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Address of correspondence

Executive Editor, ADMJ
Bashundhara Ad-din Medical College
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Email address: article.admj@gmail.com

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Editorial

The Mpox Outbreak – A Global Health Wake-Up Call

Introduction

On August 14, 2024, the World Health Organization (WHO) declared an upsurge of Mpox (formerly known as monkeypox) in the Democratic Republic of the Congo (DRC) and its spread to neighboring countries as a Public Health Emergency of International Concern (PHEIC). This declaration came as the DRC, which has long battled Mpox as an endemic disease, witnessed a dramatic rise in cases, now affecting neighboring countries like Uganda, South Sudan, and the Republic of Congo. The resurgence of Mpox raises significant concerns about preparedness, health equity, and the world's ability to respond effectively to zoonotic diseases.

Mpox: A Persistent Threat in Central Africa

Mpox was first identified in humans in 1970 in the DRC, and it has since remained endemic in parts of Central and West Africa. The virus, which is transmitted zoonotically from animals such as rodents and primates to humans, has seen sporadic outbreaks over the years. Human-to-human transmission, while less common, occurs through close contact with bodily fluids, respiratory droplets, and contaminated materials such as bedding or clothing.[1]

The 2024 resurgence in the DRC marks a significant uptick in cases, highlighting the persistence of Mpox in African regions with poor healthcare infrastructure and inadequate disease surveillance.[2] Conflict, displacement, and ecological changes such as deforestation are believed to have exacerbated the spread, as human populations increasingly interact with wildlife reservoirs of the virus.

The WHO's Declaration of a Public Health Emergency of International Concern

In response to the rising cases, the WHO declared the Mpox upsurge a PHEIC on August 14, 2024, a designation that aims to mobilize international resources and action to prevent further spread.[3] A PHEIC is the highest level of alert under the International Health Regulations (IHR), signaling the need for a coordinated global response. The 2024 Mpox crisis echoes previous outbreaks of zoonotic diseases, such as Ebola and COVID-19, underscoring the critical importance of early intervention and cross-border cooperation.

The 2024 Outbreak: Causes and Consequences

Several factors have contributed to the ongoing Mpox outbreak in the DRC and its neighboring countries. Deforestation, for instance, has increased human contact with wildlife, facilitating zoonotic spillover events.[4] Additionally, the region's fragile healthcare infrastructure has made it challenging to contain the virus once it spread beyond its typical rural confines.[5]

Neighboring countries such as Uganda and South Sudan, which already face their own public health challenges, have reported increasing numbers of Mpox cases, raising concerns about further regional spread.[6] Weak surveillance systems and under-resourced healthcare facilities have hindered timely detection and containment efforts, which are essential in preventing Mpox from becoming a more significant international health crisis.

Public Health Response: Successes and Shortcomings

Vaccine Deployment and Equity

One of the most significant components of the global response to the 2024 Mpox outbreak has been the rapid deployment of vaccines. The smallpox vaccine, which provides cross-protection against Mpox, has proven effective in reducing the severity of cases and preventing further transmission.[7] However, vaccine distribution has once again highlighted significant inequities between wealthy nations and low- and middle-income countries.

Countries like the United States and members of the European Union have stockpiled vaccines, while many African nations have struggled to secure doses despite bearing the brunt of Mpox for decades.[8] This inequitable distribution mirrors the global response to the 2022 Mpox outbreak, during which wealthier nations received the lion's share of vaccines, leaving African countries with limited access despite their endemic burden.[9]

Public Awareness and Combating Stigma

Another challenge in managing the 2024 outbreak has been public awareness and misinformation. As seen during the 2022 Mpox outbreak, early public health messaging led to stigma, particularly against men who have sex with men (MSM), who were disproportionately affected during the initial stages of the outbreak.[10] Public health campaigns in Africa and around the world have been critical in combating stigma and ensuring that at-risk populations are informed and able to seek care without fear of discrimination.

In Africa, however, the stigma associated with Mpox and other infectious diseases has made it difficult to engage vulnerable populations, particularly in conflict zones where healthcare access is already limited. Addressing these

challenges requires targeted interventions, robust public health campaigns, and collaboration between international health agencies and local organizations.[11]

Challenges and Lessons Learned

The 2024 Mpox outbreak provides several critical lessons for global public health preparedness and response.

1. Vaccine Equity

The issue of equitable vaccine distribution remains a critical challenge. Low- and middle-income countries, particularly in Africa, continue to face difficulties accessing vaccines despite the fact that Mpox has been endemic in the region for decades. Global mechanisms for equitable vaccine allocation must be improved to ensure that all countries have access to life-saving vaccines during public health emergencies.[12]

2. Strengthening Regional Healthcare Systems

The Mpox outbreak has revealed weaknesses in the healthcare systems of the DRC and its neighbors. Investment in healthcare infrastructure, including diagnostic tools, healthcare worker training, and surveillance systems, is essential to prevent future outbreaks from becoming regional or international health crises.[13] Strengthening healthcare systems will not only help contain Mpox but also prepare these countries for other emerging zoonotic diseases.

3. Surveillance and Early Detection

A robust global surveillance system is critical to detecting and responding to zoonotic diseases before they become widespread. Early detection, combined with rapid response measures, can help prevent localized outbreaks from spreading beyond national borders. In the case of Mpox, stronger surveillance in African nations could have facilitated quicker containment and a more efficient response.[14]

4. International Cooperation and Funding

The international response to Mpox must go beyond short-term emergency funding. Sustainable financial support for African countries facing endemic diseases like Mpox is critical. Long-term investment in healthcare, infrastructure, and research can help mitigate the risks posed by zoonotic diseases and ensure that countries are better prepared for future outbreaks.[15]

Conclusion

The 2024 Mpox outbreak in the DRC and its spread to neighboring countries is a stark reminder of the ongoing vulnerabilities in global health systems. The WHO's declaration of a PHEIC underscores the importance of international cooperation, equitable vaccine distribution, and the need for stronger healthcare infrastructure, particularly in regions most affected by zoonotic diseases.

Moving forward, the international community must prioritize preparedness, invest in healthcare systems in low- and middle-income countries, and ensure that future outbreaks are met with equitable and coordinated global responses. Mpox may be the current threat, but the lessons learned from this crisis will be invaluable for addressing future public health challenges.

Dr. Mohammad Mazharul Islam
Associate Professor
Department of Community Medicine
Bashundhara Ad-din Medical College,
South Keraniganj, Dhaka
E-mail: mazhar2020@gmail.com

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Original article

Effect of Regular Exercise on Some Hematological Parameters: A Cross-Sectional Analysis

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Tajkia Sultana,[1] Momtaz Begum,[2] Mousumi Tarin,[3] Roksana Islam,[4] Nahid Sultana,[5] Pranoy Kumar Chakraborty[6]

Abstract:

Background: Regular exercise is thought to play a key role in controlling the function of blood cells. Exercise is a powerful stimulus to alter hematological parameters like red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, total white blood cell count, differential count (%) of neutrophils, lymphocytes, and platelets. ***Objectives:*** To observe the effect of regular exercise on some hematological parameters in regularly exercising healthy adult males and relate the RBC parameters with exercise duration. ***Methodology:*** This cross-sectional study was conducted from July 2021- June 2022 in the Department of Physiology, Chittagong Medical College in collaboration with Lift n Life Fitness Arena gym; Muscle Mania gym, and Agrani Bank Laldighi corporate branch, Chattogram. A total of 74 male subjects, aged between 20-50 years and with a BMI of 18.5-27.5 kg/m² were included in this study by convenient sampling. 37 persons exercising regularly in the gym were included in group A. Age, height, weight, and BMI matched 37 persons were included in group B who were selected from bank officials. Collected data were analyzed by SPSS-26. Between groups, a comparison of quantitative variables was done by independent sample t-test. Pearson's correlation test was done to see the correlation of RBC parameters (RBC count, Hb, HCT, MCV) with the duration of exercise. ***Result:*** Mean values of RBC count, Hb, and HCT were significantly higher but total WBC count was significantly lower in group A (gym exercising) compared to group B (non-exercising). ($p<0.05$). MCV, DC (%) of neutrophils, lymphocytes, and platelets showed insignificant changes between groups. ($p>0.05$). RBC and MCV showed a significant positive correlation with the duration of exercise ($p<0.05$), while Hb and HCT didn't show any correlation. ($p>0.05$). ***Conclusion:*** The results of this study conclude that regular exercise has an effect on some hematological parameters in healthy adults.

Keywords: Exercise, Adult males, RBC count, Hemoglobin (Hb), Hematocrit (HCT), Mean corpuscular volume (MCV), total WBC count, differential count (%) of neutrophil and lymphocyte, platelets.

Introduction:

A sedentary lifestyle adversely affects the physical performance of human beings.[1] There is increasing evidence of the link between a sedentary lifestyle and adverse outcomes.[2] According to WHO, up to 5 million deaths per year can be prevented if the global population is more active.[3] It was reported that insufficient physical activity is

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Address of Correspondence: Dr. Tajkia Sultana, Senior lecturer, Department of Physiology, Bashundhara Ad-din Medical College, South Keraniganj, Dhaka. Email address: tajkia.sultana95@gmail.com

1. Dr. Tajkia Sultana, Senior lecturer, Department of Physiology, Bashundhara Ad-din Medical College, South Keraniganj, Dhaka
2. Prof. Dr. Momtaz Begum, Department of Physiology, Chittagong Medical College, Chattogram
3. Dr. Mousumi Tarin, Lecturer, Department of Physiology, Chattagram Maa-O-Shishu Hospital Medical College, Chattogram
4. Dr. Roksana Islam, Lecturer, Department of Physiology, Chittagong Medical College, Chattogram
5. Dr. Nahid Sultana, Lecturer, Department of Physiology, Sylhet MAG Osmani Medical College, Sylhet
6. Dr. Pranoy Kumar Chakraborty, Lecturer, Department of Physiology, Chittagong Medical College, Chattogram

highly prevalent among the Bangladeshi adult population.[4] Regular exercise improves the efficiency of various systems in the body, whereas lack of exercise results in hypovolemia, hematocrit imbalance, and immune dysfunction.[5,6] Physical activity indicates walking, cycling, swimming, sports, and active recreation that can be done at any level of skill.[7] Adults should do moderate-intensity physical activity for at least 150-300 mins or 75-150 mins physical activity of vigorous-intensity or an equivalent combination of both moderate and vigorous-intensity activity every week.[7] Exercise can increase RBC and Hb which enables the transport of respiratory gases, carries metabolites such as lactate and normalizes blood pH.[5] Oxygen-carrying capacity and oxygen binding capacity are decreased due to reduced RBC and Hb which may negatively impact health and performance.[5] Exercise causes hyperplasia of hematopoietic bone marrow and the release of several hormones and cytokines that result in increased erythropoiesis, red cell mass, and blood volume. Therefore exercise could be an appropriate non-pharmacological intervention to improve anemia in patients.[8]

The immune system is very responsive to exercise.[9] White blood cells (WBCs) are an important component of the immune system. WBC protects the body from bacteria, viruses, infections, and damaged cells that are harmful to the body.[5] It is worth mentioning that, in physically inactive persons leukocytosis and neutrophilia indicate chronic low-grade inflammation and novel risk factors for coronary heart disease, HTN, and type 2 DM.[10,11]

In the hemostatic system of the body, platelets play a crucial role. It contributes to the formation of pathologic thrombus leading to coronary artery disease and stroke.[12] Exercise has been documented to alter platelet number, size, and function.[12] It is assumed that acute and strenuous exercise increases platelet count and causes platelet activation in sedentary individuals.[12,13] But in regular exercising individuals platelet activation is inhibited and cardiovascular mortality is reduced [13] due to adaptation to hemostatic system.[14]

Hematological disorders and various non-communicable disorders can be prevented and treated with regular moderate exercise. Exercise might be a safe, promising, adjuvant, and non-pharmacological method to reduce the financial burden of these diseases. Healthy adults are the mass source of manpower. Exercise should be adopted in daily life to lead a healthy lifestyle. Therefore, this study was designed to observe the effect of regular exercise on some hematological parameters in regularly exercising adult males.

Materials and Methods:

This comparative cross-sectional study was conducted at the physiology department of Chittagong Medical College in collaboration with selected gyms and bank of Chattogram city from July 2021 to June 2022. 74 study subjects were selected by using the prevalence formula from selected gyms and bank. A convenient sampling method was used for selecting study subjects. Some 37 healthy adult males, engaged in regular exercise in the gym for at least 150 mins/week for a minimum of 12 weeks were included in group A (gym exercising), and 37 healthy age and BMI-matched adults not engaged in gym exercise or do activities like walking, jogging, swimming, cycling, yoga for <150 mins /week were included in groupB (non-exercising). Study subjects having DM, HTN, COPD, CHF, and malignancy were excluded. Smokers, alcoholics, obese, and users of any medication or supplement that affects hematological parameters were also excluded. The research protocol was approved by the Ethical Review Board of Chittagong Medical College. After obtaining written informed consent from the respondents data were collected by general examination, face-to-face interview, and using weighing machines and measuring tapes for height and weight measurement. These data were recorded on a predesigned case record form. Study subjects were instructed to refrain from exercise 48 hours prior to blood collection day. On the day of blood collection, 3 ml of blood was drawn from each participant for the hematological test. A hematology auto-analyzer (Sysmes XN 1000, Japan) was used for the complete blood count. Analysis was done according to hydrodynamic focusing (DC Detection), flow cytometry method, and SLS-hemoglobin method. Statistical analysis was done using SPSS-26 and Microsoft Excel. A p-value of <0.05 was considered significant.

Results:

A comparison of the mean values of hematological parameters for group A (gym exercising) and group B (non-exercising) is shown in Table I. Independent sample t-test was performed to compare the hematological parameters between the groups. The result of the t-test revealed that mean values of RBC count, Hb, and HCT were significantly higher but WBC count was significantly lower in gym exercising subjects. ($p<0.05$). However, the mean value of MCV, DC of neutrophil, lymphocyte, and platelet count did not differ significantly between the two groups. ($p>0.05$). In correlation of RBC parameters with the duration of exercise in the gym exercising subjects Table II revealed that RBC count and MCV significantly positively correlated with exercise duration. ($p<0.05$).

Table 1: Comparison of hematological parameters between group A (gym exercising) and group B (non-exercising). (n=74).

Attributes	Group A (gym exercising) (Mean± SD) (range) (n=37)	GroupB (non-exercising) (Mean ± SD) (range) (n=37)	P-value (t-value)
RBC count (million/cumm)	5.37 ± 0.37 (5.00-6.85)	5.13 ± 0.38 (4.00-5.91)	0.006 ** (2.81)
Hb (gm/dl)	15.14 ± 0.89 (13.60-18.00)	14.38 ± 1.28 (10.60-17.90)	0.004 ** (2.965)
HCT (%)	43.60 ± 2.87 (36.80-49.30)	42.14 ± 2.43 (34.30-50.70)	0.021** (2.37)
MCV (fl)	83.40 ± 5.25 (68.4-92.6)	82.50 ± 4.55 (67.80-90.50)	0.429 ns (0.795)
Total count of WBC (×10³/cumm)	7.66 ± 1.697 (5.2-10.12)	8.41 ± 1.451 (6.52-12.35)	0.04** (2.051)
DC of neutrophil (%)	50.70 ± 6.64 (35.00-65.00)	51.43 ± 7.71 (31.00-68.00)	0.703 ns (0.383)
DC of lymphocyte (%)	39.57 ± 7.65 (26.00-60.00)	39.73 ± 7.77 (25.00-56.00)	0.928 ns (0.090)
Platelet count (×10³/cumm)	269.24 ± 66.00 (124.00-426.00)	258.65 ± 76.01 (150.00-487.00)	0.524ns (0.640)

Independent sample t-test was applied to analyze the data.

Table 2: Correlation of RBC parameters with duration of exercise in group A (gym exercising). (n=37).

Attributes	RBC count		Hb %		HCT		MCV	
	r value	p value	r value	p value	r value	p value	r value	p value
Duration of exercise (years)	0.345	0.04**	0.015	0.93^{ns}	0.075	0.66^{ns}	0.372	0.03**

*r = correlation coefficient; **= statistically significant, ns= not significant at p>0.05 level.*

Pearson's correlation coefficient test was applied to analyze the data.

Discussion

This present study was conducted to observe the effect of regular exercise on some hematological parameters in healthy adult males. The mean ± SD of group A and group B age was 32.46 ± 8.46 and 35.89 ± 8.74 respectively. Exercise improves the hematopoietic microenvironment by osteoblastic differentiation and inhibits adipogenic differentiation in the bone marrow. Several hormones and cytokines are increased due to exercise which are associated with self-renewal, proliferation, and maturation of hematopoietic stem cells.[8] Exercise also promotes hematopoietic stem cells to produce more hemoglobin. Hematocrit is the percent saturation of hemoglobin. So, an increase in RBC follows an increase in HCT.[15] In the present study RBC, Hb, and HCT were significantly higher in group A (gym exercising). These findings are in line with previous research findings.[1,15] 12 weeks of aerobic exercise significantly increased RBC and Hb in anemic patients with breast cancer in a randomized clinical trial.[16] Contradictory findings are also present where a reduction in RBC, Hb, and HCT was found in exercising persons termed as 'pseudoanemia' mainly in the athletic population.[17,18] Al-Bewayney HMR reported a reduction in MCV in exercising individuals.[19] These reductions may be explained by hemodilution [18] via the renin-angiotensin-aldosterone system.[20] However, Baffour-Awuah B et al. (2017) [21] did not find significant differences between the two groups. MCV showed non-significant change between groups in a study.[18]

In this study, the WBC count of exercising subjects is higher than their non-exercising peers. This finding is consistent with a previous study where significant leukopenia was observed in physically active persons with lower BMI.[22] This may be explained by exercise-induced adipose tissue reduction. Thereby reduction in the release of pro-inflammatory cytokines which further reduces leukopoiesis in the bone marrow.[22] Also chronic adaptation to long-term regular exercise may contribute to this finding. However, leukopenia is beneficial because high circulating WBC is a novel risk factor for coronary artery disease and type 2 DM.[5] Chastin F et al,[10] reported insignificant change in WBC count. Improper history and lack of device-based measurement of exercise were the cause of insignificant findings.[10] DC of neutrophils and lymphocytes did not show any significant differences between groups in this study. It is assumed that WBC parameters like DC of neutrophils and lymphocytes except natural killer cells do not differ between exercising and non-exercising groups at resting conditions.[23]

The current study shows that platelet count did not differ significantly between the groups. Some studies indicated exercise increases the number of platelets [15,24] while other studies indicated exercise does not have an effect.[19,21] An Increase in platelet count may be explained by hemoconcentration [24] or epinephrine-induced splenic contraction which releases stored platelets into circulation immediately after exercise.[15]

In this study, RBC and MCV showed a significant positive correlation with exercise duration. In a study, it was observed that the 3-10 years duration of exercise had a significant positive correlation with RBC and Hb.[25] Duration of exercise plays an important role in the adaptation of blood and circulatory system. The more the exercise duration the more adaptation occurs.[25]

Conclusion

The study findings show that long-term regular exercise has an effect on hematological parameters. Chronic adaptation to exercise may explain the higher value of RBC parameters and lower count of WBC. These values are within the reference range so the differences do not pose any serious clinical problems for exercising persons. The increasing or decreasing value of the parameters is based on the type, intensity, duration of exercise, and condition state of subjects. Also age, genetic factors, physical and physiological conditions of participants might be the cause of different study findings. Participating in regular exercise has a positive effect on hematological parameters, thus increasing aerobic endurance and improving the life quality of an individual.

Limitations

The duration of our study was limited, and the sample size was too small to allow for broad generalization. Additionally, only male subjects were included, making the findings inapplicable to the female segment of the population. Furthermore, the type and intensity of exercise were not evaluated and measured.

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Conflict of interest

The authors hereby declare that no conflict of interest exists.

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Original article

Association of Immune Cells with Disease Severity of COVID-19 Patients

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Nur Mohammad Khan,[1] Rokya Sharmin Huda Fariha,[2] Md Zaber,[3] Bulbul Hossain Shuvo, [4] Shirin Tarafder[5]

Abstract

Background: COVID-19, caused by SARS-CoV-2, is associated with significant morbidity and mortality, often leading to immune dysregulation characterized by cytokine release syndrome. ***Objective:*** This study aimed to investigate the peripheral blood profiles lymphocytes of and monocytes in relation to disease severity in COVID-19 patients. ***Methodology:*** Conducted at Bangabandhu Sheikh Mujib Medical University from March 2021 to January 2022, this cross-sectional study included 84 confirmed COVID-19 patients categorized into moderate, severe, and critical groups, alongside 28 healthy controls. Peripheral blood samples were analyzed for lymphocyte subpopulations (CD4+ and CD8+ T cells) and monocyte counts using flow cytometry. Ethical clearance was obtained from the Institutional Review Board. ***Results:*** The absolute count of peripheral blood lymphocytes (T cell, B cell, NK cell) and subset of T lymphocyte including CD4+ T cells and CD8+ T cells were significantly decreased in critical group compared to moderate and severe group (P<.001). The mean lymphocyte count in critical cases was markedly lower than in healthy controls. Exhaustion marker CD94/NKG2A was increased on NK cells and CD8+ cytotoxic T cell among critical and severe group compared to moderate and healthy group. In contrast absolute count of monocyte was significantly increased in critical group (P<.001) with a mean of 1940.65/µL ***Conclusion:*** The findings underscore the immunological alterations in COVID-19 patients, characterized by decreased lymphocyte counts and increased monocyte levels, particularly in critical patients.. Monitoring peripheral blood lymphocytes, T cell subsets and monocyte may provide critical insights for understanding disease progression and informing therapeutic strategies. Monoclonal antibody targeting NKG2A for therapeutics may prevent the disease progression and decrease morbidity and mortality.

Keywords: Lymphocytes, Monocyte, CD94/NKG2A, COVID-19 patients

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Address of Correspondence: Dr. Nur Mohammad Khan, Assistant Professor, Department of Microbiology, Bashundhara Ad-din Medical College, South Keraniganj, Dhaka. Email: mubinmmc44@gmail.com

1. Dr. Nur Mohammad Khan, Assistant Professor, Department of Microbiology, Bashundhara Ad-din Medical College, Dhaka
2. Dr. Rokya Sharmin Huda Fariha, Lecturer, Department of Microbiology, Bashundhara Ad-din Medical College, Dhaka
3. Dr. Md Zaber, Assistant Professor, Department of Microbiology, Gazi Medical College, Khulna
4. Dr. Bulbul Hossain Shuvo, Assistant Professor, Department of Community Medicine, Bashundhara Ad-din Medical College, Dhaka
5. Dr. Shirin Tarafder, Professor, Department of Microbiology and Immunology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka

Introduction

COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to a global pandemic with profound public health implications, resulting in significant morbidity and mortality worldwide[1]. The disease presents with a broad spectrum of clinical manifestations, from mild respiratory symptoms to severe complications such as acute respiratory distress syndrome (ARDS) and multiple organ failure[2]. One of the hallmark features of severe COVID-19 is immune dysregulation, which is often characterized by a cytokine release syndrome (CRS) [1].This hyper-inflammatory response is associated with excessive production of pro-inflammatory cytokines, contributing to tissue damage and a poor clinical prognosis. Central to the immune response in COVID-19 are lymphocytes and monocytes[3]. Lymphocytes, particularly CD4+ T helper cells and CD8+ cytotoxic T cells, are critical for the adaptive immune response against viral infections[4]. In severe cases of COVID-19, numerous studies have reported significant lymphopenia, defined as a reduced lymphocyte count, which correlates with disease severity and worse outcomes[2]. For instance, Duans' studies[3] demonstrated that patients with severe COVID-19 had markedly lower counts of both CD4+ and CD8+ T cells compared to moderate cases, suggesting a failure of the adaptive immune system to mount an effective response to the virus. The total number of B cells, both helper T cells (CD3+CD4+) and suppressor T cells (CD3+CD8+), regulatory T cells (both naïve and induced) and NK cells significantly decreased in severe cases compared to the non-severe group[5]. The increase of neutrophil-to-lymphocyte ratio (NLR), were found in the severe group with COVID-19 compared to the mild group[5]. Low levels of CD4+T and CD8+T cells are common in severe COVID pneumonia. B cells and NK cells were also reduced both in mild and severe COVID infection [6].Total number of NK and CD8+ T cells was decreased markedly in COVID-19 patients and the function of NK and CD8+ T cells was exhausted with the increased expression of NKG2A[7]. Expression of NKG2A was reduced with restored NK and CD8+ T cells level in patients convalescing after therapy suggesting SARS-CoV-2 infection is associated with the functional exhaustion of cytotoxic lymphocytes[8]. NKG2A is an inhibitory receptor, it's expression on NK and CD8+ T cells induce functional exhaustion of NK and CD8+ T cells, leading to chronic viral infections[6]. For elimination of virus in the early stage of COVID-19 targeting NKG2A may prevent the functional exhaustion of cytotoxic lymphocytes[8]. Conversely, monocytes, which are essential components of the innate immune response, often exhibit increased counts in patients with severe COVID-19[9]. This monocytosis reflects the activation and recruitment of monocytes in response to infection and inflammation. Elevated monocyte levels contribute to the inflammatory milieu seen in severe cases and are associated with poorer clinical outcomes[4]. Furthermore, the role of monocytes in the development of CRS underscores their importance in the pathogenesis of severe COVID-19, as they can release a variety of cytokines and chemokines that exacerbate inflammation[10]. The relationship between viral load and immune response is also critical in the context of COVID-19 detectable levels[5].Given these complexities, this study aims to investigate the peripheral blood profiles of monocytes and lymphocytes in relation to disease severity among COVID-19 patients[11]. By characterizing these immune cell dynamics, we hope to contribute to a deeper understanding of the immunological landscape in COVID-19[12]. This knowledge may not only enhance our grasp of disease progression but also inform therapeutic strategies aimed at mitigating severe outcomes and improving patient management[13].

Materials and methods:

This cross-sectional study was conducted at Bangabandhu Sheikh Mujib Medical University (BSMMU) in Dhaka from March 2021 to January 2022. Subjects were selected from the BSMMU Fever Clinic, and informed consent was obtained from all participants, with ethical approval granted by the Institutional Review Board. A purposive sampling method was used, resulting in a sample size of 112, based on Morgan's table, which included 84 confirmed COVID-19 patients categorized as moderate, severe, or critical, along with 28 healthy controls. Inclusion criteria required participants to be adults (≥18 years) with confirmed COVID-19 via RT-PCR, while exclusion criteria included autoimmune disorders, co-infections, or recent immunosuppressive therapy. Peripheral blood samples were collected in EDTA tubes and processed within two hours for analysis of T lymphocyte , T cells subset (CD4+ and CD8+ T cells), B lymphocyte, NK cell and monocyte counts using flow cytometry with specific monoclonal antibodies. Data were analyzed using SPSS version 26, employing descriptive statistics and comparisons with ANOVA or Kruskal-Wallis tests, with a significance threshold set at $p < 0.05$. Confidentiality and privacy of participants were strictly maintained.

Result:

This study enrolled 84 confirmed COVID-19 patients and 28 healthy individuals as controls. The COVID-19 patients were categorized into three groups: moderate (n=28), severe (n=28), and critically ill (n=28).

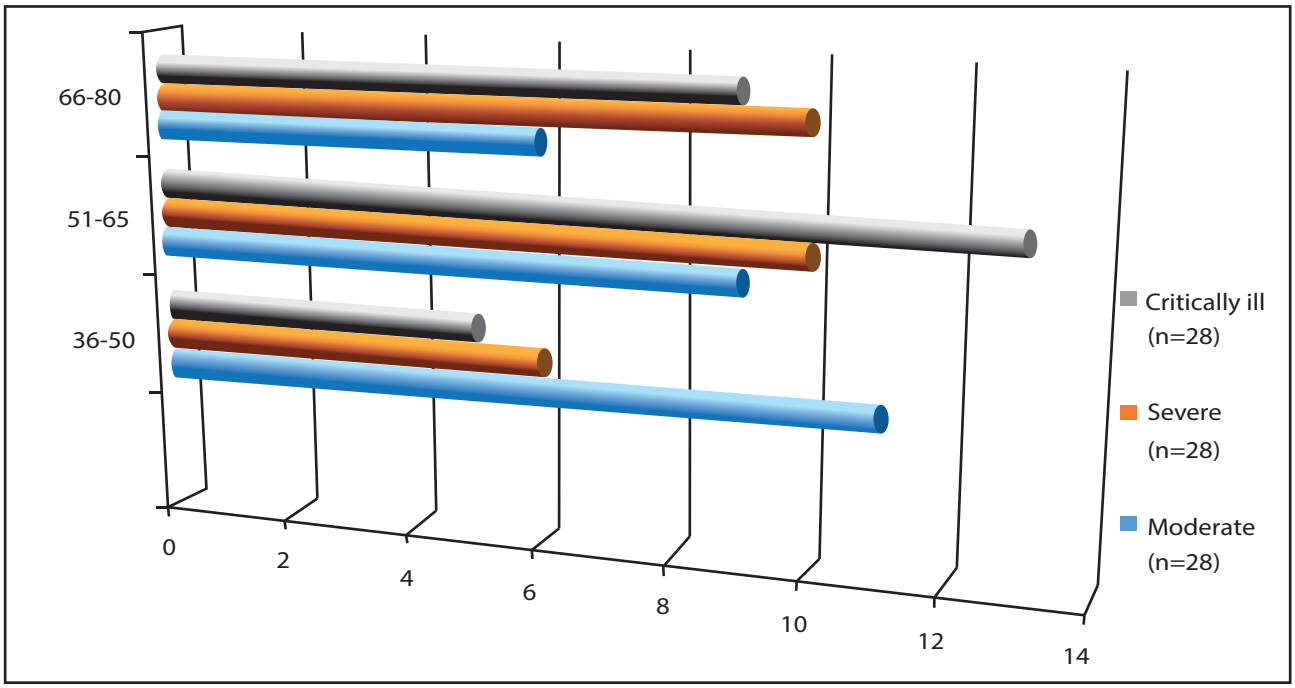

Figure 1:Frequency of age of the study cases (Fisher Exact test showed no significant statistical difference among the groups regarding age).

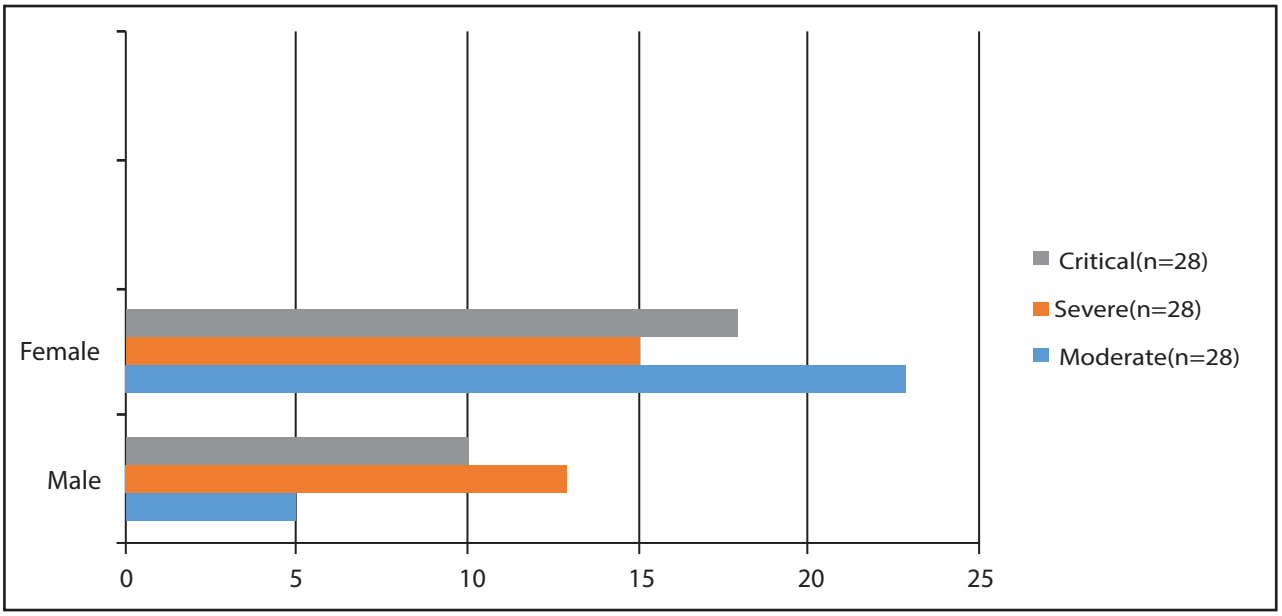

Figure 2: Gender distribution of the study cases (Chi-square test showed no significant statistical difference among the groups regarding gender).

Table 1: Summarizing the p-values for the comparison of absolute counts and percentages of peripheral blood lymphocytes among the different groups:

Comparison	Absolute Count P-value	Percentage P-value
Healthy vs Critical	P < .001	P < .001
Moderate vs Critical	P < .001	P < .001
Severe vs Critical	P < .001	P = .004
Healthy vs Severe	P < .001	P < .001
Moderate vs Severe	P < .001	P = .007
Healthy vs Moderate	P = 1.00	P = 1.00

Note: P < .05 indicates statistical significance. P-values were calculated using One-way ANOVA with post-hoc Bonferroni test.

In the study, 80.01% of patients had co-morbidities, with the critical group showing the highest prevalence at 92.85%, compared to 46.42% in the moderate group (p=0.004). Diabetes mellitus was the most common co-morbidity (63.87%), and the critical group exhibited a significantly higher frequency of diabetes (75.0%) than the moderate group (63.87%), with a p-value of 0.015.

Table 2: Frequencies of co-morbidities among different categories of patients

Variables	Total patient (n=84)(%)	Moderate (n=28) (%)	Severe (n=28) (%)	Critical (n=28) (%)	P value
Co-morbidities (any)	68 (80.01)	13 (46.42)	23 (82.14)	26 (92.85)	**.004**
Diabetes mellitus	52 (63.87)	11 (39.28)	20 (71.42)	21 (75.0)	**.015**
Hypertension	41 (51.25)	6 (21.42)	16 (57.14)	18 (64.28)	.682
Asthma	7 (8.42)	1 (3.57)	2 (7.14)	4 (14.28)	.841
Chronic kidney disease	6 (6.74)			6 (21.42)	.710
Chronic liver disease	3 (1.96)		1 (3.57)	2 (7.14)	.161
Others	4 (4.49)	1 (3.57)	2 (7.14)	1 (3.57)	.445

Table 3: This table represents circulating peripheral Blood Lymphocytes , circulating T Lymphocytes & circulating CD4+ Profiles in COVID-19 Patients Compared to Healthy Controls (N=112)

Category of patient	Peripheral blood lymphocyte		CD3+ T lymphocyte		CD4+ helper T lymphocyte	
	Mean of Absolute count, cells/uL± SD	Percentage Mean ± SD	Mean of Absolute count, cells/uL± SD	Mean of Absolute count, cells/uL± SD	Percentage Mean ± SD	Percentage Mean ± SD
Control group n=28	2586±412.56	34.25±6.21	1684.65 ± 428.41	74.40 ± 5.02	878.11 ± 276.51	45.41 ± 4.22
Moderate group n=28	2271±385.09	32.96±4.94	1392.24 ± 410.96	72.54 ± 7.32	785.54 ± 242.04	40.63 ± 6.85
Severe group n=28	1845±465.02	25.62±7.48	953.48 ± 301.78	62.47 ± 10.52	546.08 ± 189.45	36.12 ± 10.26
Critical group n=28	839±423.51	9.14±5.21	529.98 ± 259.11	55.06 ± 1.46	235.04 ± 149.39	30.25 ± 13.85

The study presents data on peripheral blood lymphocyte counts across four patient categories: Control, Moderate, Severe, and Critical groups, each consisting of 28 patients. In the Control group, the absolute count of CD3+ T lymphocytes was 2586 ± 412.56 cells/uL, making up 34.25 ± 6.21% of total lymphocytes, while CD4+ helper T lymphocytes had an absolute count of 1684.65 ± 428.41 cells/uL, constituting 74.40 ± 5.02% of total lymphocytes. In the Moderate group, the absolute count of CD3+ T lymphocytes decreased to 2271 ± 385.09 cells/uL (32.96 ± 4.94%), and CD4+ helper T lymphocytes dropped to 1392.24 ± 410.96 cells/uL, representing 72.54 ± 7.32%. The Severe group showed a further decline, with CD3+ T lymphocytes at 1845 ± 465.02 cells/uL (25.62 ± 7.48%) and CD4+ helper T lymphocytes at 953.48 ± 301.78 cells/uL, accounting for 62.47 ± 10.52%. In the Critical group, there was a marked decrease, with CD3+ T lymphocytes at 839 ± 423.51 cells/uL (9.14 ± 5.21%) and CD4+ helper T lymphocytes at 529.98 ± 259.11 cells/uL, making up 55.06 ± 1.46% of total lymphocytes. Overall, these results indicate a significant decline in both CD3+ T lymphocytes and CD4+ helper T lymphocytes as the severity of the patient condition increases from the Control to the Critical groups, suggesting an impairment in T lymphocyte populations in more severe cases (Table 3).

Table 4: Circulating CD8+ cytotoxic T lymphocytes, B lymphocytes among COVID-19 patients and healthy group (N=112) : Comparison of CD4+/CD8+ ratio in study groups (N=112)

CD8+ cytotoxic T lymphocyte			CD4+ /CD8+ ratio		B lymphocyte	
Category of patient	Mean of Absolute count, cells/uL± SD	Percentage Mean ± SD	Mean ± SD	P value	Mean of Absolute count, cells/uL± SD	Percentage Mean ± SD
Control group n=28	701.96 ± 157.01	25.45 ± 5.52	1.26±.58	**0.09**	356.08 ± 136.25	26.04 ± 5.26
Moderate group n=28	623.45 ± 257.43	723.85 ± 4.27	1.46±.31		358.63 ± 86.14	26.77 ± 5.78
Severe group n=28	312.01 ± 262.08	24.64 ± 7.41	1.51±.03		273.02 ± 168.32	30.06 ± 12.11
Critical group n=28	157.32 ± 94.23	21.74 ± 6.60	1.55±.47		198.05 ± 175.10	32.86 ± 15.85

The results of Table 4 show the counts of CD8+ cytotoxic T lymphocytes and B lymphocytes across four patient categories: Control, Moderate, Severe, and Critical groups, each with 28 patients. In the Control group, the absolute count of CD8+ lymphocytes was 701.96 ± 157.01 cells/uL, comprising 25.45 ± 5.52% of total lymphocytes, with a CD4+/CD8+ ratio of 1.26 ± 0.58 and B lymphocyte count at 356.08 ± 136.25 cells/uL. The Moderate group showed a decrease in CD8+ counts to 623.45 ± 257.43 cells/uL (23.85 ± 4.27%) and an increased CD4+/CD8+ ratio of 1.46 ± 0.31, while B lymphocytes remained stable at 358.63 ± 86.14 cells/uL. The Severe group reported a further drop to 312.01 ± 262.08 cells/uL (24.64 ± 7.41%) and a CD4+/CD8+ ratio of 1.51 ± 0.03, with B lymphocytes at 273.02 ± 168.32 cells/uL. In the Critical group, CD8+ lymphocyte counts plummeted to 157.32 ± 94.23 cells/uL (21.74 ± 6.60%), accompanied by a ratio of 1.55 ± 0.47 and a B lymphocyte count of 198.05 ± 175.10 cells/uL. Overall, these findings indicate a significant decline in CD8+ T lymphocyte counts as the severity of patient conditions increases, alongside relatively stable B lymphocyte

Table 5 : Comparative Analysis of CD94/NKG2A Expression in Circulating NK Cells and CD8+ Cytotoxic T Cells Between COVID-19 Patients and Healthy Controls (N=112):

NK cell				
Category of patient	**Mean of Absolute count, cells/uL± SD**	**Percentage Mean ± SD**	**CD94/NKG2A+ NK cell Percentage Mean ± SD**	**CD94/NKG2A+ CD8+ T cell Percentage Mean ± SD**
Control group n=28	256.08 ± 60.25	17.04 ± 2.26	46.46 ±13.58	7.56±47
Moderate group n=28	198.63 ± 86.14	13.77 ± 3.78	63.12 ±7.21	8.45±.44
Severe group n=28	173.02 ± 108.32	11.06 ± 4.11	80.09 ±6.23	12.45±.85
Critical group n=28	98.65 ± 125.10	10.86 ± 5.85	88.94 ±4.04	15.65±.41

Table 5 presents data on NK cell counts and percentages of CD94/NKG2A+ NK cells and CD94/NKG2A+ CD8+ T cells across four patient categories: Control, Moderate, Severe, and Critical groups, each consisting of 28 patients. In the Control group, the mean absolute count of NK cells was 256.08 ± 60.25 cells/uL, with 63.12 ± 7.21% being CD94/NKG2A+ NK cells and 8.45 ± 0.44% being CD94/NKG2A+ CD8+ T cells. The Moderate group showed a decrease in NK cell count to 198.63 ± 86.14 cells/uL, but an increase in the percentage of CD94/NKG2A+ NK cells to 80.09 ± 6.23%, while CD94/NKG2A+ CD8+ T cells rose to 12.45 ± 0.85%. The Severe group reported further decline in NK cell counts to 173.02 ± 108.32 cells/uL, with 88.94 ± 4.04% being CD94/NKG2A+ NK cells and 15.65 ± 0.41% for CD94/NKG2A+ CD8+ T cells. In the Critical group, NK cell count dropped significantly to 98.65 ± 125.10 cells/uL, with a corresponding percentage of CD94/NKG2A+ NK cells at 10.86 ± 5.85%. Overall, these results indicate a decrease in NK cell counts alongside an increase in the percentages of CD94/NKG2A+ NK and CD8+ T cells as the severity of the condition worsens.

Table 6 : Comparison Monocyte among COVID-19 patients and healthy group (N=112)

Category of patient	**Monocyte**	
	Mean of Absolute count, cells/uL± SD	**PercentageMean ± SD**
Control group n=28	656.08 ± 61.25	7.04 ± 2.28
Moderate group n=28	885.60 ± 116.14	9.77 ± 3.78
Severe group n=28	1453.02 ± 148.32	17.06 ± 15.11
Critical group n=28	1940.65 ± 195.10	21.86 ± 26.95

Table 6 summarizes the absolute counts and percentages of monocytes across four patient categories: Control, Moderate, Severe, and Critical groups, each with 28 patients. In the Control group, the mean absolute count of monocytes was 656.08 ± 61.25 cells/uL, comprising 7.04 ± 2.28% of total leukocytes. The Moderate group exhibited an increase in monocyte count to 885.60 ± 116.14 cells/uL, with a percentage of 9.77 ± 3.78%. The Severe group showed a further rise, with an absolute count of 1453.02 ± 148.32 cells/uL and a percentage of 17.06 ± 15.11%. Finally, in the Critical group, the mean monocyte count peaked at 1940.65 ± 195.10 cells/uL, accounting for 21.86 ± 26.95% of total leukocytes. Overall, these findings indicate a progressive increase in both the absolute counts and percentages of monocytes as the severity of the condition escalates.

Discussion:

In this study, the absolute count and percentage of peripheral blood lymphocytes were significantly reduced in the critical and severe groups compared to the healthy and moderate groups. A study reported a significant decrease in peripheral blood lymphocyte counts in severe and critical cases compared to mild and healthy individuals[4]. Additional studies also found reductions in lymphocyte counts among severe and critical patients compared to moderate cases[6]. A study highlighted a similar trend[7], noting a significant decrease in peripheral blood lymphocytes in severe and critically ill patients compared to moderate cases[4]. This decline in lymphocyte count may be attributed to increased lymphocytic infiltration in the lungs of COVID-19 patients [8] .The present study found a notable reduction in the absolute count of peripheral CD3+ T lymphocytes in both severe and critical groups compared to moderate and healthy individuals. A study observed a sustained decrease in T lymphocyte counts in severe and critical groups compared to those who were moderate and healthy[2]. Multiple studies have demonstrated that T lymphocyte counts are significantly lower in severe and critical patients compared to those who are mild or moderate [9] Consistent with these findings, a study reported significant reductions in T lymphocytes among severe and critical cases compared to healthy individuals[4]. The reduction of T lymphocytes may be linked to direct invasion by SARS-CoV-2, which can infect T cells via receptor-dependent spike protein-mediated membrane fusion, despite the low expression levels of the angiotensin-converting enzyme 2 (ACE2) receptor in T cells . Furthermore, SARS-CoV-2 infection triggers T cell-mediated immunity, leading to an increased production of inflammatory cytokines, although anti-inflammatory cytokines such as IL-4 and IL-10 may inhibit T cell activation10. In this study, a significant decrease in CD4+ helper T lymphocytes and CD8+ cytotoxic T lymphocytes was noted in COVID-19 patients compared to healthy controls. The absolute count of peripheral CD8+ T cells was significantly lower in the critical, severe, and moderate groups compared to the healthy group (P<.001). These results align with findings from Jiang studies [2] who noted a significant reduction in CD8+ T lymphocyte counts in COVID-19 patients compared to healthy controls, as well as in critical cases compared to mild cases. Several studies have reported a decrease in CD8+ T lymphocyte counts in severe and critical groups compared to healthy and moderate groups11. It is suggested that the SARS-CoV-2 virus may directly damage lymphatic organs, including the spleen and lymph nodes, leading to spleen atrophy and lymph node necrosis, which in turn induces lymphopenia [12]

No significant differences were observed in the CD4+/CD8+ ratio among COVID-19 patients and healthy individuals, a finding echoed in several other studies [9].The results from this study suggest that both CD4+ and CD8+ T cells consistently decreased in severe-critical and mild-moderate groups, with ratios also altered in healthy controls, potentially due to asymptomatic infections. A previous study found a CD4+/CD8+ ratio of 1.49 in healthy adults [2]. This study also compared the absolute count and percentage of peripheral B lymphocytes in COVID-19 patients against healthy controls, finding a significant reduction in B lymphocyte counts in the critical group compared to the moderate and severe groups, similar to observations by Sun & Xu studies[5]. In contrast, Qin studies reported no differences in B lymphocyte counts between moderate and severe groups[13]. Additionally, the mean percentage of B lymphocytes was significantly higher in the critical and severe groups compared to the healthy group, corroborating findings from Chen studies. This relative increase in B cell percentage may be due to a significant decrease in T cell counts in these patient[9]. The present study found a significant decrease in the absolute count of peripheral NK cells in the severe and critical groups compared to healthy and moderate groups. Similar findings were reported by Jiang studies[2], where NK cell counts were significantly reduced in severe and critical groups relative to healthy controls. Zhang & his group [4] also observed significant reductions in NK cell counts in severe and critical COVID-19 patients compared to moderate cases. Furthermore, Xu studies reported significant reductions in NK cell counts in severe cases compared to moderate cases[14], whereas Liu studies found no significant differences between severe and moderate groups[15]. The reduction in NK cell counts could be attributed to the migration of NK cells from peripheral blood to lung tissue, facilitated by increased levels of MCP-1 and IP-10 in COVID-19 patients [16]. In this study, the expression of CD94/NKG2A was analyzed to assess NK cell exhaustion status. The results indicated that the percentage of CD94/NKG2A-expressing NK cells was higher in the critical, severe, and moderate groups compared to the healthy group. This finding aligns with results from Zheng studies 7who reported increased CD94/NKG2A expression on NK cells in severe COV-

ID-19 patients compared to healthy individuals. However, a study found no significant differences in CD94/NKG2A expression between COVID-19 patients and healthy controls[17]. The high levels of NK cell exhaustion may result from persistent antigenic stimulation by the coronavirus or be a consequence of the associated cytokine storm, which could contribute to the progression of COVID-19. Targeting the CD94/NKG2A receptor might serve as a promising therapeutic approach to prevent NK cell exhaustion in the early stages of COVID-19 [7].

Additionally, the study detected CD94/NKG2A expression on T cells across the study groups. While the percentage of CD94/NKG2A-expressing T cells increased in severe-critical patients compared to asymptomatic and healthy individuals, the differences were not statistically significant. A study also reported a significant increase in CD94/NKG2A expression on CD8+ T cells in severe and moderate cases compared to healthy controls, along with reduced expression of functional markers such as CD107a, IFN-γ, and IL-2 on CD8+ T cells, indicating functional exhaustion[18]. Assessing these functional markers may help elucidate the extent of T cell exhaustion across different study groups.
The study found a significant increase in both the absolute count (1940.65 cells/µl) and percentage (21.86%) of blood monocytes in the critical group compared to the healthy (656.08 cells/µl, 7.04%) and moderate (885.60 cells/µl, 9.77%) groups. Previous research has indicated similar trends, with monocyte absolute counts significantly higher in severe cases (1405 cells/µl) compared to mild cases (615 cells/µl, $p < 0.0001$), along with increased percentages of monocytes in severe patients (17.4% in severe vs. 9.8% in mild, $p < 0.0001$) [15].

Conclusion:

In conclusion, this study highlights that the absolute counts of peripheral blood lymphocytes, including T cells, B cells, and NK cells, as well as T cell subsets like CD4+ and CD8+, are significantly decreased in severe and critical COVID-19 patients compared to healthy and moderate individuals. These findings suggest that lymphocyte and T cell subset counts could serve as important indicators of disease severity. Additionally, the elevated expression of CD94/NKG2A on NK and CD8+ T cells in severe and critical cases may play a role in the pathogenesis of COVID-19, potentially contributing to immune dysfunction and disease progression. Together, these insights underscore the importance of monitoring lymphocyte counts and exhaustion markers in understanding and managing COVID-19.

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Conflict of interest:

The authors hereby declare that no conflict of interest exists.

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Original article

Reproductive Health Knowledge among Male Adolescents in Rural Bangladesh

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Bulbul Hossain Shuvo,[1] Nur Mohammad Khan,[2] Rokya Sharmin Huda Fariha,[3] Md. Mahbubur Rahman,[4] Munmun Ghosh[5]

Abstract

Background: The foundation of human health is created at adolescent period. Reproductive health plays an important role here. But reproductive health knowledge and its service aren't sufficient all over the world to adolescents' people. There has a shortness of data about reproductive health condition and its knowledge and service. Therefore, adolescents should know about sexual and reproductive health and its available services to protect themselves. There is still need of doing research to find the current situation. ***Objective:*** The objectives of this study were to assess reproductive health knowledge and its available services among male adolescents in rural area of Bangladesh. ***Methodology:*** This study was cross sectional study. The target population was high school going male adolescents. The total period of this study was from January to December, 2018. Study place was selected by purposively and simple random sampling technique was used to select the male adolescents. Sample size was 214. Semi-structured questionnaires were used to collect data. The thesis protocol was approved by IRB, BSMMU. Frequency, percentage, means, chi-square tests were done by SPSS version 21. ***Results:*** The majority age group of the respondents was 11-13 years was 73.2% rest of age 14-15 years was26.8%. To calculate knowledge score of reproductive health of the respondents, here divided 3 categories after computing total questions related to reproductive health then made 3 approximate equal divisions. There were 19 of reproductive related questions. Here, category-1 was 1-6, category-2 was 7-12 and 13-19 was in category-3. We found that, 62.73% had category-1 knowledge, 24.09% had category-2 knowledge and 13.18% had category-3 knowledge about reproductive health. ***Conclusion:*** In general, it was found that reproductive health knowledge amongst rural adolescents in the study area remained low. Providing knowledge to adolescents regarding reproductive health and its services is essential.

Keywords: Reproductive health knowledge, Male Adolescents

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Address of correspondence: Dr. Bulbul Hossain Shuvo, Assistant Professor, Department of Community Medicine, Bashundhara Ad-din Medical College, Dhaka; email: shuvo2498@gmail.com

1. Bulbul Hossain Shuvo, Assistant Professor, Department of Community Medicine, Bashundhara Ad-din MedicalCollege, Keraniganj, Dhaka
2. Nur Mohammad Khan, Assistant Professor, Department of Microbiology, Bashundhara Ad din Medical College, Dhaka
3. Rokya Sharmin Huda Fariha, Lecturer, Department of Microbiology, Bashundhara Ad-din Medical College, Dhaka
4. Md. Mahbubur Rahman, Assistant Professor, Department of Pharmacology and Therapeutics, Bashundhara Ad-din Medical College, Dhaka
5. Munmun Ghosh, Assistant Professor, Department of Physiology, Bashundhara Ad-din Medical College, Keraniganj, Dhaka

Introduction

The foundation of human health is significantly established during adolescence, a critical developmental period spanning from ages 10 to 19. Adolescents constitute approximately 20% of the global population.[1] This substantial demographic segment plays a crucial role in population dynamics, contributing to increased dependency ratios and influencing public health outcomes. Adolescence is marked by profound physiological, psychological, and social changes that elevate the risk of sexual and reproductive health (SRH) issues.[2]

Recent concerns about adolescent sexual and reproductive health (ASRH) have intensified due to rising rates of sexual activity, early pregnancies, and sexually transmitted infections (STIs), including human immunodeficiency virus (HIV). The accessibility and utilization of reproductive health services are essential for mitigating these risks and supporting adolescents in navigating their developmental challenges.[3] This demographics' health is directly linked to Bangladesh's health objectives, particularly in achieving Sustainable Development Goals (SDGs). Relevant goals include SDG 3 (ensuring healthy lives and promoting well-being for all at all ages), SDG 4 (ensuring inclusive and equitable quality education and promoting lifelong learning opportunities for all), SDG 5 (achieving gender equality and empowering all women and girls), and SDG 8 (promoting sustained, inclusive, and sustainable economic growth and productive employment) (Ministry of Health and Family Welfare.[4]

Families and educational institutions are pivotal in providing adolescents with comprehensive reproductive health education. Open communication, where parents act more as supportive mentors rather than authoritarian figures, can significantly enhance adolescents' understanding of sexual and reproductive health. Schools also play a critical role in delivering accurate information and fostering a supportive learning environment.[5]

Despite the importance of reproductive health, it remains a sensitive topic in many cultures, including Bangladesh, where cultural taboos often inhibit open discussions. Consequently, many adolescents lack adequate knowledge about reproductive health, leading to ongoing issues in their development and well-being .[5-6] The fragility of the adolescent reproductive health system necessitates awareness and proactive measures to protect future fertility and prevent sexually transmitted infections, which can have long-term effects on reproductive health (American Sexual Health Association.[6-7]

Sexual and reproductive ill-health accounts for a significant portion of the global disease burden, with 20% for women and 14% for men (World Health Organization [WHO], 2008).[8] Studies indicate a widespread lack of accurate reproductive health knowledge, underscoring the need for comprehensive awareness programs. Adolescents' limited capacity to grasp complex health concepts and the consequences of their behaviors heightens their vulnerability to sexual exploitation and risky behaviors.

The burden of disease during adolescence is substantial, with nearly 35% of global disease burdens originating in this age group. Of the 1.2 billion adolescents worldwide, approximately 90% reside in developing countries.[9] Although ASRH issues have gained national attention due to the high burden of HIV/AIDS and other STIs, as well as early childbearing, there remains a gap in translating this concern into effective action. Adolescent-friendly reproductive health services (AFRHS) are a promising strategy to address these needs, yet there remains a lack of adequate research and service provision tailored to this age group.[10]

Materials and methods:

A high school-based cross-sectional study was conducted to assess the knowledge of reproductive health and the availability of related services among male adolescents at Baghutiya Omor Ali High School in Daulatpur Thana, Manikganj district. The target population comprised male high school students from the selected area. The study was carried out over a period from January to December 2018. The study location was selected using a purposive sampling method. A simple random sampling technique was employed to select participants from Baghutiya Omor Ali High School. The sample size was calculated using the WHO-recommended formula for fixed prevalence: $n = Z^2 * P(1-P)/d^2$, resulting in a sample size of 214. Data were collected using pre-tested, semi-structured questionnaires. Pretesting was conducted at Oxford High. The statistical software package SPSS version 21.0 were used for statistical analysis and p value will settled at 0.05 level. Socio-demographic characteristics were analyzed by using frequency distribution, percentage. It also presented as mean and standard deviation where applicable. Reproductive health knowledge, barrier method (condom) knowledge and STD, HIV/AIDS knowledge also presented by frequency distribution, appropriate graphs and table. Regarding reproductive health service utilization were analyzed by frequency distribution, percentage. Knowledge score was calculated by computing related variable and then made 3 categorization with approximate 3 equal distributions (category-1, category-2 and category-3) and presented by pie chart.

Result:

Table 1 shows the reproductive health knowledge of the respondents. Here maximum respondents thought, increase body structure 82 (37.3%) was the physical changes in male at adolescents age.

Table 1: Reproductive health knowledge of the respondents

Variables		Frequency (n =220)	Percent (%)
Knowledge on physical changes in male at adolescents age (multiple response)	Increase body structure	82	37.3
	Increase size of genitalia	65	29.5
	Increase growth of scrotum	49	22.3
	Pubic hair appearance	50	22.7
	Facial and armpit hair appearance	47	21.7
	Changes of voice	46	20.9
	Wet dream	36	16.4
	Don't know	116	52.7
Knowledge on physical changes in male at adolescents age (multiple response)	Increase body structure	38	17.3
	Increase size of genitalia	33	15
	Increase growth of breast	35	15.9
	Pubic hair appearance	29	13.2
	Armpit hair appearance	26	11.8
	Changes of voice	25	11.4
	Menstruation	22	10
	Don't know	157	71.4

Table 2 shows, (28.6%) respondents thought that menstruation is natural phenomenon on the other hand only 57(25.9%) thought that wet dream is natural phenomenon. In mental changes idea for male, attract to opposite sex was 56(25.6%). 86(39.1%) of respondents had no idea about ill health condition of masturbation.

Table 2: Reproductive health knowledge of the respondents

Variables		Frequency (n =220)	Percent (%)
Knowledge on wet dream	Natural phenomenon	57	25.9
	One kinds of diseases	66	30
	Result of curse	3	1.4
	Don't know	105	47.7
Knowledge on menstruation	Natural phenomenon	63	28.6
	One kinds of diseases	50	22.7
	Don't know	120	54.5
Knowledge on mental changes in male (multiple response)	Attraction to opposite sex	86	39.1
	Increase curiosity	33	15
	Increase excitement	29	13.2
	Don't know	101	45.9
Knowledge on mental changes in female (multiple response)	Attraction to opposite sex	56	25.5
	Increase shyness	86	39.1
	Others	19	13.2
	Don't know	94	45.9
Thinking of masturbation is harmful to health	Yes	82	37.3
	No	52	23.6
	Don't know	86	39.1

Table 3 shows that, maximum sources of the reproductive health knowledge to the respondents were teacher 113(61.4%) then mother 105(47.7%) and friend 88(40%). Here maximum respondents didn't attend any classes 72(32.7%) related to reproductive health.

Table 3: Sources of reproductive health knowledge to the respondents

Variables		Frequency (n =220)	Percent (%)
Sources of knowledge (multiple response)	Teacher	113	51.4
	Mother	105	47.7
	Father	53	24.1
	Brother	46	20.9
	Sister	29	13.2
	Other family member	29	13.2
	Friend	88	40
	Doctor	56	25.7
	Book	23	10.5
	Cinema/Video	10	4.5
Attending any class related to reproductive health	Yes	72	32.7
	No	148	67.3

To find out knowledge score of reproductive health of the respondents, we have computed variables of related questions to reproductive health then made 3 categories with approximate equal distribution. There were 19 reproductive health related questions. Here, category-1 was 1-6, category-2 was 7-12 and 13-19 was in category-3.

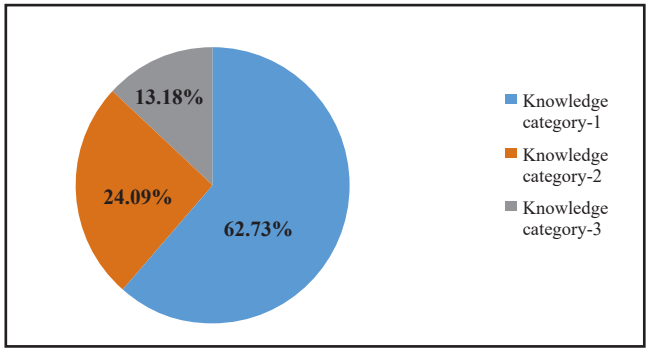

Figure 1: Respondents Knowledge score on adolescent reproductive health

Here, we got 140 (62.73%) had category-1 knowledge, 51(24.09%) had category-2 knowledge and 29 (13.18%) had category-3 knowledge about reproductive health.

Table 4 shows that, there was no association between knowledge score and age of the respondents.

Table 4: Association between knowledge score and age of the respondents

Age group of the respondents	knowledge score			Total	p value
	Category-1 0-6	Category-1 7-13	Category-1 14-19		
11-13	102	40	19	161	0.939
14-15	36	16	7	59	
Total	138	56	26	220	

*P <0.05

Table 5: Knowledge on barrier method (condom) of the respondents

Variables		Frequency (n =220)	Percent (%)
Thinking of effectiveness of condom to prevent pregnancy	Yes	83	37.7
	No	31	14.1
	Don't know	106	48.2
Usable of condom more than one time	Yes	30	13.6
	No	66	30
	Don't know	124	56.4
Thinking of effectiveness of condom to prevent STD/AIDS	Yes	77	35
	No	32	14.5
	Don't know	111	50.5
Decrease pleasure in sexual intercourse	Yes	72	32.7
	No	28	12.7
	Don't know	120	54.6

This table 5 shows the knowledge on barrier method (condom) of the respondents. 117(53.2%) of the respondents have seen of condoms. 83(37.7%) thought condom can prevent pregnancy. Majority of respondents 124(56.4%) don't know that condom can use for only one time. And majority of respondents don't have any idea of decrease pleasure of condoms during sexual intercourse.

To find out knowledge score of barrier method (condom), we have done 3 categories, category-1, category-2 and category-3. This category is done by computing whole variables related to barrier method related questions then made 3 categories with approximate 3 equal distributions. There were 12 of condom related questions. Here, score 0-4 is categorized as category-1, 5-8 as category-2 and 9-12 as category-3.

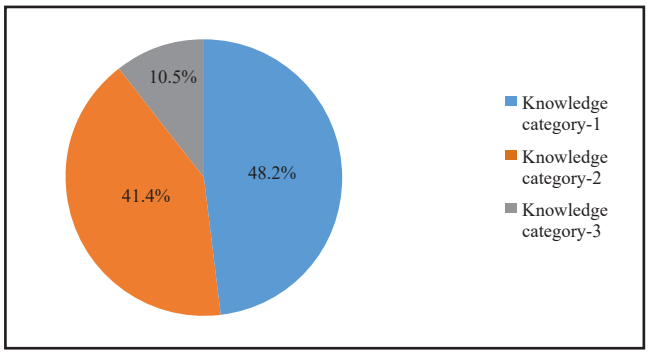

Figure 2: Respondents knowledge score on barrier methods (condom)

Here, finding is that, 106(48.2%) of respondent have category-1 knowledge on barrier method, 91(41.4%) have category-2 and 23(10.5%) have category-3 knowledge.

Discussion:

The study conducted at Baghutiya Omor Ali High School in Daulatpur Thana, Manikganj district provides a comprehensive analysis of male adolescents' knowledge of reproductive health and the availability of related services. This discussion delves into the findings, comparing them with existing literature and exploring the implications for future reproductive health education interventions.

The data indicates that a substantial portion of respondents had limited knowledge about the physical and mental changes that occur during adolescence. For instance, while 37.3% identified an increase in body structure as a change in males during adolescence, only 20.9% were aware of voice changes, and even fewer knew about wet dreams, with 52.7% admitting to having no knowledge of these changes. The awareness of female physical changes was even lower, with only 10% recognizing menstruation as a natural process, and 71.4% of respondents reporting no knowledge of female changes during adolescence.

These findings highlight a critical gap in adolescent reproductive health education, consistent with the literature that notes adolescents often lack accurate information about reproductive development. Studies such as those by Bilal, Patel, and Kulkarni (2015) emphasize that the adolescent population frequently holds misconceptions about basic biological processes due to insufficient education and cultural taboos surrounding discussions of reproductive health.[2]

One of the most concerning aspects of the study is the limited understanding of reproductive health issues among the respondents. Less than half (25.9%) of the participants correctly identified wet dreams as a natural phenomenon, while a significant portion (47.7%) didn't know about it, with 30% even believing it to be a disease. Similarly, only 28.6% recognized menstruation as natural, with over half (54.5%) admitting to a lack of knowledge. These figures suggest that despite the substantial focus on sexual and reproductive health in policy discussions, there is a lack of sufficient, practical education for adolescents in Bangladesh. This mirrors the findings of Jones et al. (2012), which highlight a global trend of insufficient sexual education among adolescents, particularly in developing countries.[9]

The research also identifies significant barriers to accessing sexual and reproductive health knowledge. Teachers were reported as the most common source of information (51.4%), followed by mothers (47.7%) and friends (40%). This dependence on teachers and family members for information indicates that many adolescents lack access to more formal or specialized resources such as healthcare professionals or educational programs. In fact, 67.3% of respondents reported that they had never attended a class related to reproductive health, reflecting a systemic failure in providing comprehensive sexual education in schools.

The limited participation in reproductive health classes underscores the need for structured educational programs. Literature emphasizes the crucial role of educational institutions in disseminating reproductive health information, and how failure to do so often results in misconceptions and risky behaviors among adolescents.

Regarding knowledge of condoms and their role in preventing sexually transmitted infections (STIs) and pregnancy, the study reveals another area of concern. Less than half (37.7%) of respondents were aware that condoms can prevent pregnancy, and only 35% knew that condoms can prevent STDs such as HIV/AIDS. Even more troubling is that 56.4% of respondents did not know that condoms are single-use only. Such findings point to a substantial knowledge gap about condom use, which is consistent with existing research that has found similar deficits in other adolescent populations, especially in rural areas.

This lack of knowledge regarding contraception is particularly alarming, as it leaves adolescents vulnerable to both unintended pregnancies and sexually transmitted infections. As noted in the study, a majority of respondents did not fully understand the protective benefits of condoms, a key issue in preventing the spread of HIV and other STIs. This gap in knowledge suggests that adolescent reproductive health programs need to prioritize contraceptive education

and ensure adolescents understand both the correct usage and efficacy of barrier methods like condoms.

Interestingly, the analysis shows no significant association between the respondents' age and their reproductive health knowledge, as demonstrated by a p-value of 0.939. This lack of correlation suggests that reproductive health knowledge is not necessarily improved by age alone and reinforces the idea that formal education and parental guidance are critical in shaping adolescents' understanding of these topics. Without structured educational interventions, adolescents are likely to remain ill-informed, regardless of age.

The findings from this study align with the broader concerns outlined in the literature regarding adolescent reproductive health, particularly in developing countries like Bangladesh. Adolescents represent a significant portion of the global population and play a crucial role in future public health outcomes. However, as this study illustrates, many adolescents lack the basic knowledge necessary to navigate the challenges of sexual and reproductive health, increasing their vulnerability to risky behaviors, STIs, and unintended pregnancies.

To address these gaps, it is essential to enhance adolescent reproductive health programs, particularly in school settings, where students can receive structured, accurate, and comprehensive information. There is also a need for increased parental involvement, where open communication about reproductive health is encouraged, helping to dispel taboos and misunderstandings. Finally, efforts should focus on ensuring that adolescents have access to youth-friendly health services, enabling them to make informed choices about their sexual and reproductive health.

Conclusion:

The study underscores the critical need for improved reproductive health education among adolescents in Bangladesh. The significant gaps in knowledge, particularly regarding condom use and understanding of basic physiological changes, reflect broader global challenges in adolescent health education. Addressing these gaps requires a multifaceted approach involving schools, families, and healthcare providers to ensure that adolescents are better equipped to manage their sexual and reproductive health responsibly.

Limitations of the Study

While this study provides valuable insights into the reproductive health knowledge of male adolescents in rural Bangladesh, there are several limitations to consider:

1. **Limited Generalizability:** The study was conducted in a single high school in a rural area, which may not be representative of the broader adolescent population in Bangladesh. The findings may differ in urban settings or other regions of the country with different socioeconomic and cultural contexts.
2. **Gender Focus:** This study focused solely on male adolescents, which limits the understanding of reproductive health knowledge and challenges faced by female adolescents. A comparative analysis including both genders would provide a more comprehensive understanding of adolescent reproductive health in the area.
3. **Self-Reported Data:** The study relied on self-reported data, which may be subject to biases such as social desirability bias, where respondents may have provided answers they believed were more socially acceptable rather than truthful responses.
4. **Cross-Sectional Design:** The cross-sectional design of the study captures a snapshot in time, making it difficult to determine changes in knowledge or behavior over time. A longitudinal study would provide more insights into how adolescents' knowledge of reproductive health evolves.
5. **Limited Scope of Questions:** While the study addresses several key aspects of reproductive health, the scope of questions may not cover all relevant areas, such as the impact of media or social influences on adolescent behavior, emotional health, and decision-making regarding sexual health.
6. **Lack of Qualitative Insights:** The study used quantitative methods, which may not fully capture the complexity of adolescents' understanding of reproductive health. Qualitative data, such as interviews or focus groups, could provide deeper insights into the reasons behind knowledge gaps and misconceptions.
7. **Potential Recall Bias:** Since the data were collected through questionnaires, there may be issues related to recall bias, where participants might not accurately remember or report past experiences or knowledge related to reproductive health.

These limitations should be considered when interpreting the results and applying them to broader adolescent health initiatives.

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Conflict of interest:

The authors declare that no conflict of interest exists.

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Original article

Adherence to Highly Active Antiretroviral Therapy in People Living with HIV/AIDS

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Khondoker Hasina Sultana,[1] Mohamaad Mazharul Islam,[2] Md. Anisur Rahman[3]

Abstract

Background: Maintaining adherence to HIV/AIDS treatment is essential to delay or prevent drug resistance and ensure the long-term effectiveness of first-line antiretroviral therapy. ***Objectives:*** This study aimed to assess the level of adherence to Highly Active Anti-Retroviral Therapy (HAART) and identify factors influencing adherence among individuals living with HIV/AIDS. ***Methodology:*** A cross-sectional study was carried out at Ashar Alo Society in Mohammadpur, Dhaka, from July 2013 to June 2014. Data were gathered from 193 participants through face-to-face interviews using a semi-structured questionnaire based on the Center for Adherence Support and Evaluation Adherence Index and a checklist for document review. ***Result:*** In the study, 53.9% of respondents were male, 43.0% female, and the rest were transgender, with a mean age of 36.8 years. Most had completed secondary school (46.6%), 29.5% were businessmen, 58.5% came from nuclear families, the average family size was 4.7, and 69.4% were married. A total of 97.4% of participants adhered to Highly Active Antiretroviral Therapy (HAART) based on Pill count and the Center for Adherence Support and Evaluation Index. Most respondents had been diagnosed with HIV for over 730 days (64.8%) and on HAART for the same period (49.7%). More than half (59.6%) took a single daily dose, with a mean of 2.75 tablets per day. Adherence was significantly higher in males ($p = 0.005$) and married individuals ($p = 0.027$). Full adherence was observed in participants with primary or higher education, age 41+, family support, recent HIV detection (68-365 days), shorter HAART duration (59-365 days), single daily dose, and baseline CD4 count ≥ 300. Non-adherence was mainly due to negligence (40%), being away from home, frustration, and being busy (20% each). ***Conclusion:*** To improve HAART adherence, continuous counseling for both patients and their families is recommended.

Keywords: HAART, HIV/AIDS, Antiretroviral Therapy, Treatment Adherence

Introduction:

Adherence to Highly Active Antiretroviral Therapy (HAART) is essential for successful HIV treatment, requiring 95% adherence to ensure optimal virological, immunological, and clinical outcomes. This prevents drug resistance and maintains the long-term effectiveness of therapy. HAART, the gold standard in HIV/AIDS management, should be offered comprehensively, including adherence counseling, regular lab tests, management of opportunistic infections, and continuous treatment

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Address of correspondence: Dr. Khondoker Hasina Sultana, Medical Officer, Infectious Disease Division, icddrb, Mohakhali, Dhaka. Email address: shorna2020@gmail.com

1. Dr. Khondoker Hasina Sultana, Medical Officer, Infectious Disease Division, icddrb, Mohakhali, Dhaka
2. Dr. Mohammad Mazharul Islam, Associate Professor, Department of Community Medicine, Bashundhara Ad-din Medical College, South Keraniganj, Dhaka
3. Prof. Dr. Md. Anisur Rahman, Professor & Head, Department of Epidemiology, NIPSOM, Mohakhali, Dhaka-1212

monitoring.[1]

Virological response to Highly Active Antiretroviral Therapy: Usually by week 24 following initiation of treatment, patient's viral load should be at the least <400 copies /ml.[2]

The introduction of highly active antiretroviral therapy (HAART) in 1996 significantly improved the management of HIV, reducing morbidity and mortality. However, since HIV is a chronic disease requiring long-term treatment, patients often face challenges with adherence to their medication regimens. Non-adherence has been identified as a major reason for treatment failure, leading to increased morbidity and mortality. Effective antiretroviral therapy is heavily dependent on patient adherence.[3]

The introduction of highly active antiretroviral therapy (HAART) in the treatment of HIV has shown dramatic results, leading to the reduction of mortality and the improvement of the quality of life of People Living with HIV/AIDS.[4]

The emergence of drug-resistant viral strains linked to suboptimal adherence in resource-poor settings poses challenges for the effectiveness of Highly Active Antiretroviral Therapy (HAART) in HIV/AIDS treatment. High patient motivation and adherence are crucial to prevent resistant strains. A 10% increase in adherence could lead to a 21% reduction in disease progression, highlighting that nonadherence increases the risk of therapy failure and drug resistance.[5,6]

Optimal adherence to antiretroviral regimens is closely associated with achieving and maintaining HIV viral suppression and preventing the development of drug-resistant virus. Missed antiretroviral doses, interruptions in therapy and improper dosing can all lead to HIV drug resistance. Adherence measures were significantly associated with VL, with 42% of suboptimally adherent patients compared with only 19% of optimally adherent patients showing virological failure ($P < 0.001$).[7]

The present significant challenges to both patients and health-care providers with respect to adherence. Without adequate adherence, antiretroviral agents are not maintained at sufficient concentrations to suppress HIV replication in infected cells and to lower the plasma viral load. In addition to being associated with poor short-term virological response, poor adherence to antiviral medication accelerates development of drug-resistant HIV.[8]

Antiretroviral adherence is the second strongest predictor of progression to AIDS and death, after CD4 count. Incomplete adherence to Antiretroviral Therapy, however, is common in all groups of treated individuals. The average rate of adherence to Antiretroviral Therapy is approximately 70%, despite the fact that long-term viral suppression requires near-perfect adherence.[9]

The main goal of Antiretroviral Therapy (ART) is to reduce HIV-related illness and death, with an initial focus on achieving sustained viral suppression. Near-perfect adherence (over 95%) to ART is crucial for this suppression. Nonadherence can lead to decreased immunological benefits and increased rates of morbidity, mortality, and hospitalization. A study involving 1,095 patients showed a clear correlation between adherence levels and CD4 count increases at 12 months, with higher adherence linked to greater CD4 cell gains.[10]

Bangladesh is a low-level epidemic but high risk country. Prevalence of Most at Risk People (MARP) {FSW, MSM, Hijra, and Transgender} and in general population is less than one percent. According to 9th round of serological surveillance (2011) the overall prevalence of HIV is 0.7%. Highest rate of HIV is among People Who Inject Drug (PWID). But the prevalence has declined to 5.3% from 7%.[11]

The introduction of HAART in 1996 changed the clinical course of HIV, with a significant decline in morbidity and mortality. Evidence suggests that HIV-positive patients have problems taking antiretroviral medication correctly and non-adherence has been recognized as one of the main causes of treatment failure.[3]

Materials and methods

This cross-sectional study aimed to determine the extent and factors affecting adherence to HAART. Both qualitative and quantitative data were gathered through interviews with respondents at Ashar Alo Society, Mohammadpur, Dhaka, a community-based NGO working with people living with HIV/AIDS (PLHIV). The study was conducted from July 2013 to June 2014.

Adults (18+), male, female, and transgender, diagnosed with HIV/AIDS, receiving HAART, and willing to participate were included in the study. Ashar Alo Society was selected purposively for collecting samples, as it provides HIV/AIDS treatment. For data collection, a semi-structured questionnaire was used, including socio-demographic data, adherence factors, the CASE Adherence Index, and reasons for non-adherence. Adherence was assessed by pill count and using the following formula:

Adherence (%) = (Total pills taken×100) ÷ (Total pills prescribed)

Ethical approval was obtained from NIPSOM and Ashar Alo Society. Informed consent was secured, and confidentiality maintained. The cross-sectional design limited causal inferences. The study was restricted to one center, had a low educational level among respondents, and few non-adherent participants, affecting the conclusions.

Result:

A total of 193 respondents were enrolled in this study. Collected data on adherence to HAART were organized into four different categories:

a) Socio-demographic and economic characteristics

b) Extent of treatment adherence to Highly Active Antiretroviral Therapy

c) Factors associated with adherence to Highly Active Antiretroviral Therapy

d) Reasons behind non-adherence to Highly Active Antiretroviral Therapy

a) Socio-economic characteristics

The study involved 193 respondents, with 53.9% male, 43.0% female, and 3.1% transgender. The mean age was 36.88 years, with the majority (28.5%) aged up to 30 years. Most respondents were Muslims (91.7%) and married (69.4%). Living arrangements included 57.5% in rural areas. Occupationally, 29.5% were businessmen and 28.5% housewives. Education levels showed 46.6% completed secondary school, while the average family income was Tk. 11,248. Less than half were the primary income source, with most residing in tin shed houses (54.9%). Family sizes averaged 4.7 members, with 59.1% having 4 to 6 members.

b) Extent of treatment adherence

Using the Center for Adherence Support and Evaluation (CASE) Adherence Index Questionnaire, where the total score ranges from 3 to 16 (with scores >10 indicating good adherence and scores ≤10 indicating poor adherence), the majority of respondents (50.3%) obtained a score of 13. One-fifth of respondents (20.2%) received a score of 11, and only 6.7% of participants achieved the maximum score of 16. A score of ≤10 was observed in only 2.5% of respondents. The mean score was 12.5 (±1.5). Based on adherence assessed via pill count, 74.1% of respondents achieved a score of 100. Only 2.6% had a score below 95, while 17.9% received a score between 97 and 99. The mean pill count score was 99.3 (±1.5). In this study, 97.4% of participants were adherent to HAART based on both the pill count and the CASE Adherence Index Questionnaire, while only 2.6% were classified as non-adherent.

c) Factors associated with adherence to HAART

Among the 193 respondents, the majority (93.8%) lived with their family, while 5.7% lived alone, and only one person (0.5%) lived with a friend. In this study, 85.5% of participants disclosed their HIV status, while 14.5% chose to keep it confidential.

Of the respondents, 67.9% managed their daily medication reminders themselves, while 32.1% were reminded by family members. The majority (86%) attended physician visits alone, 13.5% were accompanied by family, and only one person (0.5%) attended with a friend.

All participants (100%) expressed satisfaction with their healthcare provider. Most respondents (97.4%) received counseling at every follow-up visit, with only 2.6% reporting they did not. Similarly, 97.4% were satisfied with the time spent on counseling, and only 2.6% reported insufficient counseling time.

A majority of respondents (63.2%) felt comfortable taking antiretroviral drugs in the presence of others, while 36.8% did not. Additionally, 96.9% of respondents reported no history of alcohol or substance use, while 3.1% had a history of such usage.

Regarding antiretroviral drug side effects, 63.2% of respondents reported none. Itching was experienced by 12.4%, while nausea and/or vomiting, anorexia, fever, and skin pigmentation were reported by 5.7%, 4.7%, 4.1%, and 4.1%, respectively. Diarrhea and paresthesia/neuropathy were each reported by 2.1%, and 1.6% experienced skin rashes.

The majority of respondents (64.8%) had been diagnosed with HIV for more than 730 days, with 19.2% diagnosed between 366 to 730 days, and 7.8% diagnosed within 180 days. The mean duration of HIV detection was 1,306 (±993) days.

Nearly half of respondents (49.7%) had been on HAART for more than 730 days, 22.3% had been on HAART for 366 to 730 days, 15.5% for ≤180 days, and 12.4% for 181 to 365 days. The mean duration of HAART was 866 (±725) days.

A majority of respondents (90.7%) had no history of opportunistic infections, while 9.3% reported such infections. Among the respondents, 96.4% acquired HIV through sexual transmission, 3.1% through blood transfusions, and one person (0.5%) via intravenous drug use.

Most respondents (91.2%) did not require a change in drug regimens, while 8.8% reported changes. Nearly half of the respondents (43%) were on the antiretroviral regimen of TDF+FTC+EFV. A similar proportion (26.9%) were on TDF+3TC+EFV, and 26.4% were on a double combination that included EFV. Smaller proportions were on LPV/r-based regimens: 2.6% on LPV/r, TDF, and 3TC, and 1% on a double combination with LPV/r.

Of the 193 respondents, 59.6% were prescribed a double daily dose, while 40.4% were on a single daily dose. The majority (26.9%) took four tablets per day, followed by three tablets per day (24.9%), two tablets (23.8%), and one tablet (20.7%). Only 2.6% took seven tablets per day. The mean number of tablets per day was 2.75 (±1.33).

At the time of HAART enrollment, 34.7% of respondents had a CD4 cell count between 100 and 199, followed by 28.5% with counts between 200 and 299. A CD4 cell count below 100 was recorded for 26.4% of participants, while only 5.7% had counts above 350. The mean CD4 cell count was 176 (±106.8).

The study found no significant association between participants' age and adherence to HAART. In the age group of 41 years and above, adherence was 100%, followed by the 36 to 40 age group with 97.4% adherence. The lowest adher-

ence (94.5%) was observed among participants aged 18 to 30. Although five cells (50.0%) had an expected count of less than five, Fisher's Exact Test was conducted, revealing no significant association between age and adherence to HAART (p = 0.69).

In contrast, the study identified a significant association between gender and adherence to HAART. Male participants demonstrated a higher adherence rate (99.0%) compared to female respondents (97.6%), with the lowest adherence observed among transgender individuals (66.7%). Despite three cells (50.0%) having an expected count of less than five, Fisher's Exact Test was applied, and the association between adherence and gender was found to be statistically significant (p = 0.005).

Table-1: Association between Gender of the respondents and Adherence to HAART

Gender	Adherence to HAART				Total	
	Non-adherent		Adherent			
	frequency	percentage	frequency	percentage	frequency	percentage
Male	1	1.0%	103	99.0%	104	100.0%
Female	2	2.4%	81	97.6%	83	100.0%
Transgender	2	33.3%	4	66.7%	6	100.0%
Total	5	2.6%	188	97.4%	193	100.0%
Significance	Fisher's Exact Test p = .005					

The study found no significant association between respondents' religion and adherence to HAART. Among Muslim participants, 97.2% were adherent, while 100% of Hindu respondents demonstrated adherence. Although two cells (50.0%) had an expected count of less than five, Fisher's Exact Test was conducted, revealing no significant association between religion and adherence to HAART (p = 1.000).

In contrast, the study identified a significant association between marital status and adherence to HAART. Married respondents exhibited the highest adherence rate (99.3%), compared to 88.9% among single participants and 93.8% among widowed individuals. Divorced respondents showed 100% adherence. Despite four cells (50.0%) having an expected count of less than five, Fisher's Exact Test was applied, and the association between marital status and adherence was found to be statistically significant (p = 0.027).

The study found no significant association between the monthly family income of respondents and adherence to HAART. Participants with a monthly family income between 9,000 and 18,000 had 100% adherence, while the lowest adherence (94.3%) was observed among those with a monthly family income of up to 8,000. Although four cells (50.0%) had an expected count of less than five, Fisher's Exact Test was applied, showing no significant association between monthly family income and adherence to HAART (p = 0.103).

Table-2: Association between Marital status of the respondents and Adherence to HAART

Marital status	Adherence CASE				Total	
	Non-adherent		Adherent			
	frequency	percentage	frequency	percentage	frequency	percentage
Single	2	11.1%	16	88.9%	18	100.0%
Married	1	.7%	133	99.3%	134	100.0%
Divorced	0	0%	9	100.0%	9	100.0%
Widowed	2	6.3%	30	93.8%	32	100.0%
Total	5	2.6%	188	97.4%	193	100.0%
Significance	Fisher's Exact Test, p = .027					

Similarly, no significant association was found between the educational qualification of respondents and adherence to HAART. Participants with primary, higher secondary, and above qualifications exhibited 100% adherence, while the lowest adherence (91.9%) was found among illiterate participants. Despite four cells (50.0%) having an expected count of less than five, Fisher's Exact Test was conducted, revealing no significant association between educational qualification and adherence to HAART (p = 0.121).

The study also found no significant association between the reminder assistance for medication doses and adherence to HAART. Participants who were reminded by family members had 100% adherence, compared to 96.2% adherence among those who did not receive family support. Although two cells (50.0%) had an expected count of less than five, Fisher's Exact Test indicated no significant association between reminder assistance and adherence to HAART (p = 0.178).

Regarding accompaniment during physician visits, the study found no significant association with adherence to HAART. Participants who were accompanied by family or friends had 100% adherence, while those who attended physician visits alone had 97% adherence. Despite four cells (66.7%) having an expected count of less than five, Fisher's Exact Test revealed no significant association between accompaniment and adherence to HAART (p = 1.00).

The study also found no significant association between the duration since HIV detection and adherence to HAART. Participants who had been diagnosed with HIV within 68 to 365 days exhibited 100% adherence, while the lowest adherence (96.8%) was observed among those diagnosed for more than 730 days. Although four cells (50.0%) had an

expected count of less than five, Fisher's Exact Test found no significant association between the duration since HIV detection and adherence to HAART (p = 1.00).

Similarly, no significant association was observed between the duration of HAART and adherence. Participants who had been on HAART for 59 to 365 days had 100% adherence, while the lowest adherence (95.8%) was found among those on HAART for more than 730 days. Despite four cells (50.0%) having an expected count of less than five, Fisher's Exact Test revealed no significant association between the duration of HAART and adherence (p = 0.84).

The study also found no significant association between the number of daily doses and adherence to HAART. Participants who received a single daily dose exhibited 100% adherence, while those on a double daily dose had an adherence rate of 95.7%. Although two cells (50.0%) had an expected count of less than five, Fisher's Exact Test found no significant association between the number of daily doses and adherence to HAART (p = 0.082).

Lastly, the study found no significant association between CD4 count at HAART enrollment and adherence to treatment. Participants with a baseline CD4 count of ≥300 exhibited 100% adherence, while the lowest adherence (96.4%) was found among those with a CD4 count between 200 and 299, followed by those with a count between 100 and 199 (97%). Although four cells (50.0%) had an expected count of less than five, Fisher's Exact Test indicated no significant association between baseline CD4 count and adherence to HAART (p = 1.00).

d) Reasons behind non-adherence

Negligence was the main reason (40%) behind non-adherence to HAART. Away from home (20%), Frustration (20%), Busy with other things (20%) was the other reasons behind non-adherence to HAART.

Table-3: Distribution of respondents by Reasons behind non-adherence to HAART

Reasons behind non-adherence	Frequency	Percent
Away from home	1	20.0%
Frustration	1	20.0%
Busy with other things	1	20.0%
Negligence	2	40.0%
Total	5	100.0%

Discussion:

The article presents an analysis of several factors influencing adherence to Highly Active Antiretroviral Therapy (HAART) in individuals with HIV/AIDS across various countries, including Brazil, India, Ethiopia, South Africa, and Nigeria. The findings reveal that gender, age, marital status, education, and occupation significantly affect HAART adherence. Notably, most participants were male, middle-aged, and had completed secondary education. In Nigeria and Ethiopia, the majority were married, with businesspeople and civil servants being prominent occupation groups.

Adherence rates varied, with higher rates observed in India (87.6%) and lower rates in South Africa (63%). Key factors associated with better adherence included older age, higher education, male gender, family support, and higher baseline CD4 counts. Common reasons for non-adherence were forgetfulness, being away from home, and busyness. Despite relatively high adherence overall, barriers such as negligence and frustration remained prevalent.

Several studies have explored gender, age, marital status, education, and adherence to Highly Active Antiretroviral Therapy (HAART) across various countries. For instance, gender distribution in studies from Brazil, India, and France showed male predominance.[7, 12, 13] Age-related patterns in Nigeria, South Africa, and Ethiopia revealed mean ages of 39.1, 34.1, and 35.3 years, respectively.[14, 15, 16] Marital status data from Ethiopia and Nigeria indicated the majority were married, with 44.4% and 66.7% respectively.[14, 16]

Occupation profiles varied, with businesspeople and civil servants forming the majority in Nigeria[14] and similar patterns seen in Ethiopia.[16] Education levels showed that most participants in studies from Nigeria and Ethiopia had completed secondary schoo[l,14, 16] while a South African study reported a higher proportion with secondary or higher education.17 Adherence rates to HAART varied: 87.6% in West Bengal, India, 75.7% in India, and 63% in South Africa.[7, 18, 19] Significant associations were found between adherence and factors such as age, education, sex, and baseline CD4 count.[17, 18, 19] Reasons for non-adherence included forgetfulness, being away from home, and busyness, which were reported across studies.[14, 18, 20]

These findings highlight the multifaceted factors influencing adherence and the importance of addressing them through targeted interventions.

Conclusion:

Most participants were young, economically disadvantaged, and had completed primary or secondary education. The majority demonstrated adherence to HAART, as assessed through pill counts and the CASE Adherence Index Questionnaire. There were significant associations between adherence and various factors, including gender, marital status, age, educational level, family support, once-daily dosing, and higher baseline CD4 counts. Common reasons for non-adherence included forgetfulness, being away from home, frustration, and being preoccupied.

These findings emphasize the importance of targeted interventions, such as counseling, family involvement, and community support, to address these barriers. Enhancing adherence could slow HIV progression and reduce the likelihood of developing drug resistance, thereby improving patient outcomes. Despite high overall adherence, addressing these influencing factors through effective interventions could further optimize adherence and treatment success.

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Review article

Preserving Our Last Line of Defense: A Deep Dive into Antibiotic Stewardship in Bangladesh

Rokya Sharmin Huda Fariha,[1] Nur Mohammad Khan[2]

Abstract

Antibiotic resistance (AMR) has emerged as a critical global health threat, particularly in low- and middle-income countries (LMICs) like Bangladesh, where the misuse and over-prescription of antibiotics have exacerbated this issue. Widespread AMR has led to treatment failures, prolonged hospital stays, and increased healthcare costs. In response, antibiotic stewardship programs (ASPs) have been implemented in Bangladesh to promote the appropriate use of antibiotics, improve patient outcomes, and curb the growing threat of AMR. This review examines the current status of ASPs in Bangladesh, exploring their objectives, implementation strategies, key stakeholders, and challenges. Despite the establishment of ASP initiatives, significant limitations persist, such as inadequate resources, insufficient training for healthcare providers, and a lack of public awareness regarding antibiotic misuse. Moreover, the healthcare infrastructure—particularly in rural areas—is often insufficient to support effective stewardship practices. These challenges are compounded by socioeconomic barriers, including poverty and limited access to healthcare, which further hinder the adoption of ASPs in rural and underserved regions.The article provides data on current AMR trends in Bangladesh, including resistance rates for common pathogens, hospital data on treatment failures, and the economic burden of AMR on the healthcare system. These statistics underscore the urgency of addressing the issue. Additionally, the review highlights case studies that illustrate the complexities faced by healthcare professionals and institutions in implementing ASPs, as well as the unintended consequences of antimicrobial use, such as the emergence of new resistance patterns. While antibiotic stewardship programs have made some progress, there are notable gaps in their effectiveness, particularly in rural areas where healthcare resources are scarce. These areas face unique challenges, such as a lack of trained personnel and poor access to diagnostic tools. The article proposes several strategies to enhance ASPs, including the integration of digital technologies for better monitoring and reporting of antibiotic use, as well as targeted community engagement to raise awareness and promote responsible antibiotic use.In conclusion, this review emphasizes the need for a balanced approach to antibiotic stewardship—one that not only addresses AMR but also ensures the overall health and safety of patients. By fostering collaboration among healthcare providers, policymakers, and the public, Bangladesh can strengthen its ASPs and make meaningful progress in combating antibiotic resistance. This article provides actionable recommendations for enhancing antibiotic stewardship and closing existing gaps in the response to AMR, ensuring a more sustainable and effective approach to safeguarding public health in Bangladesh.

Keywords: Antibiotic stewardship programs (ASPs), Antimicrobial resistance (AMR), Antibiotics.

Introduction

Antibiotic resistance (AR) is emerging as one of the most critical public health challenges worldwide, with significant implications for global healthcare systems.[1] It threatens to reverse decades of medical progress, leading to increased morbidity and mortality, higher healthcare costs, and the

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Address of correspondence: Dr. Rokya Sharmin Huda Fariha, Lecturer, Department of Microbiology, Bashundhara Ad-din Medical College, Dhaka. Email: sharmin.fariha111@gmail.com

1. Dr. RokyaSharmin Huda Fariha, Lecturer, Department of Microbiology, Bashundhara Ad-din Medical College, Dhaka
2. Dr. Nur Mohammad Khan, Assistant Professor, Department of Microbiology, Bashundhara Ad-din Medical College, Dhaka

possibility of returning to a pre-antibiotic era where simple infections could again become life-threatening.[2] The rise of resistant pathogens is primarily driven by the misuse and overuse of antibiotics in both human medicine and agriculture, a trend that is especially pronounced in low- and middle-income countries like Bangladesh.[3] In Bangladesh, the burden of AR is exacerbated by a range of factors, including limited healthcare access, inadequate regulatory frameworks, and insufficient public awareness regarding the appropriate use of antibiotics.[4] Reports show that many healthcare providers prescribe antibiotics without proper diagnosis, contributing to unnecessary exposure and accelerating the development of resistance.[5] The situation is further complicated by the widespread availability of antibiotics over the counter, allowing patients to self-medicate without professional oversight.[6] As a result, Bangladesh is facing an alarming increase in antibiotic-resistant infections, which not only complicate treatment but also drive up healthcare costs.[7]Antibiotic stewardship programs (ASPs) are essential tools in curbing the spread of antibiotic resistance.[8] These programs typically include strategies for appropriate antibiotic prescribing, training for healthcare providers, and monitoring of antibiotic use and resistance patterns.[9] In countries like Bangladesh, where healthcare resources are limited and the burden of AR is high, ASPs are crucial in ensuring the continued effectiveness of antibiotics for future generations.[10] By promoting rational antibiotic use, these programs can improve clinical outcomes, reduce healthcare costs, and enhance patient safety.[11] These gaps include limited evidence on the full scope of AR in Bangladesh, insufficient exploration of socioeconomic and cultural factors that drive antibiotic misuse, and a lack of comparative studies across different regions or healthcare settings within the country.[12]

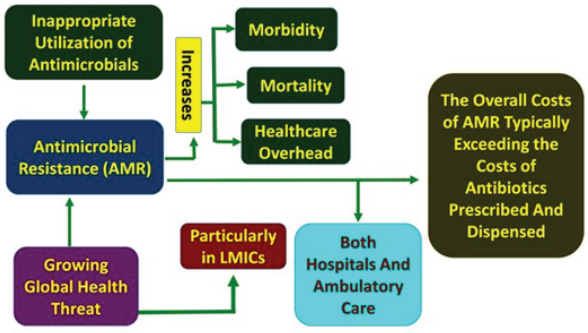

Figure 1 : Cycle of Causes of Antibiotic Resistance: Interconnected Factors and Consequences[13]

Additionally, the role of antibiotics in agriculture remains under-researched, and there is a need for clearer identification of key stakeholders and their roles in implementing ASPs. Policy and regulatory gaps, coupled with infrastructure challenges, further hinder the effective implementation of stewardship programs.[14] Public and healthcare provider awareness is also limited, and the potential for technological and innovative solutions to enhance ASPs has not been fully explored.[15] This review aims to provide a comprehensive overview of the current state of antibiotic stewardship in Bangladesh, highlighting the challenges and proposing recommendations to strengthen these efforts, ultimately safeguarding public health and curbing the growing threat of antibiotic resistance.

Overview of Antibiotic Stewardship Programs in Bangladesh

Antibiotic Stewardship Programs (ASPs) are coordinated interventions designed to improve and measure the appropriate use of antibiotics, thereby enhancing patient outcomes, reducing adverse effects, and decreasing the emergence of antibiotic-resistant bacteria.[16] In the context of Bangladesh, where the burden of antibiotic resistance is particularly acute, the establishment of effective ASPs has become critical to preserving the efficacy of existing antibiotics and ensuring public health safety.[17]

The primary objectives of ASPs in Bangladesh include:

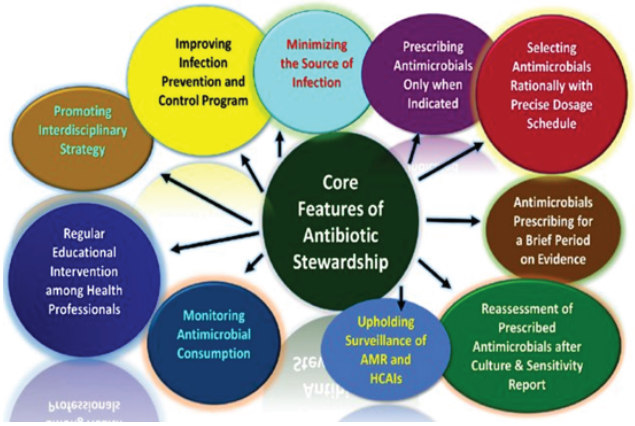

Figure 2 :Overview of an Antibiotic Stewardship Program: Key Components and Strategies[18]

Optimizing antibiotic use involves ensuring that antibiotics are prescribed only when necessary and that the correct drug, dose, route, and duration are selected, guided by evidence-based guidelines.[19] By promoting rational antibiotic use, stewardship programs aim to minimize selection pressure and the spread of resistant bacteria.[20] These programs also focus on improving patient outcomes by facilitating timely and effective treatment of infections, thereby reducing the rates of treatment failure and complications. Additionally, educating healthcare professionals and the public is crucial for raising awareness about antibiotic resistance and emphasizing the importance of appropriate antibiotic use among both providers and the general population.[21]

Monitoring and Surveillance

Effective ASPs incorporate mechanisms for monitoring antibiotic use and resistance patterns, allowing for data-driven decision-making and adjustments to stewardship strategies in Bangladesh, the implementation of these objectives is particularly challenging due to a variety of factors, including inadequate healthcare infrastructure, a lack of regulation in the pharmaceutical sector, and widespread self-medication practices.[22]

Key Stakeholders and Initiatives

The successful implementation of ASPs in Bangladesh requires collaboration among various stakeholders, including government bodies, healthcare institutions, professional organizations, and international agencies. Below are some of the key stakeholders involved in antibiotic stewardship in Bangladesh.[23]

Government Agencies

The Ministry of Health and Family Welfare (MoHFW) is the primary governmental body responsible for public health in Bangladesh. It has initiated several policies aimed at combating antibiotic resistance and promoting ASPs, such as the National Policy for Antimicrobial Resistance Control.[24]

Healthcare Institutions

Hospitals and healthcare facilities play a crucial role in implementing ASPs. Many institutions in urban areas have begun to establish their own stewardship programs, focusing on education, guidelines for antibiotic use, and monitoring practices. The involvement of both public and private healthcare sectors is vital for a comprehensive approach.[25]

Academic Institutions

Universities and research institutions contribute to ASPs through research, education, and training programs. They play a key role in developing evidence-based guidelines and conducting studies on antibiotic use and resistance in the country.[27]

International Organizations

Global health agencies, including the World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC), have been instrumental in providing technical support and resources for the development and implementation of ASPs in Bangladesh (WHO, 2015).

Pharmaceutical Companies

While pharmaceutical companies can be a source of antibiotic overuse, they can also play a role in ASPs by engaging in responsible marketing practices and supporting education initiatives aimed at both healthcare providers and the public.[28]

Non-Governmental Organizations (NGOs)

Various NGOs are active in promoting public health initiatives, including antibiotic stewardship. They often engage in awareness campaigns to educate the public about the risks of antibiotic misuse and the importance of adhering to prescribed treatments.[29]

Initiatives and Programs

Several initiatives aimed at promoting antibiotic stewardship have been launched in Bangladesh, reflecting a growing recognition of the issue of antibiotic resistance. Key initiatives include:

National Action Plan on Antimicrobial Resistance

Launched in 2017, this plan outlines a comprehensive strategy for combating antibiotic resistance in Bangladesh. It includes specific objectives related to the surveillance of antibiotic use and resistance, improving infection prevention and control, and raising awareness among healthcare professionals and the public (MoHFW, 2017).

Initiatives and Programs

Several initiatives aimed at promoting antibiotic stewardship have been launched in Bangladesh, reflecting a growing recognition of the issue of antibiotic resistance. Key initiatives include:

The Bangladesh Antimicrobial Resistance Surveillance (BARS)

This initiative aims to establish a national surveillance system for monitoring antibiotic use and resistance patterns. By collecting and analyzing data from various healthcare facilities, BARS seeks to inform policy decisions and improve stewardship efforts.[30]

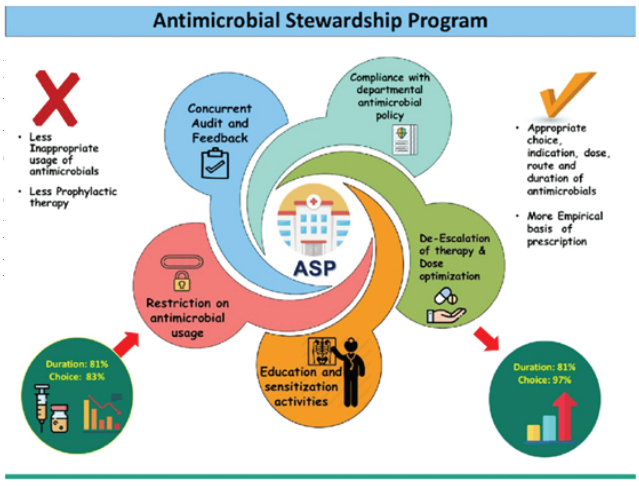

Figure 3 :Strategies for Effective Antibiotic Stewardship: Best Practices and Approaches[13]

Public Awareness Campaigns

Efforts to educate the public about antibiotic resistance and the importance of appropriate antibiotic use have been undertaken by both governmental and non-governmental organizations. These campaigns aim to change public perceptions and behaviors regarding antibiotic use, particularly self-medication practices.[32]

Collaboration with International Organizations

Bangladesh has engaged with global health organizations to implement best practices in antibiotic stewardship. Collaborations with the WHO and CDC have provided valuable resources and guidelines that have been adapted to the local context (WHO, 2015).

Research Initiatives

Academic institutions are increasingly focusing on research related to antibiotic use and resistance in Bangladesh. This research informs local guidelines and contributes to the global understanding of resistance patterns, thereby supporting evidence-based stewardship efforts.[33]

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Current Status of Antibiotic Stewardship in Bangladesh

Antibiotic stewardship programs (ASPs) are gaining traction in Bangladesh as a vital strategy to combat the growing threat of antibiotic resistance.[34] Despite facing numerous challenges, the country is making strides in implementing these programs across various healthcare settings.[35] This section examines the current status of antibiotic stewardship in Bangladesh, focusing on the implementation of ASPs in healthcare settings, government policies and guidelines, and the role of educational institutions.[36]

Implementation in Healthcare Settings

The implementation of ASPs in healthcare settings across Bangladesh is still in its nascent stages, but progress is being made, particularly in urban hospitals and medical centers. Many institutions are recognizing the need for systematic approaches to improve antibiotic prescribing practices and enhance patient care.[37]

Hospital Initiatives

Major hospitals in Dhaka and other urban areas have initiated ASPs that focus on training healthcare providers, establishing guidelines for antibiotic use, and monitoring antibiotic prescriptions.For instance, several tertiary care hospitals have developed protocols that require justification for antibiotic prescriptions, particularly for broad-spectrum agents.[38]

Multidisciplinary Teams

Successful ASPs typically involve the formation of multidisciplinary teams comprising infectious disease specialists, pharmacists, microbiologists, and clinical staff. These teams collaborate to assess antibiotic use, provide feedback to prescribers, and educate healthcare staff on best practices.Some hospitals have begun to adopt this team-based approach, facilitating a culture of stewardship within their institutions.[39]

Monitoring and Surveillance

Effective ASPs rely on robust monitoring and surveillance systems to track antibiotic prescribing patterns and resistance trends. Some healthcare facilities in Bangladesh are now implementing surveillance programs that collect data on antibiotic use and resistance, enabling data-driven decision-making. However, these initiatives are often limited by insufficient infrastructure and resources.[40]

Challenges in Rural Areas

While urban hospitals are making progress, rural healthcare facilities face significant challenges in implementing ASPs. Limited access to healthcare professionals, lack of resources, and a high prevalence of self-medication hinder effective stewardship in these regions .Addressing these disparities is crucial for the nationwide success of ASPs.[41]

Government Policies and Guidelines

The Bangladesh government has recognized antibiotic resistance as a critical public health issue and has initiated several policies aimed at promoting antibiotic stewardship.[42]

National Action Plan

In 2017, the Ministry of Health and Family Welfare (MoHFW) launched a National Action Plan on Antimicrobial Resistance, outlining strategies for surveillance, prevention, and control of antibiotic resistance (MoHFW, 2017). This plan emphasizes the need for comprehensive ASPs across all healthcare settings, including hospitals, clinics, and community pharmacies.

Regulatory Frameworks

The government has also established regulatory measures to control the sale and distribution of antibiotics. These include restrictions on over-the-counter sales and guidelines for appropriate antibiotic prescribing. However, enforcement of these regulations remains a significant challenge, as many pharmacies continue to sell antibiotics without prescriptions.[43]

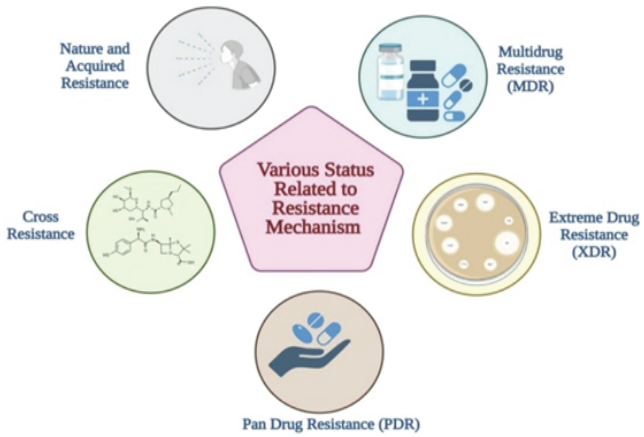

Figure 4: Summary of different statuses associated with antibiotic resistance conditions.

Guidelines for Healthcare Providers

The MoHFW has developed guidelines for healthcare providers to promote rational antibiotic use. These guidelines provide recommendations for appropriate prescribing based on local epidemiology and resistance patterns. However, widespread adherence to these guidelines is still lacking, primarily due to limited awareness and training among healthcare providers.

Public Awareness Campaigns

The government, along with NGOs, has initiated public awareness campaigns aimed at educating the general population about the dangers of antibiotic misuse and the importance of adherence to prescribed treatments. These campaigns play a critical role in reducing self-medication and promoting responsible antibiotic use.[44]

Role of Educational Institutions

Educational institutions are pivotal in the advancement of antibiotic stewardship in Bangladesh. They play a crucial role in training future healthcare professionals and conducting research to inform best practices.[45]

Medical Education

Medical schools in Bangladesh are beginning to incorporate antibiotic stewardship into their curricula. This education aims to equip future healthcare providers with the knowledge and skills necessary to prescribe antibiotics judiciously.Courses on infectious diseases often include modules on antibiotic resistance and stewardship principles.[46]

Continuing Medical Education (CME)

Many professional organizations, such as the Bangladesh Medical Association (BMA) and the Infectious Diseases Society of Bangladesh (IDSB), are organizing CME programs focused on antibiotic stewardship. These programs offer healthcare professionals opportunities to update their knowledge and skills regarding antibiotic use and resistance.[47]

Research Initiatives

Academic institutions are also engaged in research on antibiotic use and resistance patterns in Bangladesh. Studies conducted in collaboration with local and international partners contribute valuable data that inform local guidelines and practices. This research helps identify gaps in antibiotic stewardship and areas for improvement.[48]

Community Engagement

Educational institutions often partner with NGOs to conduct outreach programs aimed at raising awareness about antibiotic resistance in local communities. These initiatives emphasize the importance of proper antibiotic use and the dangers of self-medications.[49]

Figure 5: Building a Successful Antimicrobial Stewardship Program

Complications Associated with Antibiotic Stewardship

Antibiotic stewardship programs (ASPs) are essential for combating antibiotic resistance and improving patient care. However, the implementation of these programs in Bangladesh has led to several complications that impact patient outcomes, resistance patterns, and public compliance. This section explores these challenges in detail.[50]

Impact on Patient Care and Outcomes

One of the primary goals of ASPs is to enhance patient care by ensuring appropriate antibiotic use.[51] However, the transition to stewardship practices can sometimes have unintended negative effects on patient outcomes.[52] Stringent stewardship protocols can sometimes delay the administration of necessary antibiotics, as providers may need to justify their choices or seek approval, potentially worsening patient conditions and increasing mortality rates, especially in sepsis cases.[53] The complexity of clinical guidelines and algorithms associated with ASPs can confuse healthcare providers, particularly in resource-limited settings, leading to difficulties in making timely prescribing decisions.[54] Resistance to changing established prescribing habits among healthcare providers can hinder effective ASP implementation, as cultural

attitudes towards antibiotic use are often deeply ingrained, making behavior shifts challenging despite educational efforts.[55] Additionally, changes in prescribing practices may affect patient satisfaction, as patients expecting immediate symptom relief may feel dissatisfied with watchful waiting or delayed antibiotic therapy, which can undermine the patient-provider relationship and treatment adherence.[56]

Resistance Patterns and Their Implications

While the ultimate aim of ASPs is to reduce antibiotic resistance, the transition to stewardship practices can inadvertently influence resistance patterns.[57] The implementation of Antibiotic Stewardship Programs (ASPs) can lead to increased use of specific antibiotics as alternatives to restricted ones, creating selective pressure that may allow resistant strains of bacteria to thrive.[58] Additionally, guidelines based on local resistance data can be ineffective in areas with scarce or inconsistent data, leading to inappropriate antibiotic choices that further exacerbate resistance.[59] The resistance patterns in Bangladesh can have global implications, as local prescribing practices contribute to worldwide resistance trends, complicating international efforts to manage infectious diseases.[60] As resistance patterns evolve due to suboptimal antibiotic use, the incidence of infections caused by resistant organisms may increase, resulting in longer hospital stays, higher medical costs, and greater mortality, which can strain healthcare resources.[61]

Challenges in Public Compliance and Education

Public compliance and education are vital for the success of Antibiotic Stewardship Programs (ASPs) in Bangladesh, yet several challenges hinder effective engagement.[62] Many individuals remain unaware of the risks associated with antibiotic misuse, with self-medication being common and complicating ASP implementation.[63] Cultural beliefs often treat antibiotics as quick fixes for various ailments, creating expectations for their use even when unnecessary, which requires coordinated efforts from healthcare providers and community organizations to change.[59] Misinformation from unverified sources further contributes to public confusion, highlighting the need for clear, accurate educational initiatives.[64] Designing effective engagement strategies are challenging, as outreach must consider local contexts and literacy levels to resonate with diverse populations.[65] Finally, sustained public health campaigns and community engagement are essential for maintaining awareness and adherence to stewardship principles over time.[44]

Case Studies and Examples

Antibiotic stewardship programs (ASPs) in Bangladesh have seen varying levels of success and challenges. By examining specific case studies, we can identify successful implementations and glean valuable lessons from failures.[66] This section explores notable examples of ASPs in Bangladesh, highlighting both achievements and setbacks.[37]

Successful Implementations

Dhaka Medical College Hospital (DMCH) Initiative

The DMCH implemented a comprehensive ASP that focused on enhancing antibiotic prescribing practices through educational interventions and the establishment of clinical guidelines. The program involved a multidisciplinary team that included infectious disease specialists and pharmacists. Initial data showed a significant reduction in the prescription of broad-spectrum antibiotics, along with improved patient outcomes, such as decreased length of hospital stays for patients with infections.[67] This initiative demonstrates the effectiveness of teamwork and education in achieving stewardship goals.[68]

MawlanaBhashani Medical College ASP

Another successful case was at Mawlana Bhashani Medical College, where an ASP was developed focusing on continuous education and feedback mechanisms. The program included training sessions for healthcare staff and the implementation of a real-time monitoring system for antibiotic use.[69] By utilizing local resistance data, the program effectively adjusted prescribing practices, resulting in a notable decline in resistant infections. The success of this initiative underscores the importance of data-driven approaches and regular staff engagement.[70]

Bangladesh Institute of Tropical and Infectious Diseases (BITID)

BITID launched an ASP that emphasized community outreach alongside hospital-based interventions. The program conducted awareness campaigns about antibiotic resistance and proper usage in nearby communities.[71] The integration of community education not only improved antibiotic stewardship in the hospital but also fostered a culture of responsible antibiotic use among the public. The hospital reported improved compliance with antibiotic guidelines and a significant reduction in self-medication practices within the community.This case illustrates how outreach can amplify the impact of ASPs beyond clinical settings.[72]

National Action Plan on Antimicrobial Resistance (NAP)

The NAP, established by the Ministry of Health and Family Welfare, represents a national-level commitment to combating antibiotic resistance. Through this initiative, various healthcare facilities across the country received support to implement ASPs tailored to local contexts. Reports indicate that hospitals adopting these guidelines have experienced improvements in antibiotic prescribing and reductions in resistance rates, highlighting the effectiveness of coordinated national strategies (MoHFW, 2017).[73]

Lessons Learned from Failures

Several Antibiotic Stewardship Programs (ASPs) in

Bangladesh have encountered challenges that provide important lessons for future implementations. One notable failure occurred in a rural hospital lacking adequate resources, where the absence of trained personnel and diagnostic facilities limited the initiative's impact on prescribing practices.[37] In urban hospitals, some healthcare providers resisted changing established prescribing habits despite new guidelines, highlighting the need for cultural change and ongoing education.[74] Additionally, a lack of monitoring systems in a regional hospital meant that providers received no feedback on their prescribing patterns, contributing to ongoing misuse of antibiotics.[75] A community education pilot aimed at reducing misuse fell short due to low public awareness, underscoring the necessity for tailored public health campaigns.[76] Fragmentation of efforts among ASPs limited coordination and sharing of best practices, which undermined their overall effectiveness.[77] Finally, implementing generic guidelines without adapting them to local resistance patterns resulted in continued high rates of resistance, emphasizing the importance of tailoring ASPs to local epidemiological data.[72]

Future Directions and Recommendations

As antibiotic resistance continues to pose a significant threat to public health in Bangladesh, enhancing antibiotic stewardship programs (ASPs) is crucial for effective management. This section outlines future directions and recommendations, focusing on strategies for improving ASPs, the role of technology and data analytics, and the importance of community engagement.[52]

Strategies for Enhancing Stewardship Programs

Developing standardized, evidence-based guidelines tailored to local resistance patterns is crucial for promoting uniformity in prescribing practices; collaboration with health organizations can facilitate this.[78] Continuous education and training for healthcare providers through workshops and online courses enhances knowledge of antibiotic resistance and stewardship principles, addressing misconceptions and emphasizing guideline adherence.[79] Interdisciplinary collaboration among infectious disease specialists, pharmacists, microbiologists, and nursing staff can improve ASP effectiveness by fostering a culture of stewardship and enhancing guideline adherence through regular case discussions and data reviews.[80] Implementing regular audits of antibiotic prescribing practices, along with feedback mechanisms, can help hospitals monitor usage and resistance patterns, encouraging improvements and adherence to guidelines.[81] Strengthening regulations on antibiotic sales and prescriptions, including enforcing prescription-only practices and conducting inspections, is essential for ensuring compliance and reducing misuse.[82]

Role of Technology and Data Analytics

Integrating Antibiotic Stewardship Programs (ASPs) into Electronic Health Records (EHR) can streamline prescribing by providing alerts and reminders for guidelines, facilitating timely interventions.[83] Data analytics for predictive modeling of antibiotic usage and resistance trends offers valuable insights, allowing healthcare providers to anticipate resistant infections and adjust practices, ultimately improving patient outcomes.[84] Telemedicine and mobile health (mHealth) applications enhance access to healthcare and stewardship education, especially in rural areas, enabling providers to consult specialists and educate patients on responsible antibiotic use.[85] Robust surveillance systems are essential for monitoring antibiotic resistance in real-time, enabling rapid responses to emerging threats through a national database that integrates data from hospitals and laboratories.[86]

Importance of Community Engagement

Community engagement is crucial for reducing antibiotic misuse and enhancing stewardship efforts. Public awareness campaigns play a key role by educating the population about antibiotic resistance and responsible use, utilizing diverse platforms such as social media and community events.[87] Involving community health workers can further enhance this engagement, as they serve as trusted sources of information, especially in rural areas where healthcare access is limited.[88] Collaboration with local organizations, including schools and NGOs, can amplify outreach and facilitate community initiatives that promote responsible antibiotic use while gathering feedback on community needs.[76] Empowering patients to take an active role in their healthcare are also essential; educating them about their rights regarding prescriptions fosters a culture of accountability.[18] Finally, establishing feedback mechanisms, such as surveys and focus groups, provides valuable insights into public perceptions, allowing strategies to be tailored to meet community needs.[89]

Conclusion

The growing threat of antibiotic resistance in Bangladesh necessitates robust antibiotic stewardship programs (ASPs) to safeguard public health. This review highlights several critical findings. While there have been successful implementations of ASPs in various healthcare settings, challenges such as inadequate resources, resistance to change among healthcare providers, and lack of community awareness hinder their effectiveness. Complications associated with ASPs, including delays in treatment, increased resistance patterns, and public non-compliance, underscore the complexity of managing antibiotic use, emphasizing the need for comprehensive approaches that consider both clinical and community aspects. Successful case studies from institutions like Dhaka Medical College and Mawlana Bhashani Medical College demonstrate the potential for improved prescribing practices through interdisciplinary collaboration, continuous education, and community outreach. Future directions for enhancing ASPs involve standardizing guidelines, utilizing technology and data analytics, and fostering community engagement.

Public awareness campaigns, training for healthcare workers and effective regulatory frameworks are essential for promoting responsible antibiotic use. To effectively combat antibiotic resistance in Bangladesh, a collaborative effort from all stakeholders is crucial. Healthcare providers must commit to adhering to evidence-based guidelines, participating in training programs, and collaborating with interdisciplinary teams to ensure responsible antibiotic prescribing. Government and policymakers should strengthen regulations on antibiotic sales, invest in surveillance systems for monitoring resistance, and support national initiatives that facilitate the implementation of ASPs across healthcare facilities. Educational institutions need to integrate antibiotic stewardship principles into curricula and offer continuing education opportunities for healthcare professionals to stay updated on best practices.Local organizations should engage in public awareness campaigns to educate communities about the dangers of antibiotic misuse and the importance of responsible use. Finally, patients and the general public must be empowered to understand their rights regarding antibiotic prescriptions and encouraged to seek clarity from healthcare providers about their treatment options. By taking collective action and prioritizing antibiotic stewardship, stakeholders can significantly reduce the impact of antibiotic resistance, ultimately safeguarding the health of current and future generations in Bangladesh.

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Conflict of interest

The authors declare that no conflict of interest exists.

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Case report

Adolescent Menorrhagia in Bangladeshi Girls: Unveiling Challenges and Treatment Approaches

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Rokya Sharmin Huda Fariha,[1] Nur Mohammad Khan[2]

Abstract

Adolescent menorrhagia, characterized by excessive menstrual bleeding, is a prevalent but under-recognized condition in Bangladesh. This case report focuses on a 15-year-old girl diagnosed with severe menorrhagia, highlighting the challenges in timely diagnosis, treatment, and management. The patient presented with prolonged, heavy menstrual bleeding over six months, leading to symptoms of iron-deficiency anemia and significant psychological distress. Initial assessments indicated no anatomical anomalies but revealed underlying hormonal imbalances. The patient's condition was further complicated by cultural stigmas surrounding menstruation, which delayed seeking medical attention. Despite available treatment options such as hormonal therapy and iron supplementation, the patient faced barriers in accessing appropriate care. Limited healthcare awareness, societal misconceptions about menstruation, and reluctance to discuss menstrual health were significant obstacles. The patient was ultimately treated with a combination of hormonal therapy (oral contraceptives) and iron supplements, leading to a marked improvement in both menstrual bleeding and anemia. Psychological counseling was also provided to address the emotional distress caused by her condition. This case underscores the importance of early diagnosis and intervention in managing adolescent menorrhagia. It highlights the need for better healthcare provider training, especially in recognizing and treating menstrual disorders in adolescents. Moreover, it stresses the need for public education to reduce stigma and encourage open dialogue about menstrual health. By addressing these barriers, we can improve the management of menorrhagia in adolescent girls in Bangladesh, ultimately improving their quality of life and overall health outcomes.

Key word: Adolescent menorrhagia, Hormonal therapies (OCP), Cultural stigma.

Introduction

Menorrhagia, defined as excessive menstrual bleeding, is a common yet often under-recognized concern among adolescents.[1] This condition can have a significant impact on physical health, emotional well-being, and overall quality of life.[2] Adolescents like Ms. Reshma, a 17-year-old girl presenting with a three-month history of heavy menstrual bleeding and iron deficiency anemia, face unique challenges in managing menorrhagia. Prolonged or heavy menstrual bleeding often leads to complications such as anemia, which in turn can cause symptoms like fatigue, dizziness, and difficulty participating in daily activities.[3] These symptoms further exacerbate the physical and emotional challenges faced by affected adolescents.[4] The diagnosis and management of menorrhagia in adolescents require careful consideration of both primary and secondary causes. Primary causes include hormonal imbalances, such as those seen in anovulatory cycles, while secondary causes may involve structural abnormalities or underlying medical conditions, such as coagulation disorders or thyroid

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Address of correspondence: Dr. Rokya Sharmin Huda Fariha, Lecturer, Department of Microbiology, Bashundhara Ad-din Medical College, South Keraniganj, Dhaka. Email: sharmin.fariha111@gmail.com

1. Dr. Rokya Sharmin Huda Fariha, Lecturer, Department of Microbiology, Bashundhara Ad-din Medical College, Dhaka
2. Dr. Nur Mohammad Khan, Assistant Professor, Department of Microbiology, Bashundhara Ad-din Medical College, Dhaka

dysfunction.4 In Ms. Reshma's case, thorough history-taking revealed no structural abnormalities but highlighted the possible role of a hormonal imbalance, which was later confirmed through diagnostic testing. This case underscores the importance of a comprehensive evaluation that includes a detailed medical history, appropriate diagnostic investigations, and an individualized treatment plan tailored to the patient's specific needs. One of the significant barriers in the management of menorrhagia in adolescents is a lack of awareness about what constitutes normal menstrual patterns. Many young women, like Ms. Reshma, may not recognize that their symptoms require medical attention or may feel embarrassed to seek help due to the societal stigma surrounding menstruation. Patient education is therefore critical, not only in promoting awareness of normal menstrual health but also in empowering young patients to seek timely medical care. A multi-faceted approach that includes medical treatment, such as hormonal therapy or iron supplementation, along with patient education, can greatly improve outcomes for adolescents with menorrhagia.[5]

This case study of Ms. Reshma highlights the complex interplay of physiological, psychological, and societal factors that influence the management of menorrhagia in young women. By examining her case, we aim to emphasize the importance of early diagnosis, the impact of iron deficiency on overall health, and the need for a holistic, multidisciplinary approach to treatment. Ultimately, addressing the unique challenges of adolescent menstrual health is essential for improving both physical and emotional well-being in young women.[6]

Case Summary

Ms. Reshma (pseudonym), a 17-year-old female, presented to the outpatient department of SSMC with complaints of persistent menorrhagia over the past three months. Menorrhagia, characterized by heavy or prolonged menstrual bleeding, can significantly impact an adolescent's quality of life, both physically and emotionally. Ms. Reshma reported that her menstrual cycles, which previously lasted 5–7 days, had recently extended to 10–14 days. During her peak bleeding days, she needed to change sanitary pads every hour, leading to fatigue and dizziness, particularly during menstruation. She denied experiencing associated symptoms such as severe abdominal pain, fever, or any changes in bowel or urinary habits, which helped narrow down potential causes. Her medical history revealed menarche at age 13 with regular cycles every 28–30 days, and no previous episodes of heavy bleeding or gynecological issues. Notably, her mother had a similar history of heavy menstrual bleeding but had never sought medical attention. On physical examination, Ms. Reshma appeared pale but in no acute distress. Vital signs were stable (BP: 100/60 mmHg, pulse: 80 bpm), and her abdominal and pelvic exams were unremarkable, with no active bleeding noted at the time of examination.

Diagnostic Workup

Laboratory investigations revealed mild anemia (hemoglobin 10.5 g/dL) and depleted iron stores (low serum ferritin), confirming iron deficiency anemia secondary to chronic blood loss. Coagulation studies (PT, aPTT) were normal, ruling out coagulopathy. A pelvic ultrasound showed a normal-sized uterus with no structural abnormalities, such as fibroids or polyps, which could contribute to the bleeding. Based on these findings, a diagnosis of primary menorrhagia secondary to iron deficiency anemia was made.

Management Plan

Ms. Reshma was started on oral iron supplementation (Ferrous sulfate 325 mg daily) to address her anemia and replenish iron stores. Dietary recommendations included increasing iron-rich foods (e.g., lean meats, beans, leafy greens) and pairing these with vitamin C-rich foods (e.g., citrus fruits) to enhance absorption. Hormonal therapy with combined oral contraceptives (Ethinyl estradiol and Levonorgestrel) was initiated to regulate her menstrual cycles and reduce bleeding volume. The benefits and potential side effects of hormonal therapy were discussed, and Ms. Reshma was advised to report any unusual symptoms. A follow-up appointment was scheduled in four weeks to evaluate her response to treatment, assess adherence to the iron regimen and hormonal therapy, and monitor her overall well-being.

Follow-Up and Outcome

At her follow-up visit, Ms. Reshma reported significant improvement in her symptoms. She remained symptom-free for the 14 days following her initial visit, with no active bleeding or further episodes of dizziness or fatigue. Laboratory results indicated a notable improvement in hemoglobin levels, with a reduction in CRP to 6 mg/L. All other routine tests, including serum creatinine and ESR, were normal.Given the positive response, Ms. Reshma continued her treatment plan with close monitoring. Her anemia was effectively managed, and the menorrhagia significantly improved. She was educated on the importance of continued follow-up care and adherence to her prescribed regimen.

Discussion

Ms. Reshma, a 17-year-old female presenting with menorrhagia and iron deficiency anemia, highlights several important considerations in the diagnosis and management of adolescent menstrual disorders. Menorrhagia, defined as excessive menstrual bleeding, can significantly impair quality of life, leading to both physical and psychological

consequences. For Ms. Reshma, the transition from a typical menstrual cycle lasting 5-7 days to a prolonged 10-14 days, along with the need for frequent pad changes, suggests severe menstrual dysfunction, potentially leading to anemia due to chronic blood loss.

Diagnostic Process and Differential Diagnosis

The diagnosis of menorrhagia in adolescents requires careful consideration of both primary and secondary causes. In Ms. Reshma's case, the absence of severe abdominal pain, fever, or systemic symptoms, coupled with normal findings on pelvic ultrasound, helped rule out common secondary causes such as fibroids, polyps, or structural abnormalities.[4] Structural causes are more commonly encountered in older women, but in adolescents, these are less frequent, making primary causes—such as hormonal imbalances or coagulation disorders—more likely. This is consistent with findings from Munro et al., who suggest that while structural abnormalities are frequent in older women, they are less common in adolescents.[7] A thorough clinical history was instrumental in guiding the diagnostic process. Ms. Reshma's family history of heavy menstrual bleeding raised concerns about potential hereditary bleeding disorders, such as von Willebrand disease, which could predispose her to menorrhagia. This emphasizes the importance of a comprehensive family history, particularly when coagulopathies are suspected. While her laboratory findings confirmed mild anemia and low ferritin levels, ruling out other causes of bleeding through history and imaging allowed for a more focused diagnostic pathway.

Treatment Response and Clinical Management

Ms. Reshma's treatment regimen included both medical and educational interventions. After confirming iron deficiency anemia with laboratory testing, she was started on oral iron supplementation (Ferrous sulfate). Iron supplementation is crucial in correcting anemia and preventing complications such as cognitive impairment and reduced exercise tolerance, as noted by the World Health Organization (WHO, 2021). The positive clinical response to iron supplementation in Ms. Reshma underscores the importance of timely management in preventing long-term sequelae associated with untreated anemia. In parallel, hormonal therapy with combined oral contraceptives (COCs) was initiated to address the menorrhagia itself. COCs are a well-established treatment for adolescent menorrhagia as they help regulate menstrual cycles and reduce menstrual blood loss.[8] Ms. Reshma responded well to the combination of hormonal therapy and iron supplementation, with a significant improvement in her menstrual cycle and a reduction in her anemia-related symptoms, including dizziness and fatigue. The successful resolution of her symptoms after initiating these interventions aligns with previous research demonstrating that systematic follow-up care and individualized treatment plans significantly improve outcomes in adolescent patients with menorrhagia.[9] Regular follow-ups allowed for ongoing monitoring of hemoglobin levels, ensuring that Ms. Reshma's anemia was corrected, and also provided an opportunity to reassess the effectiveness of the hormonal therapy.

Patient Education and the Role of Awareness

Equally important in Ms. Reshma's management was patient education. Adolescents often lack awareness of what constitutes normal menstrual patterns, which can lead to delays in seeking medical help. Studies, including those by Kuhlmann & his group has shown that when patients are educated about their condition and the importance of adherence to treatment, they experience better outcomes. In Ms. Reshma's case, providing clear information about the nature of her condition, the role of iron supplementation, and the purpose of hormonal therapy was essential in ensuring that she adhered to her treatment plan.[10] Educating both patients and families about menstrual health is vital in reducing stigma and improving early intervention.[11]

The Role of Multidisciplinary Care

The case of Ms. Reshma also illustrates the need for a multidisciplinary approach to managing adolescent menorrhagia. While the primary focus of treatment in her case was medical—addressing both the anemia and excessive bleeding—a broader approach that includes psychological support, particularly in addressing the emotional distress caused by chronic menstrual problems, could further enhance the patient's overall well-being. Adolescents with menorrhagia often experience significant psychosocial strain, including anxiety and depression, which can affect their quality of life. Incorporating psychological counseling or support services into the treatment plan could provide additional benefits in this patient population.[12]

Conclusion

In summary, the case of Ms. Reshma highlights the clinical complexities involved in diagnosing and managing menorrhagia in adolescents. It underscores the significant physical and psychological burden of this condition, particularly when compounded by iron deficiency anemia. This case emphasizes the critical importance of a thorough and systematic approach to diagnosis, which includes detailed history-taking, appropriate diagnostic investigations, and the consideration of both primary and secondary causes of excessive bleeding. Ms. Reshma's successful management through a combination of hormonal

therapy and iron supplementation demonstrates the efficacy of targeted treatment in alleviating symptoms of menorrhagia and correcting anemia. However, this case also reveals that timely medical intervention alone is insufficient; patient education plays a pivotal role in empowering young women to recognize abnormal menstrual patterns and seek timely healthcare. The societal stigma surrounding menstrual health often delays intervention, making awareness and education essential components of management. The experience of Ms. Reshma emphasizes the need for healthcare providers to foster open, non-judgmental communication with adolescent patients, ensuring that they feel comfortable discussing menstrual health concerns. In this context, healthcare providers should receive targeted training to recognize and address adolescent menstrual disorders more effectively. Moreover, given the multi-factorial nature of menorrhagia, a multidisciplinary approach—integrating gynecological care, nutritional support, and psychological counseling—should be considered to address both the physiological and emotional aspects of this condition. This case also highlights broader implications for adolescent healthcare in regions where menorrhagia may be under-diagnosed or mismanaged due to cultural taboos and lack of awareness. Future research should focus on evaluating the long-term outcomes of various treatment approaches for adolescent menorrhagia and exploring strategies to overcome cultural and healthcare system barriers. By prioritizing both medical and educational interventions, we can improve the health and well-being of young women experiencing menorrhagia, ultimately leading to better long-term reproductive health outcomes.

Conflict of interest

The authors hereby declare that no conflict of interest exists.

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