees with Jagarlamudi et al., who reported Gram-positive organisms in 52.8% of isolates, although their Gram-negative proportion was also substantial (42.8%).¹⁷ In contrast, Kumar et al. reported a predominance of Gram-negative organisms among infections in acute leukemia, including *K. pneumoniae*, *E. coli* and *P. aeruginosa*.¹⁸ Rajendranath et al. likewise found Gram-negative organisms in 58.3% of microbiologically documented episodes compared with 41.7% Gram-positive organisms.¹⁹ Thus, the present predominance of Gram-positive bacteremia but

Gram-negative nonbacteremic infection illustrates the heterogeneity of bacterial infection according to anatomical site and specimen source.

The present microbiological pattern also shows similarities with Ali et al., who reported 73 microbiologically documented infections among 163 AML/MDS admissions (44.8%); Gram-positive organisms constituted 56% of recovered pathogens, with coagulase-negative staphylococci, including *S. epidermidis*, being the most frequent group.¹³ Kato et al. similarly demonstrated a substantial burden of febrile neutropenia and bloodstream infection during intensive AML chemotherapy.¹⁴ Collectively, these comparisons support the importance of continued microbiological surveillance during HiDAC consolidation.

Overall, this study demonstrates that infectious morbidity during HiDAC is frequent but does not follow a uniform progressive pattern across consolidation cycles. Fever and mucosal manifestations were prominent, while both Gram-positive bloodstream organisms and Gram-negative nonbacteremic pathogens contributed substantially to documented infections. The findings support careful clinical surveillance throughout each HiDAC cycle, with particular attention to mucosal injury, respiratory symptoms, and urinary or soft-tissue manifestations.

LIMITATIONS OF THE STUDY

Sample size was relatively small (n=50), which limits statistical precision and the ability to detect less frequent infectious complications. Purposive sampling was used, and the study was conducted at a single tertiary-care centre, limiting the generalizability of the findings to the wider AML population in Bangladesh. The number of patients decreased across successive HiDAC cycles. Long-term clinical outcomes, including infection-related mortality, treatment discontinuation, relapse, and survival following consolidation, were not evaluated. Neutropenia remains an important biological mechanism underlying infection risk, but the present study should not be interpreted as establishing a causal relationship between neutrophil reduction and individual infectious events.

CONCLUSIONS

Post-remission high-dose cytarabine consolidation in patients with acute myeloid leukemia was associated with a substantial but predominantly manageable burden of infectious morbidity. The most frequent clinical manifestations were unexplained fever (16/50, 32%),

mucositis (14/50, 28%), sore throat (13/50, 26%), diarrhoea (9/50, 18%), and pneumonia (8/50, 16%). Infectious manifestations generally declined across successive consolidation cycles for sore throat, proctitis, and unexplained fever, although mucositis and pneumonia showed some fluctuation, while soft-tissue and intra-abdominal infections increased slightly in later cycles despite their low absolute frequencies. Microbiologically documented infections included bacteremia in 9/50 patients (18%), predominantly caused by Gram-positive organisms (7/9, 77.8%), and non-bacteremic documented infections in 10/50 patients (20%), with Gram-negative organisms predominating (6/10, 60.0%). These findings indicate that infectious complications remain an important consideration during HiDAC consolidation and support close clinical surveillance, timely investigation of febrile episodes, and appropriate microbiological evaluation during treatment. Larger multicentre prospective studies are warranted to better define infection risk, identify clinically relevant predictors, and assess outcomes across different consolidation regimens in the Bangladeshi setting.

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Case Report

HLH-Like Hyperinflammation and Biopsy-Proven Acute Tubulointerstitial Nephritis in Probable Typhoid Fever: A Rare Immune-Mediated Multisystem Presentation

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Abstract

Typhoid fever is a systemic infection caused by Salmonella enterica serotype Typhi and remains an important public health concern in developing countries. Although it commonly involves the gastrointestinal and reticuloendothelial systems, rare immune-mediated complications with multisystem involvement have been described. We report a case of a 19-year-old male presenting with persistent high-grade fever, cytopenias, marked hyperferritinemia, acute kidney injury, and systemic inflammation suggestive of an HLH-like hyperinflammatory state associated with probable enteric fever. The patient had fever, splenomegaly, thrombocytopenia, elevated ferritin (>3000 ng/mL), hypofibrinogenemia, and mild hypertriglyceridemia, but did not fulfill complete HLH-2004 diagnostic criteria. Blood cultures were negative, possibly due to prior antibiotic exposure, while a strongly positive typhoid serological titre in the appropriate clinical and epidemiological context supported probable enteric fever. Renal biopsy demonstrated acute tubulointerstitial nephritis with acute tubular injury and minimal change disease-like glomerular alterations, suggesting an immune-mediated renal process. The patient was treated with intravenous ceftriaxone and corticosteroids due to persistent systemic inflammation and progressive renal involvement, resulting in complete clinical and biochemical recovery. This case highlights the importance of recognizing infection-associated HLH-like hyperinflammation and immune-mediated renal injury in patients with probable typhoid fever presenting with persistent fever, cytopenias, and acute kidney injury.

Keywords: Enteric fever; hemophagocytic lymphohistiocytosis; hyperferritinemia; acute tubulointerstitial nephritis; acute kidney injury; immune-mediated complication

INTRODUCTION

Typhoid fever is a systemic bacterial infection caused by *Salmonella enterica* serotype Typhi and remains endemic in many low- and middle-income countries, including Bangladesh. Transmission occurs mainly through the fecal–oral route, and the disease typically presents with prolonged fever, gastrointestinal symptoms, bacteremia and systemic inflammatory manifestations. Common complications include intestinal hemorrhage, intestinal perforation, encephalopathy, and sepsis^{1, 2}

Although enteric fever primarily affects the gastrointestinal and reticuloendothelial systems, severe immune-mediated complications have increasingly been recognized. Hyperinflammatory syndromes resembling macrophage activation syndrome (MAS) or secondary hemophagocytic lymphohistiocytosis (HLH) have rarely been reported in association with bacterial infections, including enteric fever. These conditions are characterized by dysregulated immune activation, excessive cytokine release, cytopenias, hyperferritinemia, hypofibrinogenemia, and multiorgan dysfunction³⁻⁵.

Renal involvement in typhoid fever is uncommon but may occur through several mechanisms, including immune-mediated glomerular injury, acute tubular injury, and tubulointerstitial nephritis. Biopsy-proven acute tubulointerstitial nephritis associated with HLH/MAS-like inflammatory activation in the setting of enteric fever appears to be extremely rare⁶.

We report a rare case of probable typhoid fever complicated by HLH-like hyperinflammation and biopsy-proven acute tubulointerstitial nephritis with minimal change disease-like features. The case emphasizes the importance of early recognition of atypical immune-mediated manifestations of enteric fever and the role of combined antimicrobial and immunomodulatory therapy.

CASE REPORT

Patient Information and Initial Presentation

A 19-year-old male presented with a five-day history of high-grade fever, vomiting, anorexia, and generalized weakness. There was no significant previous medical history, chronic illness, medication exposure, or known autoimmune disorder.

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On admission, the patient was febrile (103°F), tachycardic, and mildly dehydrated. Examination revealed splenomegaly without evidence of focal infection.

Initial investigations demonstrated thrombocytopenia, elevated inflammatory markers, and acute kidney injury. Serum creatinine was 2.5 mg/dL with active urinary sediment, moderate proteinuria, and dysmorphic red blood cells. Serum ferritin was markedly elevated (>3000 ng/mL), while fibrinogen was reduced and triglyceride levels were mildly increased, raising suspicion of an HLH-like hyperinflammatory state.

Clinical Timeline (CARE Guideline Format)

Time	Clinical Event
Day -5 to 0	Development of high-grade fever, vomiting, anorexia, and weakness
Day 0	Hospital admission: fever, tachycardia, dehydration, and splenomegaly detected
Day 1	Investigations revealed thrombocytopenia, AKI (creatinine 2.5 mg/dL), and elevated inflammatory markers
Day 3	Ferritin markedly elevated (1765 ng/mL); inflammatory markers remained high
Day 5–6	Ferritin increased (>3000 ng/mL), hypofibrinogenemia identified; HLH-like inflammatory state suspected
Day 6	Renal biopsy performed, showing acute tubulointerstitial nephritis with acute tubular injury
Day 6–7	Intravenous ceftriaxone initiated; dexamethasone started due to persistent inflammatory activity
Day 9	Fever resolved with improvement of inflammatory markers

Day 10 onward Renal function gradually improved with continued clinical recovery

Diagnostic Assessment and Differential Diagnosis

The differential diagnosis included infectious, inflammatory, and hematological causes of fever with cytopenias, hyperferritinemia, and acute kidney injury.

The following conditions were evaluated:

- Dengue fever:** Excluded by negative dengue testing and clinical assessment.
- Malaria:** Excluded by negative malaria investigations.
- Leptospirosis:** Considered because of fever with renal involvement, but testing was negative.
- Viral hepatitis associated systemic inflammation:** HBsAg and anti-HCV were negative.
- Autoimmune vasculitis or connective tissue disease:** ANA, C-ANCA and P-ANCA were negative, with renal biopsy not supporting immune complex glomerulonephritis.
- Secondary HLH due to other infections (EBV/CMV/tuberculosis):** No clinical or laboratory evidence suggested these causes.

Blood cultures were negative; however, the patient had received three doses of oral cefixime (400 mg) before admission, which may have reduced culture yield. A high typhoid antibody titre (TH 1:640) in the appropriate endemic setting, a compatible clinical presentation, exclusion of alternative diagnoses, and a response to ceftriaxone supported a diagnosis of probable enteric fever.

Assessment of HLH-2004 Diagnostic Criteria

HLH-2004 Criterion	Finding in the Present Case
Fever	Present
Splenomegaly	Present
Cytopenia affecting ≥2 lineages	Partial (thrombocytopenia; leukocyte fluctuation)
Hypertriglyceridemia	Mild elevation present
Hypofibrinogenemia	Present
Hemophagocytosis	Not demonstrated
Ferritin >500 ng/mL	Present (>3000 ng/mL)
Reduced NK-cell activity	Not performed
Elevated soluble CD25	Not performed

The patient met several features suggestive of HLH/MAS spectrum activation but did not meet the complete HLH-2004 diagnostic criteria. Therefore, the condition was described as an HLH-like hyperinflammatory state rather than definitive HLH.

Treatment and Outcome

The patient was treated with intravenous ceftriaxone 2 g daily for 14 days. Due to persistent fever, increasing ferritin levels, thrombocytopenia, and ongoing systemic inflammation, dexamethasone therapy was initiated and gradually tapered over two weeks.

Following treatment, the patient showed clinical improvement with defervescence by hospital day 9, gradual normalization of inflammatory markers, and improvement of renal function.

Renal biopsy demonstrated acute tubulointerstitial nephritis with dense inflammatory infiltrates and acute tubular injury. Immunofluorescence showed mesangial IgM and C3 deposition in an entrapment pattern without evidence of primary immune complex glomerulonephritis, supporting an immune-mediated renal injury.

Laboratory and Results Presentation

Table I summarizes the sequential hematological, inflammatory, renal, autoimmune, and infectious parameters during hospitalization. Initial laboratory evaluation revealed thrombocytopenia (platelet count $90 \times 10^3/\mu\text{L}$) with fluctuating leukocyte counts during hospitalization. Inflammatory markers were markedly elevated, including C-reactive protein (maximum 146.7 mg/L) and serum ferritin (>3000 ng/mL), suggesting significant systemic inflammatory activation. Hypofibrinogenemia (166.5 mg/dL) and mildly elevated triglyceride levels further supported an HLH/MAS-like hyperinflammatory state.

Renal assessment demonstrated acute kidney injury with serum creatinine of 2.5 mg/dL at admission, persistent elevation during the early hospital course, and gradual improvement following treatment. Urinary evaluation revealed active sediment, moderate proteinuria (24-hour urinary protein 1.7 g/day), and dysmorphic red blood cells, raising suspicion of immune-mediated renal involvement.

Autoimmune investigations, including antinuclear antibody (ANA), cytoplasmic and perinuclear antineutrophil cytoplasmic antibodies (C-ANCA and P-ANCA) were negative. Viral screening for hepatitis B and hepatitis C was negative.

Blood cultures remained negative. However, the patient had received oral cefixime (400 mg) prior to admission, which may have reduced microbiological yield. Typhoid serology demonstrated an elevated TH titre (1:640). Considering the compatible clinical presentation, endemic setting, exclusion of alternative infections, and favorable response to ceftriaxone, a diagnosis of probable enteric fever was considered.

Table I: Sequential Hematological, Inflammatory, Renal, Autoimmune, and Viral Parameters During Hospitalization

Parameter	Ref. Range	Day 1	Day 3	Day 4	Day 5	Day 6	Day 7	Day 9	Day 10
Haematological Parameters									
Haemoglobin (g/dL)	13.0 – 17.0	17.0	14.4	13.4	12.8	14.6	15.3	13.2	12.6
WBC ($\times 10^3/\mu\text{L}$)	4.0 – 11.0	5.1	6.5	5.5	8.03	7.5	8.0	9.0	11.0
Neutrophils (%)	40 – 75	71	86	86	88	87	90	78	82
Lymphocytes (%)	20 – 45	19	11	10	9	11	7	19	15
Platelets ($\times 10^3/\mu\text{L}$)	150 – 400	90	90	60	120	160	100	180	125
Inflammatory Markers									
CRP (mg/L)	< 5	92	—	—	126.5	146.7	97.0	67.5	29.8
Ferritin (ng/mL)	12 – 300	—	1765	—	—	—	3359	2306	—
Fibrinogen (mg/dL)	200 – 400	—	—	—	—	—	166.5	—	—
Haptoglobin (mg/dL)	32 – 205	—	—	—	—	—	0.70	—	—
LDH (U/L)	140 – 280	—	993	—	—	—	—	509	—
Renal Parameters									
Creatinine (mg/dL)	0.7 – 1.2	2.5	2.4	2.3	2.3	2.3	2.4	1.8	1.6
UTP-24hrs (g/24hrs)	< 0.15	—	1.7	—	—	—	—	—	—
Autoimmune Markers									
ANA (Au/mL)	< 40	—	—	5.27	—	—	—	—	—
C-ANCA (U/mL)	< 5.00	—	—	1.50	—	—	—	—	—
P-ANCA (U/mL)	< 20	—	—	8.34	—	—	—	—	—
Viral Screening									
HBsAg	< 1.00	—	—	0.01	—	—	—	—	—
Anti-HCV	< 1.00	—	—	0.15	—	—	—	—	—

Abbreviations: Ref.= reference; WBC= white blood cell count; CRP= C-reactive protein; LDH= lactate dehydrogenase; ANA= antinuclear antibody; C-ANCA= cytoplasmic antineutrophil cytoplasmic antibody; P-ANCA= perinuclear antineutrophil cytoplasmic antibody; HBsAg= hepatitis B surface antigen; Anti-HCV= antibody to hepatitis C virus; UTP-24hrs= urinary total protein in 24 hours.

Figure 1, a line graph, displays the daily temperature trend. Fever persisted during the initial hospital days and peaked at 104°F on hospital day 2, then gradually resolved after initiation of antimicrobial and corticosteroid therapy, with normalization by day 9.

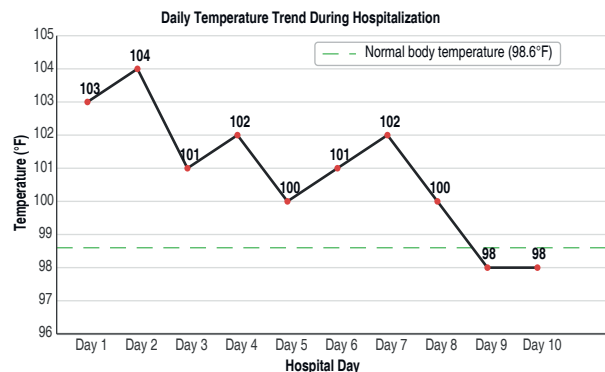


Figure 1: Daily Temperature Trend during Hospitalization

Figure 2 illustrates the renal biopsy findings. Light microscopy showed dense interstitial inflammatory infiltrates composed predominantly of lymphocytes, plasma cells, and eosinophils with associated acute tubular injury.

Immunofluorescence revealed mesangial IgM and C3 deposition in an entrapment pattern without evidence of primary immune complex-mediated glomerulonephritis. Overall, the findings were consistent with acute tubulointerstitial nephritis with minimal change disease-like glomerular alterations.

(A) Dense interstitial inflammatory infiltrates with lymphocytes, plasma cells and eosinophils consistent with acute tubulointerstitial nephritis (H&E $\times 400$). (B) Acute tubular injury with tubular dilatation and epithelial cell sloughing (H&E $\times 400$). (C) Tubular epithelial flattening and reactive epithelial changes without crescent formation (H&E $\times 400$). (D) Glomerulus with preserved architecture surrounded by tubular injury and interstitial inflammation (H&E $\times 200$). (E, F) Mesangial IgM and C3 deposition in an entrapment pattern without evidence of immune complex glomerulonephritis, consistent with minimal change disease-like changes.

(Abbreviations: H&E = hematoxylin and eosin; IF = immunofluorescence).

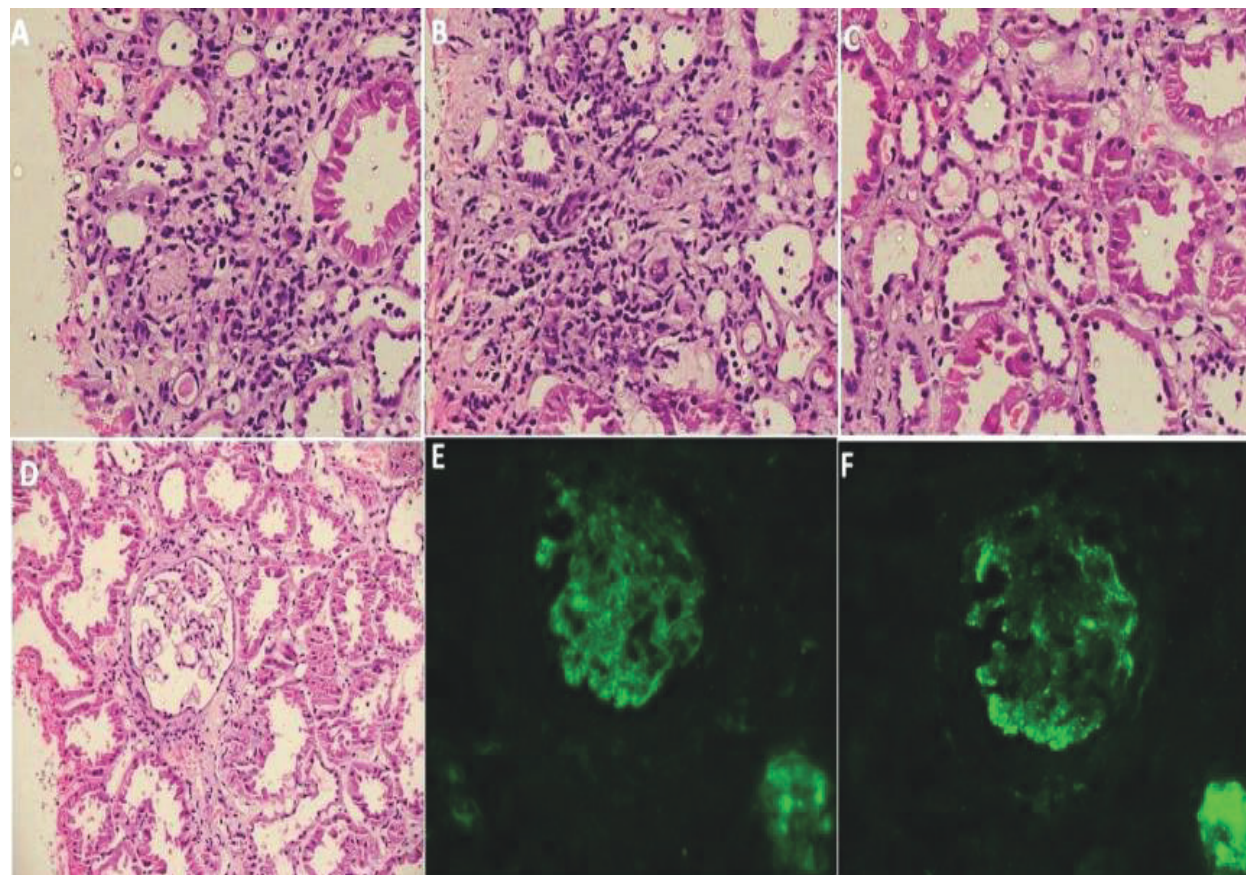


Figure 2: Renal Biopsy Findings on Light Microscopy and Immunofluorescence

DISCUSSION

Typhoid fever remains an important systemic infection in tropical and developing regions and continues to cause significant morbidity despite advances in antimicrobial therapy. The disease typically presents with prolonged fever, gastrointestinal manifestations, and systemic inflammatory responses; however, severe immune-mediated complications are uncommon and may be overlooked.^{1, 2}

In the present case, probable enteric fever was complicated by marked hyperinflammation, cytopenia, hyperferritinemia and acute kidney injury, representing an HLH-like inflammatory phenotype. Hyperferritinemia, hypofibrinogenemia, and thrombocytopenia are recognized features of macrophage activation and secondary HLH spectrum disorders. However, this patient did not meet all HLH-2004 criteria, and therefore the diagnosis was considered an HLH-like hyperinflammatory state rather than definitive HLH.⁷

The pathogenesis of infection-associated hyperinflammation involves uncontrolled activation of macrophages, antigen-presenting cells, and cytotoxic lymphocytes, resulting in excessive cytokine production and systemic tissue injury. Secondary HLH is increasingly recognized as a continuum of immune dysregulation triggered by infections, malignancies, and autoimmune diseases rather than a single uniform disease entity.^{4, 5}

Previous reports have described HLH-like manifestations associated with enteric fever, although such presentations remain rare. Swaminathan and Naveed highlighted the diagnostic challenge of distinguishing infection-associated inflammatory syndromes from other hyperinflammatory conditions, particularly in patients presenting with persistent fever, cytopenias, and markedly elevated ferritin levels³. In the current case, the coexistence of renal involvement further complicated the clinical picture and required evaluation for both infectious and autoimmune causes.

Renal complications of typhoid fever are uncommon but have been described, including acute tubular injury, glomerulonephritis, and tubulointerstitial nephritis⁶. The present case is notable because renal biopsy confirmed acute tubulointerstitial nephritis with acute tubular injury and minimal change disease-like changes. The absence of immune complex glomerulonephritis and negative autoimmune markers favored an immune-mediated tubulointerstitial process rather than primary renal autoimmune disease.

The relationship between enteric fever and renal injury may involve multiple mechanisms, including immune complex deposition, inflammatory cytokine-mediated injury, and direct infection-related immune activation. In this patient, the combination of systemic hyperinflammation and renal biopsy findings suggests that immune dysregulation played an important role in disease manifestation.

The management of infection-associated HLH-like inflammatory states remains challenging because immunosuppression may theoretically worsen infection, whereas uncontrolled inflammation may contribute to organ dysfunction. Current recommendations suggest that selected patients with severe secondary HLH/MAS may benefit from immunomodulatory therapy alongside appropriate antimicrobial treatment⁹. In this case, persistent fever, rising inflammatory markers, thrombocytopenia, and renal involvement prompted the addition of dexamethasone after initiation of ceftriaxone. The subsequent clinical improvement and normalization of inflammatory parameters suggested that inflammatory activation contributed substantially to the severity of illness.

To the best of our understanding, the occurrence of HLH-like hyperinflammation likely associated with enteric fever, alongside biopsy-confirmed acute tubulointerstitial nephritis, constitutes a rare clinical manifestation. This case underscores the importance for healthcare professionals to identify atypical immune-mediated complications arising from prevalent tropical infections, especially in instances where persistent fever, cytopenias, hyperferritinemia, and acute kidney injury manifest concurrently.

LIMITATION OF THIS CASE REPORT

The major limitation of this report is the absence of microbiological confirmation of *Salmonella Typhi* infection. Negative blood culture may have been influenced by prior antibiotic exposure. Although typhoid serology has limitations regarding specificity, the diagnosis of probable enteric fever was supported by the clinical presentation, epidemiological context, exclusion of alternative diagnoses, and response to appropriate antimicrobial therapy.

CONCLUSION

Probable typhoid fever may rarely be associated with severe immune-mediated complications, including HLH-like hyperinflammation and acute tubulointerstitial nephritis. Persistent fever accompanied by cytopenias, marked

hyperferritinemia, hypofibrinogenemia, and renal dysfunction should prompt evaluation for infection-associated hyperinflammatory states.

Although microbiological confirmation was unavailable in this case, the clinical findings, serological evidence, exclusion of alternative causes, and therapeutic response supported probable enteric fever as the underlying trigger. Early recognition and appropriate combination of antimicrobial therapy with carefully selected immunomodulation may improve outcomes in patients with severe inflammatory manifestations.

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Obituary news January-2026

BMA would like to express deep condolence on deaths of the following notable physicians in recent past:

Sl. No.	Name	Date of Death
1	Professor Dr. Hosne Ara Tahmin Charu Former Additional Director General (ADG), DGHS Former Principal Dhaka Medical College	08/12/2025
2	Dr. Dilu Ara Begum Former Additional Director General (ADG), DGHS	02/12/2025
3	Dr. Azmun Nahar Jihan Ex Student of Chattogram Medical College (52bach)	30/11/2025
4	Dr. Nasim Ahmed Sumon Dermatologist, Shaheed Suhrawardy Medical College, Dhaka	26/11/2025
5	Dr. Mahbubur Rahman Rashid Associate Professor of Dermatology, North East Medical College & Hospital, Dhaka	25/11/2025
6	Professor Dr. Matiur Rahman Renowned Urologist Ex. President, Bangladesh Renal Association	19/01/2025
7	Dr. Iffat Mokarrama Oshi (42nd BCS Health) and Resident Physician Department of Gastroenterology, Sir Salimullah Medical College Hospital Ex-student, Dhaka Medical College's (K-71 batch)	20/10/2025
8	Prof. Dr. Mohsinuzzaman Chowdhury Ex. Principal, Cumilla Medical College & Ex. Secretary BMA Cumilla Branch	27/09/2025
9	Dr. Sourav Saha Ex Student of Rangpur Medical College (44bach)	22/09/2025
10	Dr. Md. Sirajul Islam Former Superintendent, Lalmonirhat Sadar Hospital	03/09/2025
11	Dr. Fakhrul Alam Faruq Ex Student of Sir salimullah Medical College (1st Bach)	01/09/2025

May Allah bless the departed souls.

Our heartiest commiseration to the deceased's family, our prayers are with them during this difficult moment of their life.