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Personalized Medicine

Pradip Kumar Dutta^{1*}

Personalized medicine is an imminent practice of medicine. It uses an individual's genetic profile to guide decisions with regard to the prevention, diagnosis, and treatment of disease. It helps to make proper medication, appropriate dose and regimen for an individual patient by using genetic profile. Personalized medicine is being advanced through data from the Human Genome Project.¹ Its field is broad. It can be used for the diagnosis of various diseases like Cancers, Alzheimer, Hepatitis, Cardiac diseases, Autoimmune diseases, Brain tumours, Renal carcinomas and Prostate cancer etc.² Another name of personalized medicine is precision medicine. It is based on pharmacogenomics and genomics.³ It is a type of targeted treatment, It is an evolving field where physicians combine some diagnostic test with medical history of patients and develop targeted medicine for individual patient.⁴

Concept of Personalized Medicine:⁵

The '4 PS'

Personalised medicine is sometimes conceptualised as a '4P' model:

Predictive-determining the risk/susceptibility and treatment response

Preventive-allowing early intervention to prevent the disease altogether

Personalised - according to the genetic make-up of the person and their disease

Participatory-involving the patient in decisions on prevention or treatment

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The aim of personalised medicine is generally perceived to be the "right treatment for the right person at the right time".

Difference between Conventional Medicine and Personalized Medicine:

Conventional medicine deals with organ or system based approach, while personalized medicine is based on molecular mechanism. Precision medicine have various advantages over conventional medicine like optimum therapy required, increased safety and efficacy, decreased adverse drug reaction, enhanced patient compliance, reduced cost, time and clinical trials failure rate.²

Tools for Detecting, Diagnosis and Treatment of Disease⁵

i) 'Omics' Technologies:

Omics technologies define molecular mechanisms of the human body. Examples include 'genomics' (The study of genes and their function) 'glycomics' (The study of cellular carbohydrates) 'lipidomics' (The study of cellular lipids) 'metabolomics' (The study of molecules involved in cellular metabolism) 'pharmacogenomics' (The study of how genetic variations influence an individual's response to medicines) and 'proteomics' (The study of proteins). These analyses can provide information on the molecular and cellular processes of diseases. These technologies have mostly been used as research tools. Translating -omics into clinical applications enable a better understanding of human health and disease and plays a crucial role in diagnosis, treatment and prevention of illness.

ii) Biomarkers:

Biomarkers are measurable indicators of healthy and pathological processes in the body. They can belong to different types of biochemical molecules such as proteins, DNA, RNA or lipids. Also novel genetic biomarkers are continually being discovered. They can be used in different stages of disease. Some are 'diagnostic biomarkers' (To identify and diagnose

a disease as early as possible) some are ‘risk biomarkers’ (To detect a person's risk of developing a disease) some are ‘prognostic biomarkers’ (To detect evolution or progression of a disease) and still some are ‘predictive biomarkers’ (To assess the response to and toxicity of a treatment). In developing medicines, sub-dividing (‘Stratifying’) patients into groups according to their biomarker profile allows decisions on which medicines are best suited for a particular patient group. Single-Nucleotide Polymorphisms (SNPs) can act as biomarkers to help locate genes that confer an increased or decreased susceptibility to complex common diseases. To identify SNPs, researchers conduct genome-wide association studies. The large sets of information gained are stored into – ‘biobanks’ – so that they are available to researchers worldwide

Some examples of personalized medicine.^{2,5}

- i) In lung cancers monoclonal antibody or tyrosine kinase inhibitors are radiolabelled and injected and their targets of epithelial growth factor receptor or vascular endothelial growth factor receptor binding was detected by Positron Emission tomography (PET) scan
- ii) In rheumatoid arthritis TNF-alpha inhibitor application inhibiting interferon pathway is detected by gene expression.
- iii) In renal cancers different monoclonal antibody is applied as per biomarker expression.
- iv) Gene sequencing showing faulty gene (BRCA1) in a person may stimulate prophylactic operation (Like mastectomy or oophorectomy) to avoid cancers.

Accessibility of Personalized Medicine to Patients and Healthcare Professional⁵ :

Personalized medicine is patient centered. It involves informed consent and respects patient's decisions about health-related issues. So, patient should be pre-educated. They need to be 'empowered' to become participants in their own healthcare provision. The newer terminology is “Health literacy”. It is the ability of individual patient to access, understand, appraise and apply health information to make their own sound health decisions.

Appropriate education of healthcare professionals is considered key to the integration of personalized medicine into mainstream clinical care. A prerequisite is that healthcare professionals across disciplines (General practitioners, obstetricians, nurses, pharmacists etc) understand the role of -omics technologies and know how to use them in their day-to-day practice. They will need to be aware of the latest relevant diagnostic, prognostic and predictive tests, and how to interpret the data and use it as guidance for clinical decisions.

Challenges in Implementing Personalized Medicine:²

- i) Translational gap
- ii) Data protection, confidentiality and right to information
- iii) Regulatory clarity
- iv) Cost.

Precision medicine is now getting attention for its potentiality and uniqueness. The personalized medicine is based on the discovery of individual genes, which cause disease. Because of this exciting technique we can accurately apply the treatment with reduced amount of side effects. This is a cost-effective approach to develop new medicine by combining clinical, family history and genetic profile.²

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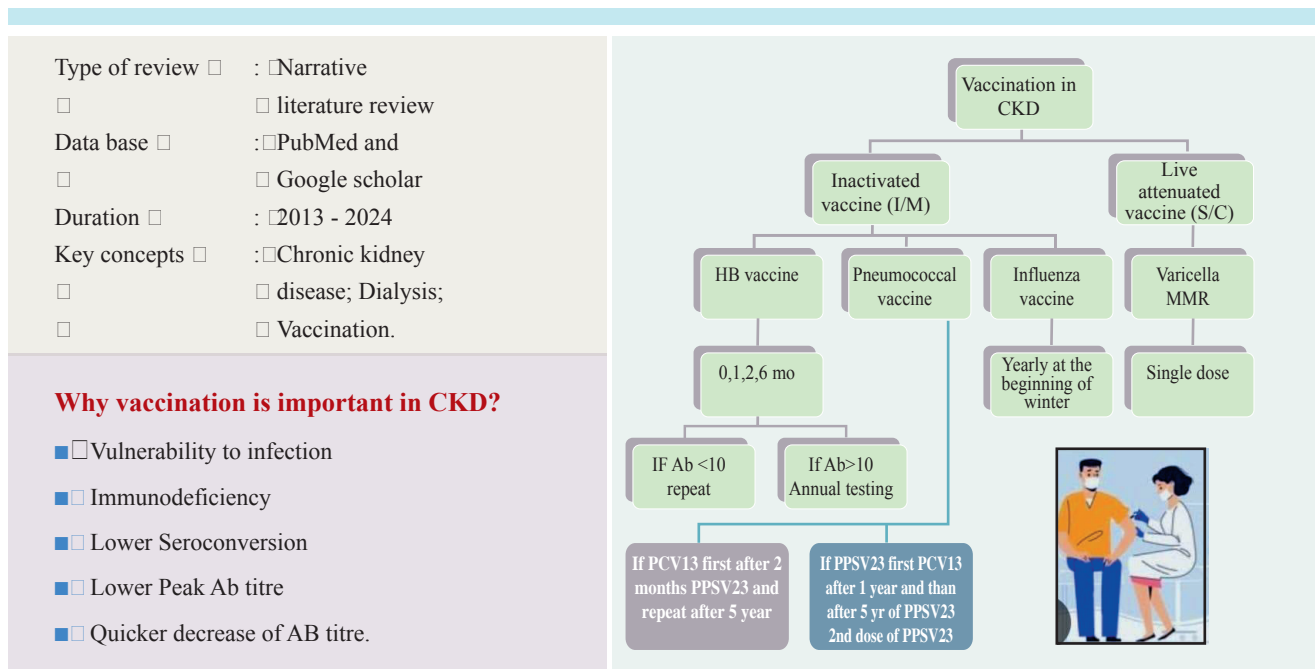
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Vaccination in Patients with Chronic Kidney Disease : An Overview

Dilip Kumar Roy^{1*}

GRAPHICAL ABSTRACT

Vaccination in Patients with Chronic Kidney Disease : An Overview



Conclusion: Early utilization, increasing Ag dose and appropriate frequency will ensure safety of vaccination in CKD.

Roy D K et al.

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ABSTRACT

Background: Infections are recognized as the most common cause of hospitalization and mortality in End-Stage Renal Disease (ESRD) patients. Vaccinations may reduce the incidence or morbidity of certain illnesses. Given their vulnerability to infection, effective vaccination strategies are of paramount importance to protect

patients with Chronic Kidney Disease (CKD). Because of the immune system deficiencies associated with CKD, seroconversion rates to vaccinations are lower, peak antibody titers are lower, and antibody levels decrease more quickly. Kidney Disease Improving Global Outcomes (KDIGO) recommend the Annual influenza vaccination in adults with CKD. Vaccination with polyvalent pneumococcus vaccine every 5 years unless contraindicated in CKD stages 4 and 5 and patients at high risk of pneumococcal infection and Immunization against Hepatitis B Virus (HBV) in adults with a progressive CKD having GFR <30 mL/min/1.73 m².

Methodology: The current study is a narrative review of published studies and articles by searching PubMed and

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Google Scholar with search strategy using appropriate keyword and titles.

Conclusion: The response of vaccination should be evaluated by an appropriate serological testing. The early utilization of vaccines in at-risk populations for CKD and increase antigen dose and frequency of vaccination in targeted patient populations has improved clinical outcomes by reducing many viral and bacterial infections in the CKD population.

Key words: Chronic kidney disease; Dialysis; Vaccinations.

INTRODUCTION

CKD is associated with premature ageing compared with the general population.¹ This accelerated ageing process leads to alterations in the immune system that predispose individuals to the subsequent development of infections, cancer, autoimmunity and cardiovascular disease.² Infections are recognized as the most common cause of hospitalization and mortality in ESRD patients.³ In fact, the incidence of the common infections [Urinary Tract Infections (UTIs)] pneumonia, sepsis) are three times greater among CKD patients who have not yet initiated dialysis than in the general population, whereas, dialysis patients have higher annual mortality rates caused by sepsis compared with the general population.⁴ Infection is the second leading cause of death in patients with CKD, and increases risk for cardiovascular events.⁴⁻⁷ Infections are more likely in persons with CKD, perhaps because of a compromised mucocutaneous barrier, infections of catheter insertion or dialysis catheters and in transplant recipients and different types of CKD the use of immune suppressive medicines. The effect of infections in CKD patients are increased hospitalizations for bacteremia and/or septicemia, increased risk for cardiovascular events and elevated incidence of bacterial pneumonia. In fact, the dysfunctional immune system of the late-stage CKD patients, with impaired innate and adaptive immunity, are at risk for many infections, some of which are vaccine preventable.^{8,9} Vaccinations may reduce the incidence or morbidity of certain illnesses. As a preventive measure, vaccination has saved more lives than any other medical intervention.^{10,11} The aim of the review is to discuss strategy of vaccination in Chronic Kidney Disease (CKD).

SEARCH STRATEGY

Available studies and abstract were identified through PubMed and Google scholar. The key search concepts were "Chronic kidney disease; Dialysis; Vaccinations". Seventy five (75) articles were founded. Filter was applied and relevant articles from the reference lists of the reviewed articles from 2013 to 2024 were sought out.

DISCUSSION

Impaired Immune Response in CKD Patients

In CKD population B lymphocyte and CD4+ T lymphocyte are decreased as well as there is decreased T-cell response to antigenic stimuli. Moreover Immunoglobulin G synthesis is lowered in response to vaccination, although total antibody productions is not affected.¹² Several studies have discussed the potential link between endothelial dysfunction and impaired immune function.¹³⁻¹⁵ Uremic toxins, oxidative stress, endothelial dysfunction, low-grade inflammation as well as mineral and bone disorders all are involved and may contribute to the impaired immune system in these patients.

Vaccine Response in Chronic Kidney Disease

Patients with ESRD have a reduced response to vaccination due to immune dysregulation.¹⁶ Compared with vaccinated patients without ESRD, for example, patients on dialysis have a lower antibody titer and an inability to maintain adequate antibody titers over time.^{17,18} A number of studies have shown lower rates of seroconversion following pneumococcal immunization in individuals with CKD, with some research reporting differing rate for the dialysis, pre dialysis, including transplant patients. When compared to patients with CKD or nephrotic syndrome, individuals who had had a transplant or were on dialysis had a 41% lower chance of maintaining protective antibody levels after one year. Only 52% of individuals who had lost protective antibody levels responded to revaccination with a substantial immunological response, which then faded after 6 months.¹⁹ The relatively low antibody response to vaccination also appears to correlate with the degree of kidney failure but not with the specific mode of dialysis.²⁰ Among patients with CKD, including those with kidney failure, the number of vaccination non-responders is considerable, which has led to adjustments in their vaccination regimens, especially for vaccines against Hepatitis B Virus (HBV) or the H1N1 influenza A virus subtype.¹¹

Vaccination Benefits in Chronic Kidney Disease

The flu vaccination seems to be linked to a decreased risk of hospitalization or fatality in patients.²¹ Pneumococcal immunization is only moderately effective in individuals with CKD. Booster dose of the pneumococcal immunizations administered to dialysis or pre dialysis CKD patients essentially prevented pneumococcal infections throughout a two-year follow-up period. Vaccines are important to help prevent serious diseases in CKD, those on dialysis, and immunocompromised people, such as Kidney Transplant (KT) recipients. The goal of vaccination is to increase chances of fighting off that infection quickly.

Vaccination in CKD: General Considerations

The Centers for Disease Control and Prevention (CDC) guidelines for vaccination in CKD summarized in the recommendations of the Advisory Committee on Immunization Practices (ACIP) which recommend for all adults the diphtheria/tetanus, the annual inactivated influenza vaccine, the Measles/Mumps/Rubella (MMR) and the varicella vaccine if not contraindicated. In CKD and dialysis, it adds the hepatitis B vaccine in adapted dose as well as the pneumococcal vaccine.²² Moreover, KDIGO recommend the following guidelines in CKD patients.²³ i) Annual influenza vaccination in adults with CKD ii) Vaccination with polyvalent pneumococcus vaccine every 5 years unless contraindicated in CKD stages 4 and 5 and patients at high risk of pneumococcal infection iii) Immunization against hepatitis B in adults with a progressive CKD and have GFR <30 mL/min/1.73 m². American guidelines of vaccination in adult solid organ transplantation updated by the American Society of Transplantation (AST) and the Infectious Disease Society of America in 2013 recommended vaccination during pre and post transplant workup.^{24,25}

Hepatitis B vaccine

Patients with CKD and ESRD are at increased risk of infection with HBV. Analysis of the Dialysis Outcomes and Practice Patterns Study (DOPPS) revealed an overall prevalence of 3.3%, ranging from a low of 0% in the UK and a high of 6.6% in Italy.²⁵ This is compared to < 2% of the general population of North America and Western Europe.^{26,27} The increased exposure to blood products coupled to impairment of both innate and adaptive immunity contributes to acute infection and fulminant hepatic disease, with up to 80%

progressing to chronic carrier state.²⁸ With strict infection control measures and HBV vaccination, the rates of hepatitis B infection in dialysis patients have declined dramatically.²⁹

ESRD patients have a reduced response to HBV vaccination. Only 50 to 60 percent of ESRD patients develop antibodies following HBV vaccination.^{30,31} HBsAg-specific Th cells were detected in 50% of patients without evidence of humoral immunity (HBsAg-antibody), suggesting protection even without seroconversion.³² Numerous guidelines recommend hepatitis B vaccination of patients with CKD, including dialysis, hemodialysis, peritoneal dialysis and home dialysis patients.^{33,34}

Hepatitis B (HB) vaccine has been available since 1982.³⁵ The most recently recommended vaccine is HepB-CpG, which is prepared by combining purified recombinant hepatitis B surface antigen with small synthetic immunostimulatory Cytidine-phosphate-Guanosine Oligodeoxynucleotide (CpG-ODN) motifs (1018 adjuvant). This 1018 adjuvant binds to Toll-like receptor 9, which in turn stimulates a directed immune response to hepatitis B surface antigen.³⁶ In a study of almost 500 hemodialysis patients, 3 doses of HepB-CpG induced significantly higher seroprotection, earlier seroprotection, and more durable seroprotection than 4 double doses of Engerix-B; it has a similar safety profile and was generally well tolerated.³⁷

Because of the generally low response rate among patients with ESRD, the following strategies i) Doubling the dose of vaccine.³⁸ ii) Giving an HBV vaccine that uses a novel immunostimulatory adjuvant.^{39,40} iii) Beginning the vaccination series as soon as CKD is recognized and the patient is known to be HbsAg and antibody negative.²⁰ iv) Administering an additional vaccine series to patients on dialysis with antibody titers ≤10 international units/L one to two months after completion of the first series.¹⁸ v) For patients on HD, the need for booster doses should be guided by annual testing of the anti-HB levels have been used.^{33,41-43} A European Consensus group on hepatitis B immunity recommends for immunocompromised patients a regular testing for anti- HBs, and a single booster dose when the titer is inferior to 10 mIU/mL⁴¹⁻⁴³. There appears to be no benefit to repeated boosters in those whose antibody titers remain ≤10 international units/L. Administering a single booster dose if the antibody titer falls to ≤10 international units/L in the patient who initially developed an antibody response to vaccination or after natural infection.^{44,45}

Currently, recommendations for adults (Table I) on dialysis are either 40 µg of Recombivax administered at 0, 1 and 6 months or Engerix-B administered at 0, 1, 2 and 6 months.⁴⁶⁻⁴⁹ Vaccine should be given intramuscular in deltoid regions. HBV-antibody titer should be assessed 1 to 2 months after the final dose. If the latter is <10 mIU/mL, repeating the entire dosing series is suggested with an evaluation of the antibody response in 1 to 4 months. The HB vaccine has been confirmed to be safe, and there is no evidence indicating it causes any complications or side effects.⁴¹

Table I Dosing schedule for hepatitis B immunizations in adult patients with kidney disease

Vaccine	Dose	Schedule	
Engerix B	High Dose	0, 1, 2 and 6 months	● High dose Vaccine recommended in advanced kidney disease and for patients on maintenance hemodialysis
Recombivax	40 µg	month	● Optimal dosing in early kidney disease not well defined
HB			● Titers should be checked to ensure appropriate response.
Heplisav	Slandered dose	0 and 1 month	● To date there is no specific recommendations for Heplisav in patients with ESKD or earlier stages of kidney disease.
			● So, dosing is extrapolated from general guidelines.

Vaccines for influenza

Influenza vaccination has clear health benefits in ESRD.⁵⁰ Analysis of antibody response suggests the majority of dialysis patients achieve protective antibody titers and repeated seasonal vaccination may enhance protection.⁵¹⁻⁵⁵ Suga et al. described that patients with CKD were able to respond to the available influenza vaccine, however, the response was suboptimal.⁵⁶

Observational studies of patients on dialysis have reported that a high-dose influenza vaccine is associated with a more sustained antibody response and a lower hospitalization rate compared with a standard-dose vaccine.^{57,58} However, another study failed to establish the benefit of Vaccination.^{58,59} CDC recommends a single 0.5mL dose of inactivated influenza vaccination for all patients with renal dysfunction and close contacts.⁶⁰ Influenza vaccine should be given annually before the beginning of the

influenza season for persons 6 months of age or older on dialysis. After the age of 12 years, one dose of whole or split virus vaccine should be given.⁶¹ Noteworthy, that live-attenuated influenza vaccine is contraindicated in high-risk conditions such as kidney transplant recipients and has not been tested in CKD, ESRD, or in organ transplantation.^{62, 63, 64}

Table II Dosing schedule for Influenza (flu) in adult patients with kidney disease⁶⁵

Vaccine	CKD stage 3-4	CKD stage -5, ESKD	Booster
Influenza (flu) - Inactivated	0.5 mL IM or SC annually in October	0.5 mL IM or SC annually in October	Not proven to be generally necessary. Cumulative effect over several flu seasons may be present.

Pneumococcal Vaccines

Streptococcus pneumoniae is the most commonly identified bacterial cause among dialysis patients, and in renal transplant recipients with community-acquired pneumonia.^{66,67} Mortality from infectious complications are 14 -16 fold higher for dialysis patients following pneumonia, compared with the general population.⁴ Vaccination against pneumococcal disease is associated with decreased mortality among patients with ESRD.⁶⁸

The Advisory Committee on Immunization Practices (ACIP) guidelines recommend (Table III) that CKD and KT patients aged 19 years or older, should receive PCV13 followed by PPSV23 (At least 8 weeks later).⁶⁹

Table III Dosing schedule for pneumococcal immunization in adult patients with kidney disease⁷⁰

Initial Vaccine	Subsequent Vaccination needs
PCV13	8+ week later give PPSV23, then 5 years later give a second dose of PPSV23
PPSV23	1 year later give PCV 13 and 5 year after initial PPSV23 vaccine give second dose of PPSV23
Either (Previously vaccinated with PPSV23 or first dose given is PPSV 23)	All patients should get an additional PPSV23 vaccine at age 65 years if initial vaccine series started before age 65.

Evidence is limited on the immunogenicity of the pneumococcal vaccines in CKD and HD patients. Over time, anti-pneumococcal antibody wanes in end-stage renal disease patients following both PPSV23 and PCV13 administration.⁷¹ In PPSV23 patients, PCV13 elicited significantly higher antibody levels compared to PPSV23.⁷² PCV13 has shown immunogenicity in KT recipients⁷³. The study also confirmed the safety of the PCV13, with no evidence of de novo anti human leukocyte antigen antibodies, no biopsy-proven rejection, and no reported cases of invasive pneumococcal infection.⁷³ In another study of KT recipients (n = 49) administered PPSV23, the anti-pneumococcal antibody response at 15 months was 77% of the response at 1-month post vaccination.⁷⁴

Varicella and Zoster Vaccines

CKD patients are more likely to develop shingles. In Taiwan, a retrospective cohort study of the national health insurance register database showed that KT recipients had the highest risk of zoster followed by those on peritoneal dialysis.⁷⁵ Among patients on dialysis, a zoster infection is associated with a higher mortality and administration of the zoster vaccine is associated with a lower risk of developing zoster when compared with unvaccinated controls.^{76,77}

As per recommendations of the ACIP patients with ESRD who are ≥50 years old should receive the Recombinant (Non-live) Zoster Vaccine (RZV).²⁹ The live viral vaccine should not be used in KT recipients.⁷⁸ Kidney patients non-immune to varicella and not on active immunosuppression, should be given two doses of vaccine 4–8 weeks apart, or a second dose if they previously received only 1 dose. Vaccine should be avoided in patients with blood dyscrasias, hematologic and lymphatic malignancies; primary or acquired immunodeficiencies, cellular immunodeficiencies, hypogammaglobulinemia; on high-dose systemic immunosuppressive therapy and on oral steroids.^{79,80}

Timing of Vaccination

Patients with ESRD either KT candidates, or not the vaccines should be administered as early as possible provided that a minimum time interval is maintained between vaccination and subsequent transplantation. For inactivated vaccines, vaccination should be completed at least two weeks prior to transplant. For live vaccines (e.g. MMR vaccine) vaccination should be completed at least four weeks prior to transplant and is generally contraindicated post transplantation when patients are immunosuppressed.⁸⁰

CONCLUSION

Over the past 10 years there has been a steady improvement in understanding human immunologic response to vaccination. The early utilization of vaccines in at-risk populations for CKD and increase antigen dose and frequency of vaccination in targeted patient populations has improved clinical outcomes by reducing many viral and bacterial infections in the CKD population. Clinicians should be encouraged to review vaccination status as part of routine office visits, either directly by the clinician, or by other providers or staff in the office. Patients should be aware of the extensive safety of vaccines and the risks of vaccine-preventable illness, including the negative impact on their kidney function. Given the growing amount of data that immunizations are beneficial, quality improvement strategies aimed at increasing vaccination rates for patients including all stages of the infection are critical.

DISCLOSURE

The author declared no conflicts of interest.

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



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Bacteriological Profile and Antibiotic Susceptibility Pattern of Uropathogens Causing Urinary Tract Infection: A Cross-Sectional Study from a Tertiary Care Hospital, Chattogram, Bangladesh

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GRAPHICAL ABSTRACT

Bacteriological Profile and Antibiotic Susceptibility Pattern of Uropathogens Causing Urinary Tract Infection: A Cross-Sectional Study from a Tertiary Care Hospital, Chattogram, Bangladesh

Cohort		Results			
Study design : Cross sectional study		Pathogen	E. Coli (n=41)	Klebsiella (n=25)	Pseudomonas (n=16)
Sample Size - 270		Antibiotics	S (%)	S (%)	S (%)
Male - 98 (36.30%)		Amoxicillin / Clavulanic Acid	36.21	11.54	NT
Female - 172 (63.70%)		Cefixime	29.21	19.23	NT
Age (Years) 18-85		Ceftriaxone	37.93	30.77	NT
Types of Pathogens		Amikacin	84.48	65.38	60.00
E. Coli 43.16%		Ciprofloxacin	17.24	19.23	0.00
Klebsiella 26.32%		Nitrofurantoin	75.52	69.28	73.05
Pseudomonas 16.84%		Meropenem	53	58	45
Others 13.68%		Levofloxacin	NT	NT	NT
		Age in years	Culture positive (n=95)	Percentage	Sex
		18-49	44	46.316%	Male 98
		≥50	51	53.684%	Female 172
					Sample (n)
					32 (32.65%)
					63 (36.63%)
					p value
					p = .028
		Attack Rate for Male to Female is 1:1.76 			

Conclusion: E. Coli is the commonest pathogen in UTI. Female patients are more culture positive than male patients. E. Coli, Klebsiella and Pseudomonas are more sensitive to Amikacin and Nitrofurantoin than Meropenem.

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ABSTRACT

Background: Urinary Tract Infection (UTI) is an infection in any part of the urinary system. It is one of the main health issues that impact people of all ages and both sexes. UTI that is caused by antibiotic-resistant bacteria can make the treatment difficult and can lead to complications. This study was conducted to find out the prevalence of pathogens causing UTI and their antibiotic susceptibility pattern.

Materials and methods: This cross sectional study was carried out at the Department of Microbiology, Marine City Medical College and Bangabandhu Memorial Hospital from July 2022 to December 2022. A total of

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270 patients with typical symptoms of UTI (Triad of urgency, frequency and dysuria) were selected by purposive sampling. Patients on any antibiotic medication or did not give consent were excluded from the study. A clean catch Mid-Stream Urine (MSU) sample was taken in a sterile, wide-mouthed container following the appropriate instructions and informed consent from the patients. All the samples were brought to the microbiology lab and processed for analysis.

Results: In this study, out of 270 cases 98 (36.30 %) were male and 172 (63.70 %) were female with a male to female ratio of 1:1.76. Rate of isolation of uropathogens in male and female was 32.65% and 36.63 %, respectively. This study shows that 35% of isolates were culture positive and 65% were culture negative. Most frequent female pathogen was *E. coli* (n=32), and male pathogen was *Klebsiella* (n=15). Moreover, isolated organisms were found mostly diabetic patients (26.32%), followed by unknown causes in 16.84% patients. *E. coli* and *Klebsiella* showed sensitivity to Gentamicin, Nitrofurantoin and Meropenem that is (89%), (73%), (75.52%), (69.28%), (53%) and (58%) and showed less sensitive to 3rd generation Cephalosporin. *E. coli* was highly resistant to 3rd generation cephalosporin- Ceftazidime (73%), followed by ciprofloxacin (74%), Cefepime (68%), Cefixime (67%), Amoxicillin-clavulanic acid (60%) and Piperacillin-Tazobactam (57%). Nitrofurantoin shows less resistant (10%). *Klebsiella* shows most resistance to 3rd generation Cephalosporin. *Pseudomonas* showed 100% resistance to Ciprofloxacin and Levofloxacin.

Conclusion: *E. Coli* is the commonest pathogen in UTI and there is difference between male and female subjects with regards to positive culture. *E. Coli*, *Klebsiella* and *Pseudomonas* are more sensitive to Amikacin and Nitrofurantoin than Meropenem.

Key words: Antibiotic Susceptibility; Bacteriological Profile; Urinary tract infection.

INTRODUCTION

The term urinary Tract Infection (UTI) refers to the existence and ongoing growth of germs in the urinary tract. Women are more likely than men to get a UTI, primarily because of their shorter urethra, lack of prostatic secretion, pregnancy and ease of fecal flora infection of the urinary system.¹ The infection is common in the community and hospital. It is estimated that about 150 million cases of UTI occur each year in the world.² At the age of 24 years, about one in three women will have experienced at least one UTI episode

that required antibiotic therapy.³ Gram-negative bacteria were identified from 75–95% of cases of uncomplicated UTIs, which are most common in young, sexually active, non-pregnant, premenopausal women.⁴ These bacteria included *E. coli*, *Proteus*, *Klebsiella*, *Pseudomonas*, *Acinetobacter*, *Serratia* and *Morganellamorgagniae*. Gram-positive bacteria such as *Enterococcus*, *Staphylococcus* particularly coagulase negative staphylococci, *Streptococcus agalactiae* and other less commonly isolated organisms are linked to the remaining instances.⁵ The majority of UTIs are caused by *E. coli*.⁶

The distribution of UTI-causing bacteria antibiotic susceptibility data varies with time and geographically.⁷ Since the introduction of UTI chemotherapy, the number of bacteria producing UTIs that are resistant to drugs has grown.⁸ As a requirement for any hospital infection control program, the Infectious Disease Society of America advises doctors to stay up to date on the local susceptibility pattern of organisms causing urinary tract infections and to track changes in their susceptibility.⁹ Empirical treatment, on the other hand, limits the ability to monitor antibiotic response and predisposes uropathogens that cause UTI to resistance.^{10,11} Despite their use as practical methods for efficient resource use, empirical management plans must be regularly updated to account for shifting pathogen susceptibility patterns. This is particularly true for developing nations, where the lack of resources for routine antibiotic sensitivity tests compounds an additional challenge.¹¹

In recent years, the resistance of uropathogens to previously effective antibiotics has become a global phenomenon.¹²⁻¹⁴ Antimicrobial Resistance (AMR) is currently estimated to account for more than 700,000 deaths per year worldwide. If no appropriate measures are taken to halt its progress, it is projected to cost approximately 10 million lives and about US \$100 trillion per year by 2050.¹⁵ In contrast to other health issues, AMR is a problem that concerns every country, irrespective of its level of income and development. According to the WHO report from 2014, Africa and South-East Asia are the regions with no established AMR surveillance systems.¹⁶

It is essential to have up-to-date, locally based information of the microorganisms causing UTIs and their antibiotic susceptibility testing to provide optimal therapy.¹⁷ However, we think that the prescribed medicines may be significantly resistant to antibiotics;

hence, if these medications are prolonged empirically, the chance of treatment failure increases. Thus, the study's objectives were to evaluate antibiotic resistance to other medications as well as recommended therapies and to spot patterns of resistance to a variety of potentially beneficial substitutes for the treatment of UTIs in this tertiary hospital, Chattogram.

MATERIALS AND METHODS

This cross sectional study was carried out at the Department of Microbiology, Marine City Medical College (MCMC) and Bangabandhu Memorial Hospital (BBMH) from July to December 2022. A total of 270 patients with typical symptoms of UTI (triad of urgency, frequency and dysuria) were selected by purposive sampling. Patients on any antibiotic medication or did not give consent were excluded from the study. A clean catch Mid-Stream Urine (MSU) sample was taken in a sterile, wide-mouthed container following the appropriate instructions and informed consent from the patients. All the samples were brought to the microbiology lab and processed. The colour and turbidity of the urine were inspected macroscopically and the amount of pus cells, bacteria and budding yeast cells were counted on a wet mount. To culture, the samples were inoculated onto Blood, Mac Conkey agar and Chromogenic UTI agar then incubated for 18-24 hours at 37°C. In the culture plates, growth greater than 10⁵ cfu/ml was regarded as positive. According to conventional operating procedures, colony morphology, motility and biochemical assays were used for additional identification and confirmation.¹⁸

Antibiotic susceptibility testing followed the Clinical Laboratory Standards Institute (CLSI 2022) criteria, antibiotic susceptibility testing was performed on Muller Hinton Agar using Kirby Bauer's disc diffusion method. After choosing and inoculating identical bacterial colonies into peptone water broth, the mixture was cultured for two hours at 37°C. Using a sterile swab, the test organism was scattered onto a Muller Hinton agar plate after being adjusted to 0.5 McFarlands standard.

Gram negative organisms were treated with Amikacin (30µg), Gentamicin (10µg), Cefotaxime (30µg), Cotrimoxazole (25µ), Norfloxacin (10µ), Levofloxacin

(5µ), Ampicillin (10µg), Cefepime (30µg), Nalidixic acid (30µg), Nitrofurantoin (300µg), Imipenem (10µg) and Piperacillin-Tazobactam (10µg/100µg). Furthermore, for gram-positive organisms, 30µg of Cefoxitin, 30µg of Linezolid, 120µg of high-level Gentamicin, and 30µg of Vancomycin were utilized. *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC 25923 are used as the strains of quality control.¹⁹

All the data was processed and analyzed using Microsoft Excel for Windows. The summarized data were presented in the form of tables and figures. The ethical clearance was obtained from the proper authorities before commence the study.

RESULTS

In this study, out of 270 cases 98 (36.30 %) were male and 172 (63.70 %) were female with a male to female ratio of 1:1.76. Rate of isolation of uropathogens in male and female was 32.65% and 36.63 %, respectively (Table I). This study shows that 35% of isolates were culture positive and 65% were culture negative. The age range was 18 to >80 years. Among 95 growth positive patients, most affected age group was 40-59 (Male 8, female 16) years. Most frequent female pathogen was *E. coli* (n=32) and male pathogen was *Klebsiella* (n=15). *E. coli* was the predominant isolate 41 (43.16 %), followed by *Klebsiella* 25 (26.32 %). *E. coli* and *Klebsiella* were sensitive to Gentamicin, Nitrofurantoin and Meropenem that is (89%), (73%), (75.52%), (69.28%), (53%) and (58%) and showed less sensitive to 3rd generation Cephalosporin (Table IV).

Table I Gender distribution for rate of isolation in urine culture (n = 270)

Sex	Sample (n)	Growth of Uropathogen, n (%)	No Growth of Uropathogen, n (%)
Male	98	32 (32.65)	66(67.35)
Female	172	63(36.63)	109(63.37)
Total	270	95(35.19)	175(64.81)

Table II Age and sex distribution of 95 culture positive patients with frequency of bacterial pathogen according to age (n=95)

Variables	E. Coli (n=41)		Enterococci (n=9)		Klebsiella (n=25)		Pseudomonas spp. (n=16)		S. saprophyticus (n=2)		S. Aureus (n=2)	
	43.16%		9.47%		26.32%		16.84%		2.11%		2.11%	
Sex (M/F)	M	F	M	F	M	F	M	F	M	F	M	F
18-29 (5/7)	1	3	1	1	4	1	1	1	-	-	-	-
30-39 (3/5)	1	2	-	1	1	1	1	1	-	-	-	1
40-49 (8/16)	3	6	1	-	5	1	1	4	-	-	-	1
50-59 (5/17)	1	10	1	-	1	5	1	1	-	1	-	-
60-69 (3/5)	1	2	1	1	1	1	-	1	-	-	-	-
70-79 (4/10)	2	7	1	-	1	-	1	1	-	-	-	-
>80 (4/3)	1	1	1	-	2	1	1	1	-	1	-	-
Total (95)	10	31	6	3	15	10	6	10	-	2	-	2

Table III Common risk factors found in UTI patients (n=95)

Risk Factor	Frequency (%)
Diabetes	25(26.32)
Pregnancy	14(14.74)
Neurological	9(9.47)
Post Menopausal	10(10.53)
Presence of Catheter	10(10.53)
History of Previous UTI	11(11.58)
Unknown	16(16.84)

Table IV Antibiotics sensitivity and resistance pattern of the most prevalent bacteria

Pathogen	E. Coli (n=41)		Klebsiella (n=25)		Pseudomonas (n=16)	
Antibiotics	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)
Amoxicillin/Clavulanic Acid	36.21	60.34	11.54	80.77	NT	NT
Piperacillin/Tazobactam	15.52	57.09	19.23	66.92	60.00	25.36
Cefixime	29.31	67.24	19.23	80.77	NT	NT
Ceftazidime	37.93	73.45	15.38	79.23	40.00	58
Ceftriaxone	37.93	61.72	30.77	61.54	NT	NT
Amikacin	84.48	12.07	65.38	30.77	60.00	40
Gentamicin	89.66	8.62	73.08	19.23	40.00	6
Nalidixic Acid	32.76	67.24	42.31	57.69	NT	NT
Ciprofloxacin	17.24	74.14	19.23	73.08	0.00	100
Nitrofurantoin	75.52	10.34	69.28	15.08	73.05	22.34
Trimethoprim/Sulfamethoxazole	37.93	48.28	34.62	38.46	NT	NT
Cefepime	15.03	68	18.20	71	40.00	54
Meropenem	53	35	58	37	45	51
Levofloxacin	NT	NT	NT	NT	NT	100
Aztreonam	NT	NT	NT	NT	NT	34

* NT= Not Tested.

DISCUSSION

UTI is emerging as an important community acquired and nosocomial bacterial infection. Moreover, antimicrobial resistance became a major health problem in different parts of the world.^{20,21} Among the 270 UTI patients 98 (36.30%) were male and 172 (63.70%) were female with male-female ratio 1:1.76. Paudel L et al. showed in their study that 79% female and 21% male were affected by UTI.²² High prevalence of UTI among female population may be due to short and wide urethra and proximity to anus that makes easy for bacteria to ascend in the urinary tract and decrease of normal vaginal flora (Lactobacilli).²³

The age range of the participants in my study was 18 to >80 years, with women in the 40–49 age group making up 25.26% of the sample. It closely resembles a study done in Bangladesh that found women in the 40–45 age range are most likely to experience UTI.^{22,24} In many developing and underdeveloped nations, including Bangladesh, antibiotics like ciprofloxacin, cephradine, nalidixic acid, amoxicillin, and cotrimoxazole are still used to treat gram-positive and gram-negative bacterial infections, including UTIs. Ciprofloxacin was formerly thought to be the best medication for both simple and complex UTIs, but because it has not been used wisely, this broad-spectrum antibiotic has completely lost its effectiveness against UTIs and other common illnesses. A similar situation with cephalosporins of the first, second, and third generations is also observed.

It is conceivable that a small number of ESBL-producing uropathogens, particularly from Gram-

negative isolates that were too small to be isolated for our analysis, may have contributed to resistance to various cephalosporin generations. In the current environment, nitrofurantoin was found to be a moderately high effective agent among all antimicrobials used to practically all uropathogens, and other investigations have showed comparable results.²⁵⁻²⁶

Twenty-five (26.32%) of the patients in our study had diabetes and several of them also had recurrent UTIs. A similar study was conducted in the Saudi Arabia and showed the overall prevalence of UTIs in diabetic patients was 25.3%.²⁷ Another important risk factor for UTI is pregnancy and in our study, it was 14.74%. A study showed that UTI among pregnant women was 15.37% which is similar to our study.²⁸ Most hospital acquired UTIs are associated with urinary catheters, a commonly used device among hospitalized patients. We found 10 (10.53%) cases are due to catheter associated UTI. The overall incidence of symptomatic catheter induced UTI was 16.8%.²⁹

There is a large group 16 (16.84%) in where we could not find out any identifiable risk factor. A total of 6 types of bacterial pathogens were isolated from urine culture. *Escherichia coli* 41 (43.16%) was the most common bacterial pathogen in both symptomatic and asymptomatic groups. Other pathogens were *Klebsiella* 25 (26.32%) and *S. aureus* and *S. saprophyticus* 2 (2.11%), *Pseudomonas* 16 (16.84%), *Enterococcus* 9 (9.47%). So, gram negative bacilli were 86% of total uropathogens and the remaining 14% were gram positive organisms including *S. aureus* and *Enterococcus*. Our study was similar to the study from Dhaka Medical college, they also found 88%-gram negative bacilli and 12%-gram positive organisms.³⁰

In our study *E. coli* was highly resistant to 3rd generation Nitrofurantoin shows less resistant only 10%. *Klebsiella* shows most resistance to 3rd generation Cephalosporin. *Pseudomonas* showed 100% resistance to Ciprofloxacin and Levofloxacin. This study found similarity with a study from Rajshahi, Bangladesh.³¹

This is great news because most of the relatively less expensive oral UTI treatments are becoming less and less effective, which is especially helpful for prevention of minor UTIs. Like nitrofurantoin, gentamicin and ceftriaxone was also found to have moderate to high susceptibility to most uropathogens, however, one must remember that their utilization is restricted due to the parenteral route and patient noncompliance.

LIMITATIONS

The present study had certain limitations like limited sample size, brief study duration, conducted in single center and was no comparison group.

CONCLUSION

E. Coli is the commonest pathogen in UTI and there is significant difference between male and female subjects with regards to positive culture. *E. Coli*, *Klebsiella* and *Pseudomonas* are more sensitive to Amikacin and Nitrofurantoin than Meropenem.

RECOMMENDATION

Every institute should have a different Antibigram to start the empirical treatment.

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AUTHORS CONTRIBUTIONS

Conception and design - SA

Data Collection - SA, SK, AAK, TK

Analysis and interpretation of data - SA, FFBH

Manuscript preparation - SA, SK, AAK, TK, FFBH

DISCLOSURE

All the authors declared no conflicts of interest.

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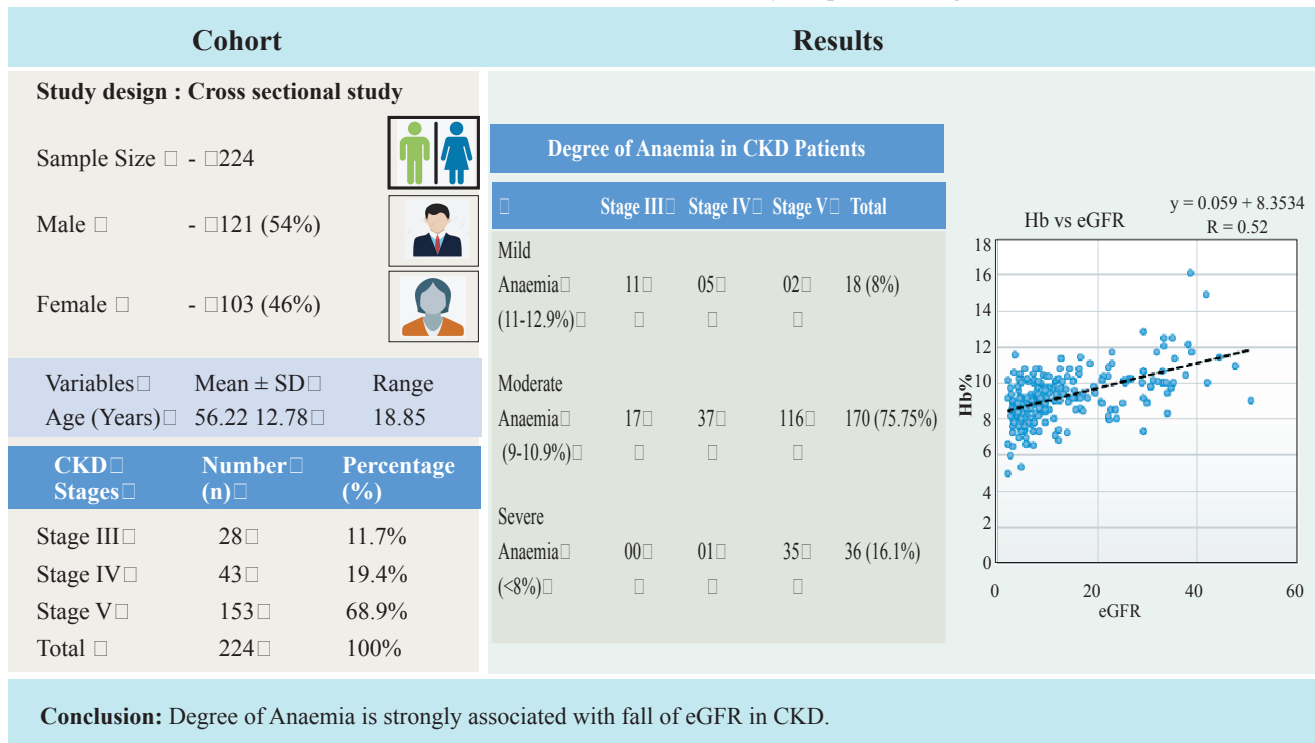
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Association of Anemia with CKD: A Cross Sectional Study in a Tertiary Hospital, Chattogram

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GRAPHICAL ABSTRACT

Association of Anemia with CKD: A Cross Sectional Study in a Tertiary Hospital, Chattogram



Hussain F et al.

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ABSTRACT

Background: Chronic Kidney Disease (CKD) is a worldwide public health problem. Major outcomes of CKD include progression of CKD to End Stage Renal

Disease (ESRD) development of different complication due to impaired kidney function and increased risk for development of Cardiovascular Disease (CVD). One of the common complications of CKD is the anemia which is associated with increased risk for CVD, increased morbidity and mortality especially in high risk group. Anemia is one of the nontraditional risk factor for CVD. The purpose of this study is to find out an association of anemia with CKD.

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Materials and methods: A cross-sectional study was conducted in the Department of Biochemistry in collaboration with Department of Nephrology, Marine City Medical College and Hospital (MCMCH). Two hundred and twenty four (224) subjects aging above 18

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years were included in this study by purposive sampling method. The study group was divided into three different groups according to the different stages of CKD as stage 3 (eGFR=30-59 ml/min/1.73m²) stage 4 (eGFR=15-29 ml/min/1.73m²) and stage 5 (eGFR <15 ml/min/1.73m²). Important variables in this study were serum Hemoglobin, serum creatinine and eGFR. eGFR was calculated by Cockcroft and Gault equation $eGFR = (140 - \text{Age in years}) \times \text{Weight (Kg)} \times [0.85 \text{ if female}] / 72 \times [\text{Serum Creatinine (mg/dL)}]$.

Results: This study showed a positive significant correlation between eGFR and Hb% in the study cases. ANOVA test was done to show the distribution of eGFR in three stages of CKD with mean and the differences were statistically significant ($F = 775.05, p < 0.00001$).

Conclusion: The current study established that the degree of Anaemia is strongly associated with fall of eGFR in CKD.

Key words: Anemia; Chronic Kidney Disease (CKD); Cardiovascular Disease (CVD); Diabetes Mellitus (DM); End Stage Renal Disease (ESRD); Erythropoietin.

INTRODUCTION

Chronic kidney disease is a worldwide public health problem. Major outcomes of CKD include progression of CKD to End Stage Renal Disease (ESRD) development of different complication due to impaired kidney function and increased risk for development of Cardiovascular Disease (CVD).¹ One of the common complications of CKD is the anemia which is associated with increased risk for Cardiovascular Disease (CVD) increased morbidity and mortality especially in high risk group.² Anemia is one of the nontraditional risk factor for CVD.³ Development of anemia in CKD is basically due to complete or relative deficiency of erythropoietin. Besides erythropoietin deficiency, different factors including blood loss, decreased half-life of red blood cells, iron deficiency, inflammation etc. may contribute to develop anemia in CKD.⁴ Some studies reported that Hb-level start to decrease even in early renal deficiency around 70 ml/min in male and 50 ml/min in female.⁵ Furthermore, anemia in CKD aggravates the adverse outcomes in CKD and worsens the comorbidities of diabetes and hypertension.³ Early identification of anemia in CKD retards the development of end stage renal disease and consequently improves from CVD morbidity and mortality.⁶ CVD is the leading cause of mortality in

patients having CKD and accounts of 58% patients dies from CVD in CKD.⁷ Even mild form of renal insufficiency has been reported to be linked with increased incidence of CVD. Incidence of mortality due to CVD in CKD patients has 10 to 20 times higher when compared with general population.^{8,9} Thus we had undertaken this study to find out the association of anemia in patients with different stages of CKD in hospital based setting.

MATERIALS AND METHODS

A cross sectional study of Two hundred and twenty four (224) subjects aged above 18 years over a period of one year from January to December 2022 was carried out in the Department of Biochemistry in collaboration with Department of Nephrology, Marine city Medical College and Hospital (MCMCH). The study group was divided into three different groups according to the different stages of CKD as stage 3 (eGFR 30-59 ml/min/1.73m²) stage 4 (eGFR 15-29 ml/min/1.73m²) and stage 5 (eGFR <15 ml/min/1.73m²). Important variables in this study was serum Hemoglobin, serum creatinine and eGFR. eGFR was calculated by Cockcroft and Gault equation $eGFR = (140 - \text{Age in years}) \times \text{Weight (Kg)} \times [0.85 \text{ if female}] / 72 \times [\text{Serum Creatinine (mg/dL)}]$.⁹ Adult Subjects irrespective of gender with CKD stage 3, stage 4 and stage 5 were included in this study. Subjects with CKD stage 5 who were under dialysis, subjects who are psychologically unstable, Bed ridden subjects, Pregnancy, Malignancy, HIV positive subjects, Hepatitis, HbsAg positive subjects were excluded from this study.

Data was collected using a pre-tested structured questionnaire with all the variables of interest after taking informed and written consent. A medical history was taken and a physical examination was performed. After having the written consent from the participants, patients having CKD were eligible for the assessment of anemia. Demographic and anthropometric data including age, sex, weight, height, BMI and blood pressure were collected from the participants. Using standard phlebotomy procedures 5 mL of blood was drawn by venous puncture under all aseptic precaution and collected blood sample was divided into two vials i.e. in EDTA vial for hematological tests and in plain vial for biochemical test. After clotting of blood in the plain vial, serum was separated, within an hour; by centrifugation at 3000 – 5000 cycles for 5 min. Serum hemoglobin and serum creatinine level were the

laboratory parameters. Laboratory standard operation procedures were maintained for all laboratory analysis.

Statistical analysis was done Statistical Package for the Social Sciences (SPSS) for Windows Version 23.0. Association between anemia and chronic kidney disease was tested by ANOVA test. Scattered diagram was used to test significant correlation. Comparison of mean value of continuous data was tested by student's t-test. p-value less than 0.05 was considered significant. All the data were represented in tables and figures. Before commence the study institutional consent was taken.

RESULTS

Out of 224 patients 46% (103) were female and 54% (121) were male. The mean values of age (56.22 ± 12.78), weight (62.49 ± 8.89), S. creatinine (6.69 ± 4.46), eGFR (13.35 ± 10.81) and blood Hb% (9.27 ± 1.43) were summarized [Table I]. There were significant differences of eGFR ($p=0.008$) and Hb ($p < 0.00001$) between male and female cases, but no significant difference of serum creatinine was observed between male and female cases in this study [Table II]. ANOVA test was done which revealed that the Hb% distribution in three stages of CKD with mean were 10.85% in stage 3, 9.71% in stage 4, 8.86% in stage 5 and the differences were statistically significant ($F = 32.68$, $p < 0.00001$) [Table III]. ANOVA tests also showed the distribution of eGFR in three stages of CKD with mean in stage 3 ($35.83 \text{ ml/min/1.73m}^2$) stage 4 ($2.92 \text{ ml/min/1.73m}^2$) stage 5 ($8.64 \text{ ml/min/1.73m}^2$) and the differences were statistically significant ($F = 775.05$, $p < 0.00001$) [Table IV]. Our study showed that 8% cases had mild anaemia, 75.9 % cases had moderate anaemia and 16.1% cases had severe anaemia [Table V]. The present study revealed a positive significant correlation between eGFR and Hb% in the study cases [Figure 2].

Table I Baseline characteristics of the study cases (n = 224)

Variables	Mean± SD	Range
Age (Years)	56.22 ± 12.78	18-85
Weight (Kg)	62.49 ± 8.89	40-91
S. Creatinine (mg/dl)	6.69 ± 4.46	1.42-21.5
eGFRml/min/1.73m ²	13.35 ± 10.81	2.0-50.9
Blood Hb%	9.27 ± 1.43	5.1-16.1

Table II Serum creatinine, calcium and Hb level between male and female cases (n = 224)

Variables	Male (n=121) (Mean± SD)	Female (n=103) (Mean± SD)	Significance
S. Creatinine (mg/dl)	5.20 ± 4.72	6.74 ± 4.15	$p=0.89$ Not Significant
eGFRml/min/1.73m ²	15.09 ± 11.4	11.3 ± 9.6	$p=0.008$ Significant
Blood Hb%	9.71 ± 1.50	8.77 ± 1.13	$p < 0.00001$ Significant

Table III Distribution of serum Hb level according to CKD stages with ANOVA test significance (n = 224)

Variable	CKD Stage	Number (n)	Mean± SD	Range	Significance
Hb%	Stage III	28	10.85 ± 1.74	8.3-16.1	$F = 32.68$
	Stage IV	43	9.71 ± 1.15	7.4-12.9	$p < 0.00001$
	Stage V	153	8.86 ± 1.18	5.1-11.6	Highly Significant
	Total	224	9.27 ± 1.43	5.1-16.1	Significant

Table IV Distribution of eGFR according to CKD stages with ANOVA test significance (n = 224)

Variable	CKD Stage	Number (n)	Mean± SD	Range	Significance
eGFR (ml/min/1.73m ²)	Stage III	28	35.83 ± 5.23	29.9-50.2	$F = 775.05$
	Stage IV	43	21.2 ± 4.63	15.0-29.2	$p < 0.00001$
	Stage V	153	7.04 ± 3.21	2.0-14.3	Highly Significant
	Total	224	13.35 ± 10.81	2.0-50.9	Significant

Table V Percentage distribution of low Hb level in the study cases (n = 224)

Severity of Anaemia	Stage III	Stage IV	Stage V	Total (n)	Percentage (%)	
Mild	M: 11-12.9% F: 11-11.9%	09 02	05 00	02 00	18	8%
Moderate	M: 8-10.9% F: 8-10.9%	06 11	23 14	64 52	170	75.9%
Severe	M: <8% F: <8%	00 00	01 00	09 26	36	16.1%
	Total	28	43	153	224	100%
		(11.7%)	(19.4%)	(68.9%)		

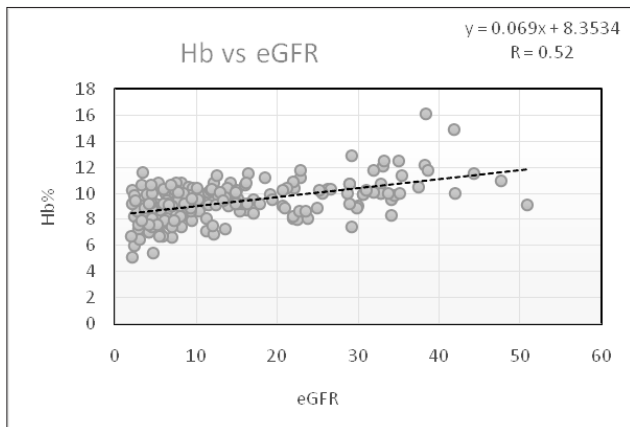


Figure 2 Scatter diagram shows positive significant correlation between eGFR and Hb%.

DISCUSSION

The study group was divided into three different groups according to the different stages of CKD as stage 3 (eGFR 30-59 ml/min/1.73m²), stage 4 (eGFR 15-29 ml/min/1.73m²) and stage 5 (eGFR <15 ml/min/1.73m²). Out of 224 patients 46% (103) were female and 54% (121) were male. There were significant differences of eGFR and Hb between male and female cases, but no significant difference of serum creatinine was observed between male and female cases in this study. ANOVA tests for the Hb% and eGFR distribution in three stages of CKD (Stage 3, 4 and 5) was statistically significant. Our study showed that 8% cases had mild anaemia, 75.9% cases had moderate anaemia and 16.1% cases had severe anaemia. The present study revealed that there was a positive significant correlation between eGFR and Hb% in the study cases. Our study reported a high prevalence of anemia in CKD stage 4 and Stage 5. The high incidence of anemia in overall CKD patients in our study may be reported due to significant number of anemia in late stage CKD in whom the mean value of hemoglobin concentration were found to be 9.71 ± 1.15 gm/dl and 8.86 ± 1.18 gm/dl respectively, for CKD stage 4 and 5. Afsar et al. and Suiga et al. reported that 75% and 73.1% respectively had anemia in CKD patients.^{10,11} Both of their findings were higher than our findings. In our study, 68.30% of patients had advance stages of CKD stage 5. Disproportionately distribution of advance renal disease in whom very high number of anemia may be accounted for different high prevalence of anemia in CKD in different studies. Mc Clellan et al conducted a study in a large number patients i.e. 5222 patients in a US multicenter survey by using cut off

point of hemoglobin concentration 12 gm/dl to define anemia had documented overall incidence of anemia in CKD was 47.75% which was not similar to our study.¹² However, McClellan et al reported 26.7% had anemia in stage 3 CKD had progression to 75.5% had anemia in stage 5 CKD. Valderrabano et al. documented the much higher incidence of anemia in CKD patients was 68% though they used cut off point for hemoglobin concentration 11 gm/dl to define anemia which was similar to our studies.¹³ Different factors are associated with CKD such as absolute and/or relative erythropoietin hormone deficiency, inflammation and oxidative stress may advocate the development of anemia in CKD. High degree of anemia may be related to the peculiarity to the environment including parasitic infestation e.g. hookworm infestation, malnutrition, deficiencies of iron, folate, vitamin B12 etc. Iron profile, folic acid and vitamin B12 were not assessed in this study which is our limitation. Regardless of this limitation, our study advocates the high prevalence and strong association of anemia with CKD. Some other factors including platelet dysfunction causes an increased risk for gastrointestinal bleeding, shortening of half-life of RBC and hemolysis due to uremic toxin accumulation. The extent of anemia increases progressively with the declining glomerular filtration rate.¹⁴ In our study the incidence of anemia was found 68% in stage 5 CKD. Our result corroborate with the study of Valderrabano et al. Furthermore, significant decreased of hemoglobin level, PCV, RBC counts, MCV, MCHC and MCH with the stages of CKD accounts for anemia of CKD is also as a part of anemia due to chronic disease besides erythropoietin hormone deficiency. Thus a comprehension study is required in large population for the estimation of prevalence of anemia in CKD. In conclusion, we documented a high prevalence of anemia in CKD stage 5. Thus a strong association between anemia and CKD was found. Anemia in CKD is the established risk factor for the development of cardiovascular disease. Therefore, it is necessary to identify anemia in CKD as soon as possible and manage them properly before development of cardiovascular disease.

LIMITATION

The study has certain limitations which includes short duration of time, small sample size and cross sectional study. Iron profile, folic acid and vitamin B12 were not assessed in this study which is another limitation.

CONCLUSION

The study revealed a strong association between anemia and CKD establishing that the degree of Anemia is strongly associated with fall of eGFR in CKD.

RECOMMENDATIONS

Study on different tertiary level hospital of different parts of Bangladesh involving a large population size will be more representative of entire country. Further prospective multicenter study in large scale is necessary to better understand the strategy anaemia in CKD.

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AUTHORS CONTRIBUTION

Conception and design - FH, PKD

Data collection - FH, RKS

Analysis and interpretation of data-FH, PKD

Manuscript preparation - FH, PKD, RKS.

DISCLOSURE

All the authors declared no conflicts of interest.

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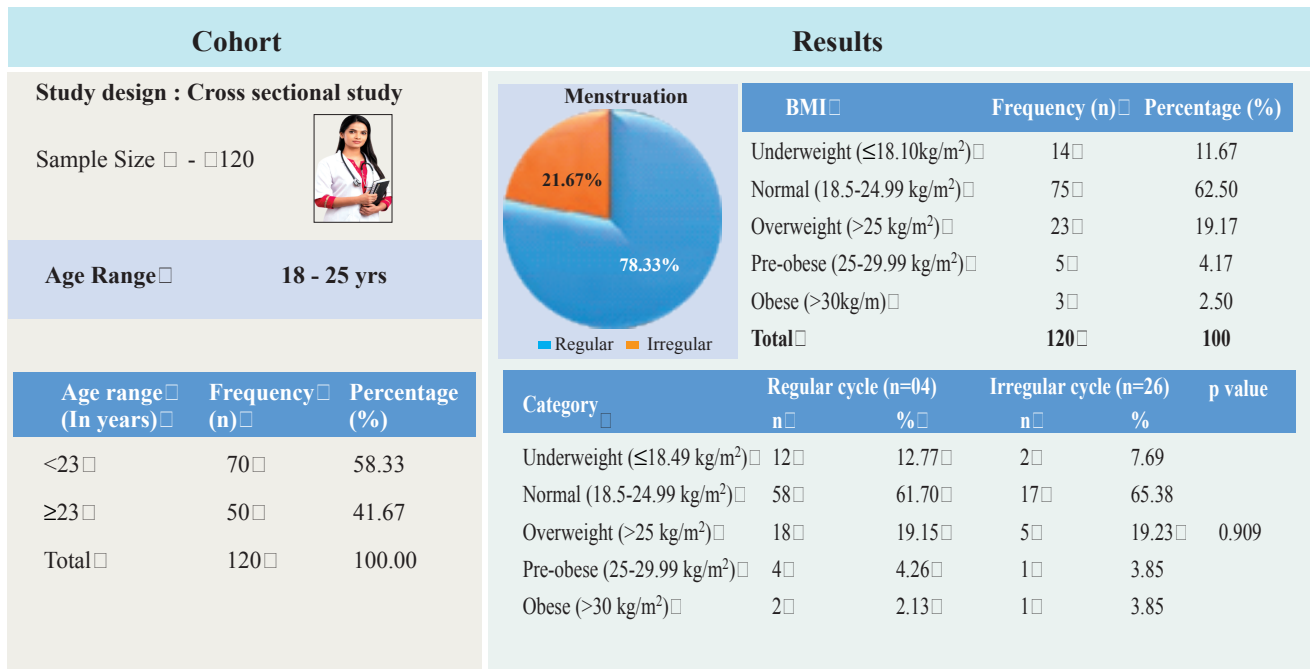
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Association of BMI with Menstrual Irregularities in Medical Students

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GRAPHICAL ABSTRACT

Association of BMI with Menstrual Irregularities in Medical Students



Conclusion: There exists a notable prevalence of irregular menstruation (21.67%) among medical students. However the association between BMI categories and irregular menstruation was statistically not significant.

Afroz S S et al.

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ABSTRACT

Background: The menstrual cycle is a recurring process involving the shedding of the uterine lining, serving as a vital sign for assessing health. It typically lasts 21 to 45

days, with variations common, especially after menarche. Menstrual irregularities are widespread, affecting 64% of girls globally and up to 87% in South Asian countries like India. Factors influencing menstruation include hormonal fluctuations, genetics and BMI. Obesity, prevalent among women, can disrupt the menstrual cycle due to excess estrogen production from fat cells, leading to various irregularities. In Bangladeshi women, menstrual disorders like dysmenorrhea and menorrhagia are common, affecting significant percentages. The study aims to evaluate the association between BMI and irregular menstruation in medical students.

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Materials and methods: The cross sectional, conducted at the Department of Endocrine, Marine City Medical College & Hospital, Chattogram, Bangladesh, involved 120 medical students over a specified period. Consent was obtained from participants who were queried about menstrual irregularities using a structured questionnaire. Inclusion criteria comprised medical students who had reached menarche and were aged 18-25 years. BMI categories were established, and data were analyzed using SPSS version 26.0, employing percentages, proportions and the Chi-square test for statistical significance.

Results: Out of the total sample, 58.33% were below 23 years old. Most (78.33%) had regular menstruation, while 21.67% had irregular cycles. The majority (62.50%) had a normal BMI, with 19.17% overweight and 11.67% underweight. Pre-obese and obese were observed in 4.17% and 2.50% of the study population. Among those with regular cycles, distribution across BMI categories varied slightly compared to those with irregular cycles. However, no statistically significant association was found between BMI and menstrual irregularity ($p=0.909$).

Conclusion: The study found a significant prevalence of irregular menstruation among medical students. Despite a higher occurrence in overweight individuals (19.23%), BMI's association with irregular menstruation is statistically insignificant.

Key words: Association; BMI; Menstrual irregularities.

INTRODUCTION

The menstrual cycle represents a regular physiological occurrence marked by the cyclic shedding of the progesterational endometrium, often accompanied by the loss of blood. Considered an additional vital sign, menstruation serves as a valuable tool in assessing normal development and in ruling out pathological conditions in adolescents.¹ Variability in the frequency, volume, and pattern of menstruation are its defining characteristics.² During the first menstruation, most women bleed for two to seven days.³ Typically, most normal menstrual cycles fall within the range of 21 to 45 days, although variability is common even within the first year after menarche. Short cycles, lasting fewer than 20 days and long cycles, lasting more than 45 days, may also occur. By the third year following menarche, approximately 60% to 80% of menstrual cycles tend to fall within the range of 21 to 34 days, which is typical of adult cycles.^{3,4} While it's rare to

discover a significant pathology to account for menstrual irregularities, changes in pattern are not uncommon. The menstrual cycle's pattern can have a notable impact on a girl's reproductive life, prompting concerns for both the patient and their families. A survey indicated that approximately 64% of girls experience at least one issue related to menstruation.² In south Asian country like India, the prevalence of menstrual disorders has been reported to be as high as 87%.⁵ Factors that often influence the regularity and flow of a woman's menstrual cycle encompass hormonal fluctuations, genetics, underlying medical conditions and Body Mass Index (BMI).⁶ BMI is a straightforward measure of weight relative to height. It is calculated by dividing a person's weight in kilograms by the square of their height in meters.⁷ According to the classification by the World Health Organization (WHO) underweight (18.49 kg/m²) normal (18.5 to 24.99 kg/m²), overweight (25 kg/m²), pre-obese (25 to 29.99 kg/m²) and obese (30 kg/m²).⁷ The prevalence of obesity is higher in women than men. In a recent study, the prevalence of general obesity was found as 25.2% in Bangladeshi women.⁸ Excessive weight and obesity have been linked to irregular menstrual cycles, which can diminish fertility and elevate the risk of hormone-sensitive cancers in women.⁹ Obesity and menstruation are linked due to the presence of lipids like cholesterol in adipocytes, which can be converted into a form of estrogen known as "Estrone." In obese women, excess fat cells serve as estrogen-producing centers, leading to hormonal imbalances that can result in menstrual irregularities such as oligomenorrhea, polymenorrhea, menorrhagia, metrorrhagia, and secondary amenorrhea.¹⁰ Based on a study, the prevalence of menstrual disorders, with dysmenorrhea, menorrhagia, oligomenorrhea and amenorrhea affecting 32.1%, 18.5%, 11.2% and 5.7% of Bangladeshi women.¹¹ There have been several research done in the past to address issues with irregular menstruation, but there aren't many data on the connection between menstrual irregularities and BMI. For more investigation, an etiological association between menstruation problems and BMI may be examined. The purpose of this study was to evaluate the association between BMI and irregular menstruation.

MATERIALS AND METHODS

A cross sectional study was conducted in the Department of Endocrine, Marine City Medical College & Hospital, Chattogram, Bangladesh. The study

enrolled a total of 120 medical students from January to December 2022. All medical students above 18 years of age, who attained menstrual irregularities were including in this study. Student receiving HRT for mental disorder, pregnancy and willing to participate in this study were included. Before data collection, consent forms were obtained from each participating student. Socio-demographic information was gathered utilizing a predefined and pre-tested questionnaire. Each participant was questioned about any menstrual irregularities, with the details duly noted. Regular menstruation was characterized by a menstrual cycle lasting between 21 to 35 days, while irregular menstruation was indicated by cycles shorter than 21 days or longer than 35 days. Anthropometric measurements, including height, weight, waist circumference, and hip circumference, were taken with participants standing upright, feet together, and arms at their sides. Height was measured in centimetres, while weight was recorded using a kilogram scale. Body Mass Index (BMI) categories were defined as follows: Underweight ($\leq 18.49 \text{ kg/m}^2$) Normal ($18.5-24.99 \text{ kg/m}^2$) Overweight ($>25 \text{ kg/m}^2$) pre-obese ($25-29.99 \text{ kg/m}^2$) and Obese ($>30 \text{ kg/m}^2$).¹¹ All data were gathered, inputted and processed in SPSS version 26.0. Data analysis was conducted utilizing percentages and proportions presented in tabular format. The Chi-square test assessed the statistical significance of associations between variables. Significance was determined at a threshold of $p < 0.05$. Institutional consent was obtained before commence the study.

RESULTS

Among the study population, 70(58.33%) individuals were aged below 23 years, and 50(41.67%) individuals were aged 23 years or older (Table I). Mostly 78.33% of the study population had regular menstruation and rest of 21.67% had irregularity (Figure 1). Table II shows the distribution of participants based on Body Mass Index (BMI) where the majority of 75(62.50%) participants had normal BMI, 23(19.17%) individuals were classified as overweight, and 14(11.67%) were underweight. A smaller portion of the sample (4.17%) were pre-obese, while only three individuals (2.50%) were categorized as Obese. Table III compares individuals with regular menstrual cycles ($n=94$) and those with irregular ($n=26$) across BMI categories. For individuals with regular menstrual cycles, the distribution across weight categories is as follows:

12(12.77%) individuals are underweight, 58(61.70%) individuals have normal BMI, 18(19.15%) individuals are overweight, 4(4.26%) individuals are categorized as pre-obese and 2 (2.13%) individuals are classified as obese. On the other hand, among individuals with irregular menstrual cycles, 2(7.69%) individuals are underweight, 17(65.38%) individuals are within the normal weight range, 5(19.23%) individuals are overweight, 1(3.85%) individual is pre-obese and 1(3.85%) individual is obese. The p-value for the distribution across weight categories is 0.909, suggesting no statistically significant difference in weight distribution between individuals with regular and irregular menstrual cycles.

Table I Age distribution of the study population ($n=120$)

Age range (in years)	Frequency (n)	Percentage (%)
<23	70	58.33
≥ 23	50	41.67
Total	120	100.00

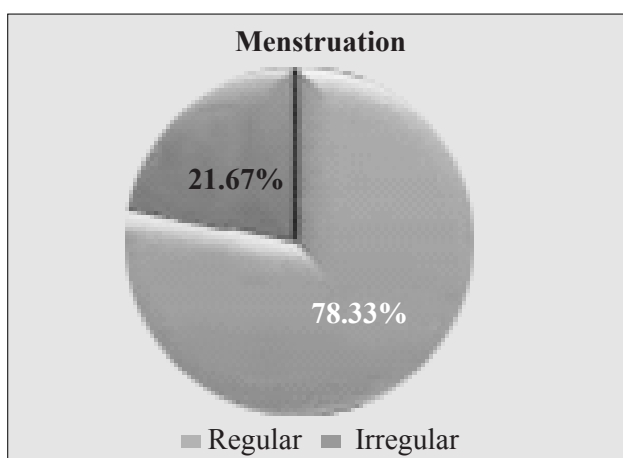


Figure 1 Distribution of menstrual irregularity ($n=120$)

Table II BMI classification of the study population ($n=120$)

BMI	Frequency (n)	Percentage (%)
Underweight ($\leq 18.49 \text{ kg/m}^2$)	14	11.67
Normal ($18.5-24.99 \text{ kg/m}^2$)	75	62.50
Overweight ($>25 \text{ kg/m}^2$)	23	19.17
Pre-obese ($25-29.99 \text{ kg/m}^2$)	5	4.17
Obese ($>30 \text{ kg/m}^2$)	3	2.50
Total	120	100

Table III Correlation between BMI with menstrual irregularities

Category □	Regular cycle □ (n=94) □		Irregular cycle □ (n=26) □		p-value
	n □	% □	n □	% □	
Underweight ($\leq 18.49 \text{ kg/m}^2$) □	12 □	12.77 □	2 □	7.69 □	0.909
Normal ($18.5-24.99 \text{ kg/m}^2$) □	58 □	61.70 □	17 □	65.38	
Overweight ($>25 \text{ kg/m}^2$) □	18 □	19.15 □	5 □	19.23	
Pre-obese ($25-29.99 \text{ kg/m}^2$) □	4 □	4.26 □	1 □	3.85	
Obese ($>30 \text{ kg/m}^2$) □	2 □	2.13 □	1 □	3.85	

DISCUSSION

Obesity is a risk factor which is associated with both short- and long-term health effects for women as well as for their offspring. It is a growing public health challenge in women of reproductive age. Obese individuals often experience disruption of the menstrual cycle, including irregular menstrual cycle, abnormal menstrual flow and duration and increased pain associated with menstrual cycle.¹² Most studies investigating the association between BMI and abnormalities of the menstrual cycle focused on a younger women population, aged between 18 to 25 years and there was no information on history of childbirth.¹³⁻¹⁵ In our current study, we investigated the association between BMI and menstrual cycle characteristics in women with a wide range of ages (Aged 17 to 53 years) using ethnicity-specific WHO classification of BMI. This could represent such associations in women of a reproductive age. Our study was done on 120 participants, where most of the individuals (58.33%) were aged below 23 years. The result of our study is comparable with research where the age of most of the subjects falls between 26 to 35 years and 15-25 years comprise 32% of all participants.¹⁶ In the present study, 21.67% subjects had complaint of irregular menses. Castillo-Martinez et al showed similar findings in his study on female patients aged 18 to 40 years who attended an outpatient obesity clinic in Mexico that 30% had menstrual cycle irregularities.¹⁷ The prevalence of menstrual irregularity in a study by Cakir et al among university students in Turkey were 31.2%.¹⁸ A study done in India on 399 subjects, where they found 23.3% of the students had menstrual irregularities.¹⁰ These findings are almost similar to our study, which is 21.67%. In our study 19.23% of irregular cases were related to overweight, 3.85% of cases was related to pre-obese and 3.85% of cases was related to obese (Table III). A study done of

Asian country like India, they found much higher percentage in irregularity with pre-obese and obese.¹⁶ Tang et al. reported 25% overweight and 5% obese females in their study which is comparable with our study as well as our findings.¹⁹ On the contrary, prevalence of overweight and obesity was 5.4% and 6.5% respectively among college going girls in Mysore District, Karnataka as shown in study by Srinivas et al.²⁰ According to our study, among overweight individuals 19.23% had irregular cycles. Similarly, for those classified as pre-obese 3.85% had irregular cycles. Lastly, among participants classified as obese (BMI > 30 kg/m²), 2.13% had regular cycles, and 3.85% had irregular cycles. Our result indicates a statistically insignificant ($p > 0.05$). association between obesity grading and menstrual cycle irregularity. Conversely, the study of Srikanth et al. found that among the overweight group, 3 individuals had irregular cycles. Within the obese grade 1 category, 13 individuals with irregular cycles and for the obese grade 2 group, 25 individuals experienced irregular cycles. Their outcome suggests statistically significant ($p \leq 0.05$) connection between the grading of obesity and the irregularity of the menstrual cycle.¹⁶ Study conducted by Tang et al. concluded that overweight females had the length of menstrual cycle of 23-60 days, whereas obese females had the cycle of 20-35 days.¹⁹ It has been documented that being 15% overweight was associated with a significantly higher chance of having a menstrual cycle longer than 43 days.²¹

LIMITATIONS

Firstly, the study's sample size needs to be bigger, limiting the generalizability of findings. Additionally, the study only focuses on medical students, neglecting broader demographic representation. Furthermore, the reliance on self-reported data for menstrual irregularities may introduce recall bias, impacting the accuracy of results. Lastly, the cross-sectional design prohibits establishing causality between BMI and menstrual irregularities, warranting further longitudinal investigation.

CONCLUSION

Based on the comprehensive analysis conducted in this study, it can be concluded that there exists a notable prevalence of irregular menstruation among medical

students, with approximately 21.67% reporting menstrual irregularities. While the study found a higher proportion of irregular menstruation among overweight individuals (19.23%) compared to those classified as pre-obese (3.85%) and obese (3.85%), the association between BMI categories and irregular menstruation was found to be statistically insignificant ($p > 0.05$).

RECOMMENDATION

A need for further exploration and larger-scale studies to elucidate the complex relationship between body mass index and menstrual irregularities, potentially contributing to better management and interventions in clinical settings.

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AUTHORS CONTRIBUTION

Conception and design - SSA

Data collection - SSA, MNI

Analysis and interpretation of data - SSA, MR, MNI

Manuscript preparation - SSA, MNI, MR.

DISCLOSURE

All the authors declared no conflicts of interest.

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Heart Disease in Pregnancy: A Cross Sectional Observational Study in Chittagong Medical College Hospital

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GRAPHICAL ABSTRACT

Heart Disease in Pregnancy: A Cross Sectional Observational Study in Chittagong Medical College Hospital

Cohort	Results	
<p>Study design : Cross sectional descriptive</p> <p>Sample Size □ - □35 </p> <p>Mean age 27 - 46</p> <p>Literacy</p> <p>Literate 28 (80%)</p> <p>Illiterate 7 (20%)</p> <p>Residence</p> <p>Rural 30 (86%) </p> <p>Urban 5 (14%) </p> <p>ANC visit</p> <p>Nil □ 4 </p> <p>Irregular □ 20</p> <p>Regular □ 11</p> <p>Heart disease</p> <p>Congenital heart Disease 9 (26%) </p> <p>Acquired heart disease 26 (74%) (Including Prepartum heart disease)</p>	<p>Maternal outcome</p> <ul style="list-style-type: none"> ● PTL □ 7 ● PPH □ 1 ● ICU referral □ 19 (54%) ● Death □ 2 (5,7%) ● New onset of heart disease □ 19 (54%) □ IHD □ 3 □ CM □ 10 □ Arrhythmia □ 3 	<p>Neonatal outcome</p> <p>Normal birth weight 26 (74%)</p> <p>NICU referral 4 (11%)</p> <p>Death 2 (5.7%)</p> 

Conclusion: Post partum ICU referral is in 50% of patients, Neonatal outcome is still better, NICU referral in only in 11% patient. Though morbidity is high in pregnancy but mortality in both mothers and neonate low, only in 5.7% of patients (Both mother and baby)

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ABSTRACT

Background: Heart disease is an important cause of maternal and neonatal mortality and morbidity both in antepartum and postpartum period. An increased

prevalence of cardiovascular disease has been found in women of child bearing age which varies between 0.3-3.5%. Purpose of this study was to observe prevalence and its outcome among the pregnant women with heart disease admitted in Chittagong Medical College Hospital (CMCH).

Materials and methods : It was a cross sectional descriptive study in Department of Obstetrics and Gynecology, Chittagong Medical College Hospital from January 2020 to June 2020 among 35 admitted pregnant women with heart disease.

Results : Acquired Heart disease was found among maximum 26 (74.3%) patient. Out of 35 patients, 10 (28.6%) patients had history of cardiac surgery.

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Concerning maternal outcome, 11 patients developed cardiac complications like dilated Cardiomyopathy (CM), either intrapartum or postpartum. 68.6% required Caesarean Section (CS). Obstetric complications developed among 8 (22.9%) patients and most of them (87.5%) developed Preterm Labor (PTL). Intensive Care Unit (ICU) referral was needed for 19 (54.3%) patients and 2 died. 11.4% neonates admitted in Neonatal Intensive Care Unit (NICU) and perinatal death was 5.7%.

Conclusion : CS was required in about one third of patients with heart disease. Regular ante natal visit was only in one-third of patients. Peripartum cardiomyopathy was observed in half of patients.

Key words: Heart disease; Obstetric complications; Pregnancy.

INTRODUCTION

Pregnancy and heart disease are regarded as high-risk scenarios. Pregnant women with underlying heart disease may have increased morbidity and mortality due to increased cardiac demands.¹ In the latest 'Confidential Enquiry into Maternal and Child Health Report (CEMACH)' in UK, Heart disease was the leading cause of mortality overall and the leading cause of indirect maternal deaths. A 1% increase in maternal mortality is complicated by it.² Higher prevalence of heart disease in pregnancy is due to older age at first pregnancy, a notable improvement in the treatment of congenital heart disease, and rising rates of diabetes, hypertension and obesity.^{3,4,5} The primary cause of indirect maternal mortality is due to cardiac problems in 20.5 % of all causes.^{6,7} The majority of pregnant women with heart disease have successful pregnancies, however neglecting to diagnose and treat pregnant patients can have dangerous effects on the developing foetus and the mother.⁸

Congenital heart disease is most frequent (75% to 82%) in the western world, with shunt lesions predominating in 20% to 65% of cases. Even though it is on the decline, rheumatic heart disease still accounts for the bulk of occurrences in underdeveloped nations, accounting for 56% to 89% of all cardiovascular disorders that occur during pregnancy.⁴ The rate of fetal death rises as the mother's functional ability declines, in cases when the mother has NYHA class IV disease, the rate of fetal death is thirty percent.⁹ Multidisciplinary approach by obstetricians, cardiologists, anesthesiologists, neonatologists with appropriate care in proper place like fetal-maternal unit may decrease it.¹⁰

Chittagong Medical College Hospital is the second largest hospital of the Bangladesh and only referral hospital (Level 3) of greater Chattogram division covering 40,000 square k. meter area and serving about 30 million population. In total, 62 pregnant women with heart problems were hospitalized to CMCH in 2019, according to institutional records. To observe the maternal and neonatal outcome among pregnant women with heart disease admitted to the obstetrics ward of Chittagong Medical College Hospital was the primary goal of the research.

MATERIALS AND METHODS

Purposive sampling was done in this cohort of 35 pregnant with heart disease admitted in the Department of Obstetrics and Gynecology at Chittagong Medical College Hospital (CMCH) from January to June 2020. It was a cross sectional descriptive study. A pre-made structured questionnaire comprised information on maternal and neonatal outcomes, clinical presentations, past medical history, and cardiac problems of the patients, in addition to sociodemographic differentials. Written informed consent was acquired from the subjects. Pregnant mother with pre-existing heart diseases or presenting with features of heart diseases during admission were included and with co-morbid conditions like severe anemia, thyroid disorders and Heart failure due to noncardiac causes were excluded. SPSS version-25, a computer program, was used to process and analyze the data (Statistical Package for Social Science). Various statistical techniques were used to analyze the data. A p value of less than 0.05 was regarded as statistically significant. The study was approved by ethical review committee of CMCH.

RESULTS

The mean age was 25 years. 54.3% of women had primary level of education. Most of the patients (97.1%) were homemaker and 57.1% were from lower class. Majority (85.7%) were from rural area. The gestational age was 35-38 weeks (Table I)

ANC visit was irregularly taken by 57.1% patients. Most of the ANC profile (71.4%) was without complications (Table II).

Maximum (74.3%) patients had heart disease following complication of pregnancy. Among those Peripartum cardiomyopathy was frequently reported (46.2%). Others are Mitral stenosis (15.4%), Pulmonary hypertension (3.8%), Arrhythmias (11.5%) and Ischemic

Heart Disease (15.4%). Atrial septal defect (44.4%), Ventricular septal defect (22.2%), Tetralogy of Fallot (22.2%) were the common congenital Heart diseases (Table III).

NYHA classification among the patients showed that 16 (45.7%) patients were grade-I, 8(22.9%) grade-II, 1(2.9%) grade III and 10 (28.6%) patients were grade-IV (Figure 1)

10 (28.6%) patients had history of cardiac surgery. PTMC was 30% and ASD closure was also 30% (Table IV)

Regarding maternal outcome, 68.6% required caesarian section and eleven patients had assisted Vaginal Delivery (VD). Obstetric complications were developed among 8 (22.9%) patients and most of them (87.5%) developed PTL. ICU referral was needed for 19 (54.3%) patients and 2 women died. CCF was the most frequent cardiac consequence (2 cases). Regarding neonatal outcome, most of the baby (94.3%) were alive. Only 4 baby (11.4%) needed for NICU referral. Maximum (74.3%) baby's birth weight was within normal range and median (IQR) APGAR score was 8 (7-8) (Table V).

11 patients who had develop cardiac complications, most of them had post-partum (27.3%) and intrapartum (9.1%) dilated cardiomyopathy (Figure 2)

Table I Socio-demographic characteristics of the patients (n=35)

Characteristics			
Age (Years)	Mean ± SD	27.46	4.847
	Range	18-35	
		Frequency	Percentage
Educational qualification			
	Illiterate	7	20%
	Primary	19	54.3%
	SSC	8	22.9%
	Graduation	1	2.9%
Occupation			
	Homemaker	34	97.1%
	Employed	1	2.9%
Monthly family income			
	Low	20	57.1%
	Lower middle	15	42.9%
Residence			
	Rural	30	85.7%
	Urban	5	14.3%

Data are expressed as mean ± SD (Range) and frequency (Percentage).

Table II Obstetrics profile of the study subjects (n=35)

Characteristics	Frequency	Percentage
ANC visit		
Nil	4	11.4%
Regular (4)	11	31.4%
Irregular (5-10)	20	57.1%
ANC profile		
Without complication	25	71.4%
Left Heart Failure	7	20%
Dilated Cardiomyopathy	2	5.7%
Myocardial Infraction	1	2.9%

Data are expressed as frequency (Percentage).

Table III Heart disease types (n=35)

Characteristics	Frequency	Percentage
Congenital Heart disease (9)		
ASD	4	44.4%
VSD	2	22.2%
TOF	2	22.2%
Coarctation of Aorta	1	11.1%
Acquired Heart Disease (n=26)		
Mitral stenosis	4	15.4%
Pulmonary hypertension	1	3.8%
Arrhythmias	3	11.5%
Ischemic Heart Disease	4	15.4%
Cardiomyopathy	12	46.2%
MR & PH	1	3.8%
MS & Arrhythmias	1	3.8%

Data are expressed as frequency (Percentage).

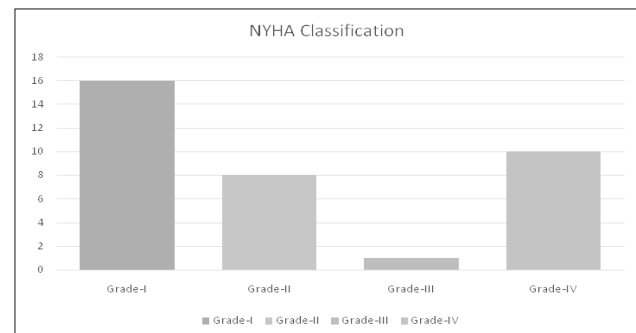


Figure 1 Distribution of NYHA classification among the patients (n=35)

Table IV Surgical history of the patients (n=10)

Name of surgery	Frequency	Percentage
TOF repair	1	10%
VSD repair	2	20%
PTMC	3	30%
ASD closure	3	30%
Pericardiectomy	1	10%

Data are expressed as frequency (Percentage)

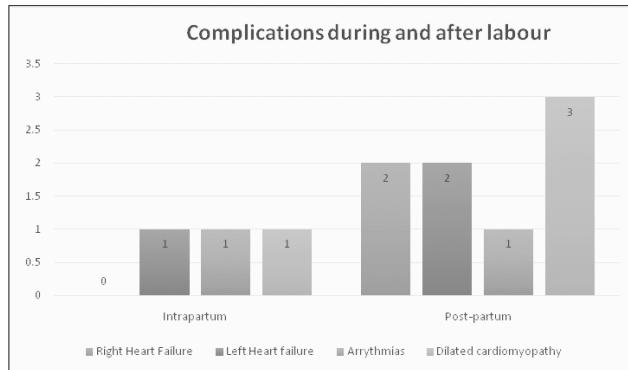


Figure 2 Cardiac complications during and after labour (n=11)

Table V Maternal and neonatal outcome of the patients (n=35)

		Frequency	Percentage
Maternal out come			
Obstetric complications	Present	8	22.9%
	Absent	27	77.1%
Type of complications			
Consequences of delivery	Preterm labour	7	87.5%
	PPH	1	12.5%
	Uneventful	14	40.0%
	ICU referral	19	54.3%
	Death	2	5.7%
Neonatal outcome			
Viability	Alive	33	94.3%
	Death	2	5.7%
NICU referral	Required	4	11.4%
	Not required	31	88.6%
		2.606	0.6
		1-4.2	
Birth weight#	Very low birth weight	2	5.7%
	Low birth weight	7	25.7%
	Normal birth weight	26	74.3%
	APGAR score		
	Median	8	
	IQR	7-8	

Data are expressed as mean ± SD (Range) median (IQR) and frequency (Percentage). # mean birth weight : 2.206kg.

DISCUSSION

The study found that pregnancy with heart disease had an average age of 27.46 ± 4.8 years (Range: 18-35). A recent study by Khan et al. reported similar results

(27.58±5.6 years).¹¹ According to Abbasi et al. 74.5% were of 20-30 years of age.¹² Pujitha et al. published similar data on the age distribution, showing that 50% of the population was between the ages of 21 and 25.¹³ In present case series 54.3% of women had primary level of education. As early childhood marriage happened in Bangladesh frequently, so less educational qualification is usual for this country. A similar finding was made in the survey conducted by Shanthibala and Shanthirani which showed that 36.17% of people were illiterate and 44.17% had completed only primary school.¹⁴ In our study, most of the patients (97.1%) were homemaker. Similarly 90.2% were house wife reported by Abbasi et al.¹² Majority (85.7%) were from rural area. Similarity found in the study of Shanthavibala and Shanthirani and Abbasi et al. 38 weeks gestational age was the median (IQR: 37–39). Pujitha et al. showed that 22 (68.8%) patients was in 37-40 gestational weeks.^{14,12,13}

ANC visit was irregularly taken by 57.1% patients. Among them ANC profile (71.4%) was without complications. As Bangladesh has improved in MCH care at every level of healthcare system, so most of the pregnant mother got ANC services easily. Another study by Bangal et al. showed out of 35 participants 13 (37%) were unbooked and 22 (63%) were booked.¹⁵

In the study ASD (44.4%), VSD (22.2%), TOF (22.2%) were the common congenital Heart diseases. And Mitral stenosis (15.4%), Pulmonary hypertension (3.8%), Arrhythmias (11.5%), Ischemic Heart Disease (15.4%), Cardiomyopathy (46.2%) were the common acquired Heart diseases. Among the patients, rheumatic heart disease affected 70.37%. According to a study by Khan et al. congenital heart disease (49.09%) was the most often found form, next to RHD (41.82%).¹¹ The congenital lesion known as Ventricular Septal Defect (VSD) accounted for 16.36% of all cases. Mitral regurgitation (34.5%) was found to be the most frequent valvular lesion, then mitral stenosis (10.91%). According to Abbasi et al. the majority of individuals (86.3%) had rheumatic heart disease, whereas 9.8% had congenital heart disease.¹² The percentage with peripartum cardiomyopathy was 3.9%. Among RHD With 21 (41.2%) cases, mitral stenosis was the most prevalent condition. 9.8% of patients had mitral regurgitation, 17.6% had mitral stenosis and regurgitation and 11.8% had both mitral regurgitation and aortic regurgitation. ASD accounted for 5.9% of all lesions in congenital heart disease cases.

Regarding NYHA classification this study showed that 16 (45.7%) patients were grade-I and 10 (28.6%) patients were grade-IV. Khan et al. revealed in their study that the majority of patients (69.09%) belonged to Classes 1 and 2, 9.09% to NYHA Classes 3 and 21.82% to Classes 4.¹¹ Our study is also comparable to Abbasi et al. and Shanthavibala and Shanthirani 28.6% patients had history of cardiac surgery in this study.^{12,14} PTMC was 30% and ASD closure was also 30%. Of the patients, 18.18% had undergone heart surgical correction, reported by Khan et al.¹¹ Closure of the Atrial Septal Defect (ASD) was the most often performed corrective surgery (9.09%). Another studies Pujitha et al. and Akhter et al. reported the similarity.^{13,10} Present study showed, out of 11 patients develop post-partum (27.3%) and intrapartum (9.1%) dilated cardio myopathy. In the study by Khan et al. Heart disease affected 18.18% of cases. Congestive heart failure was the most frequent cardiac consequence, occurring primarily in the intrapartum interval (80%).¹¹

Preterm labor (27.3%), preeclampsia (18.1%) and anemia (45.6%) were the most frequent non-cardiac problems. Seven individuals had cardiac problems, five of which needed intensive care unit treatment. The majority of patients (81.25%) had vaginal births, whereas six patients (18.75%) underwent cesarean sections. Similar to this study, the most frequent prenatal complication among cases in the Khan et al. study was premature labor (23.63%), followed by hypertensive disease of pregnancy (18.18%).¹¹ Among the cases, the percentage of instrumental delivery was greater. The percentage of maternal deaths among those with heart disease was 5.45%, which is about the same as the current study's 5.7% rate. Regarding neonatal outcome, most of the baby (94.3%) were alive. Only 11.4% needed for NICU referral. Maximum (74.3%) baby's birth weight was within normal range and median (IQR) APGAR score was 8 (7-8). Similar to this study, Salam et al. observed that none of the live newborns had congenital heart disease. Approximately 85.6% of these mothers gave live-birth. 75.3% of patients had an APGAR score of above 9 out of 10 and 72.8% of all newborns weighed more than 2 kg.¹⁶

LIMITATION

Sample size was small in a single center and study design was descriptive.

CONCLUSION

CS was required in about one third of patients with heart disease. Regular ante natal visit was only in one-third of patients. Peripartum cardiomyopathy was observed in half of patients. ICU referral was required in more than half of patients but one tenth of baby required NICU referral. In spite of high morbidity both maternal and neonatal mortality were low (Both 5.7%)

RECOMMENDATIONS

A favorable outcome requires both appropriate clinical follow-up throughout pregnancy and proper examination of the mother's circumstances prior to conception. Educating the people living in remote areas the value of routine prenatal checkups and hospital deliveries is imperative. The establishment of reasonably priced cardiac surgical facilities in rural areas will undoubtedly contribute significantly to the reduction of pregnancy-complicated heart disease mortality and morbidity. Pre Pregnancy counseling and multi disciplinary approach may be offered to all women with heart disease to prevent pregnancy related complications.

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AUTHORS CONTRIBUTIONS

Conception and design - RB, AB

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Analysis and interpretation of data - RB, BB, SYA

Manuscript preparation - RB, AB, AA, ZR, BB, SYA.

DISCLOSURE

All the authors declared no conflicts of interest.

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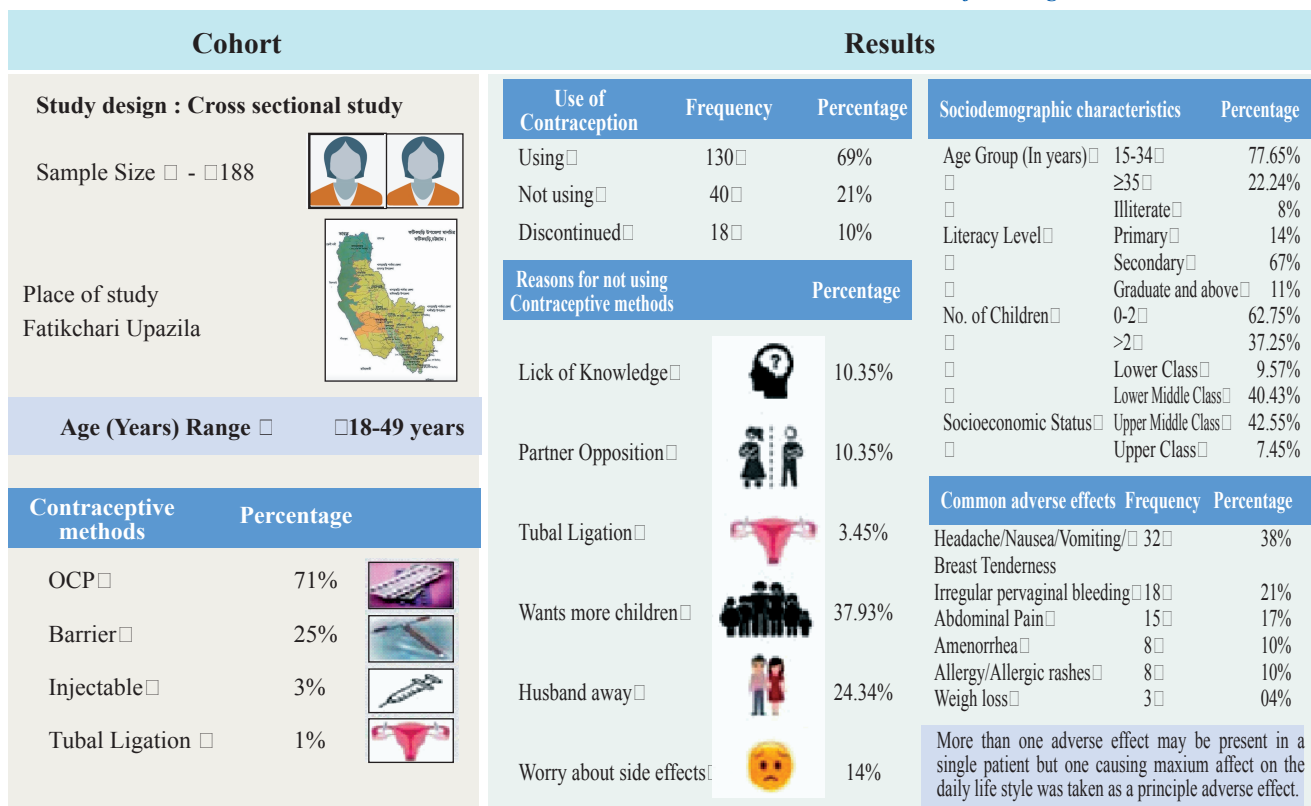
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Study on Contraceptive Practices among Reproductive Age Group Women in a Selected Rural Area of Chattogram

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GRAPHICAL ABSTRACT

Study on Contraceptive Practices among Reproductive Age Group Women in a Selected Rural Area of Chattogram



Conclusion: 70% of the study population used contraceptive device and the common device was OCP (71%). "One third of the population not using contraceptives" was due to their desire to have more children.

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ABSTRACT

Background: This report investigates contraceptive practices among women of reproductive age in a rural community of Fatikchari Upazila, Chattogram, Bangladesh. Contraception plays a pivotal role in family planning, aiming to reduce pregnancy-related complications and deaths, improve maternal and child health outcomes and prevent unplanned pregnancies. Despite significant progress in Bangladesh's Contraceptive Prevalence Rate (CPR) approximately one-third of

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pregnancies remain unplanned, indicating unmet family planning needs and challenges with contraceptive adherence.

Materials and methods: A descriptive cross-sectional study involving 188 female participants was conducted, utilizing a mixed-method questionnaire to gather socio-demographic and contraceptive practice data.

Results: Most participants (69%) reported current contraceptive use, primarily oral contraceptive pills (71%) and barrier methods (25%). Reasons for contraception included birth spacing (49.23%) and family completion (33.85%). Adverse effects were reported by 44.62% of users, including headaches and irregular bleeding. Reluctance towards permanent contraception was evident (6.39% opted for it). Reasons for non-use included desire for more children (38%) and concerns about side effects (14%). These findings highlight the importance of addressing misconceptions, improving access to comprehensive family planning services and enhancing user satisfaction to promote sustained contraceptive use.

Conclusion: 70% of the study population uses contraceptive device and the common is OCP (71%). About 1/3rd of the population not using contraceptives was due to their desire to have more children. However the percentage of contraceptive use was more among the middle class population and the common adverse effects were headache, nausea and vomiting.

Key words: Barrier method; Birth spacing; Contraceptive prevalence rate.

INTRODUCTION

Contraception is the deliberate use of artificial methods, such as various tools, substances, medications, sexual practices, or surgical operations, to avoid becoming pregnant or impregnated during sexual activity. With the use of condoms, diaphragms and other devices, these techniques aim to stop sperm from getting to the ovum, suppress ovulation, stop implantation and other strategies. Pregnancy-related issues, birthing complications and unsafe abortions were known to account for over half of all deaths in Bangladesh among women of reproductive age.¹ Many experts discovered that family planning offers many benefits for the mother, children, father, and the family as a whole, most of these complications especially pregnancy-related difficulties and deaths could be avoided with appropriate family planning.²

One of the mainstays of family planning is contraception, which can help prevent food poverty in

the home and poor health outcomes for women and children. Additionally, using condoms, a popular form of contraception can help to prevent the spread of HIV and other STI's. Hormonal therapies can alleviate discomfort and irregular bleeding in women who menstruate on every month. Contraceptives are unavoidable and practical for both men and women to prevent undesired pregnancies, choose the size of a family and enhance the spacing between childbirths and reduce abortion.³

In fewer than forty years, Bangladesh's Contraceptive Prevalence Rate (CPR) increased sevenfold, from 8% in 1975 to 62% in 2014.⁴ Nevertheless despite these advancements, about one-third of pregnancies remain unplanned, which may be linked to unfulfilled family planning needs as well as technique discontinuance and switching. Understanding that contraceptive usage-effectiveness and user adherence are just as important to reproduction as prevalence of contraceptive use is crucial. The Total Fertility Rate (TFR) would be 30% lower if unintended pregnancies were prevented, as married women in the nation are currently having 0.7 more children than they would like. The unmet demand for family planning may also contribute to this, but it's crucial to investigate how well family planning initiatives work to address problems associated with the use of contraceptive methods.⁵

In this study we wanted to observe the contraceptive practices of reproductive age group women in a rural community of Fatikchari Upazila, Chattogram.

MATERIALS AND METHODS

A descriptive type of cross sectional study was conducted in some selected villages of Fatikchari Upazila, Chattogram over a period of month from 2nd January to 30th January 2023. The selection of the sample was made by using purposive sampling technique. The sample size was 188 women of reproductive age group. The study was conducted through a pre-tested mixed type of questionnaire. After taking informed consent, the data were collected by face to face interview. The first section of the questionnaire carried the socio-demographical characteristics such as age, sex, marital status, education, occupation, family types, number of children etc. The second portion included information regarding contraceptive practices of the reproductive age group women. Widows, divorced and wife of expatriate workers were excluded from this study. Data were

analyzed with Microsoft excel for data processing and statistics. Ethical approval was taken before commence the study.

RESULTS

This descriptive cross sectional study included 188 female participants who were residents of Fatikchari Upazila and were in their reproductive age. Majority (45.74%) of the participants belonged to the age group of 25-34 while the mean age was found around 30.5 (± 4.53) years. Distribution of the participants according to their educational status showed that around 32% of them have studied up to SSC level while the second major level was secondary (28%). Majority (46.81%) of them belonged to a nuclear family while largest number of them (35.1%) had at least two children. Distribution of the participants according to their socio-economic status showed that they belonged mostly to upper middle class (42.55%) however, there was a close percentage in lower middle class (40.43%).

Table I Distribution of respondents according to sociodemographic characteristics (n=188)

Age Group (In years)	Frequency (In number)	Percentage
15-34	146	77.65%
≥ 35	42	22.34%
Literacy Level		
Illiterate	15	8%
Primary	26	14%
Secondary	53	28%
SSC	61	32%
HSC	13	7%
Graduate and above	20	11%
Family Type		
Joint	64	34.04%
Nuclear	88	46.81%
Extended	36	19.15%
No. of Children		
0-2	59	62.75%
>2	35	37.25%
Socioeconomic Status		
Lower Class	18	9.57%
Lower Middle Class	76	40.43%
Upper Middle Class	80	42.55%
Upper Class	14	7.45%

Table II Distribution of the respondents according to use of contraception (n=188)

Use of Contraception	Frequency	Percentage
Using	130	69%
Not using	40	21%
Discontinued	18	10%

While intending to learn about contraceptive practices of the reproductive age group women of Fatikchari Upazila, it was found that majority (69%) women were using contraception at that moment while 21% are not using and 10% of them have discontinued using. The most common form of contraceptive method used by the participants was OCP (71%) when the second most common form was barrier method (25%). Birth spacing was found to be the commonest reason (49.23%) for using contraceptives and family completion was the second most common (33.85%). Maximum number of the participants (55.63%) did not report on suffering from any adverse effect. Among the participants who have suffered from adverse effects (44.62%) majority complained of suffering from headache, nausea, vomiting, breast tenderness (38%) when the second most common complain was irregular per vaginal bleeding (21%). A vast difference was found when they gave opinion on adopting permanent method of contraception as there was a whopping difference between yes (6.39%) and no (93.62%). The commonest reason for not using contraceptives was they want more children (38%) when the second common reason was husband stays away (24%) and about 14% worry about the side effects. Same kind of reasoning was noticed while looking for causes of discontinuation of using contraceptive methods.

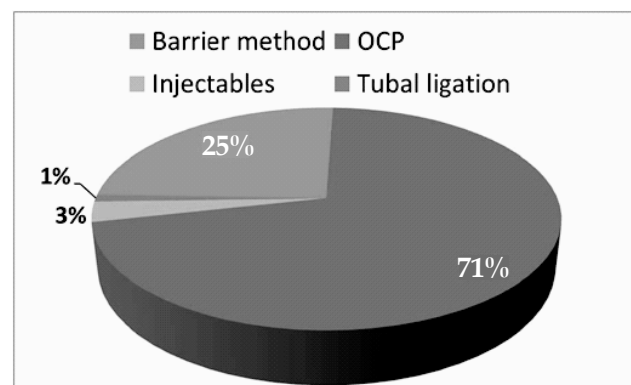


Figure 1 The common type of contraceptive methods adopted by reproductive age group women in Fatikchari Upazila

Table III Common adverse effects among women using contraception (Out of 84)

Common adverse effects	Frequency	Percentage
Headache/Nausea/Vomiting/		
Breast Tenderness	32	38%
Irregular per vaginal bleeding	18	21%
Abdominal Pain	15	17%
Amenorrhea	8	10%
Allergy/Allergic rashes	8	10%
Weight loss	3	04%

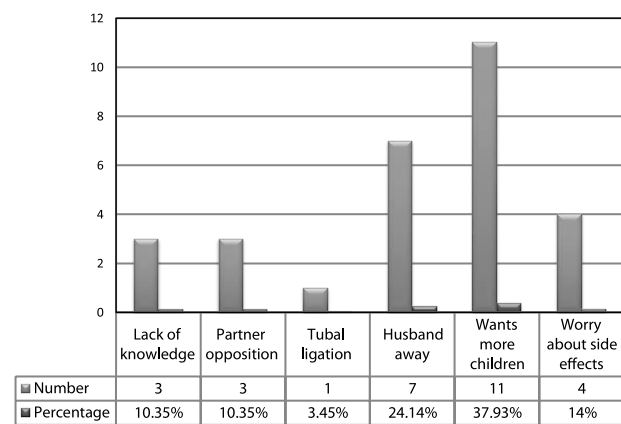


Figure 2 Number of women not using contraceptive methods for various reasons

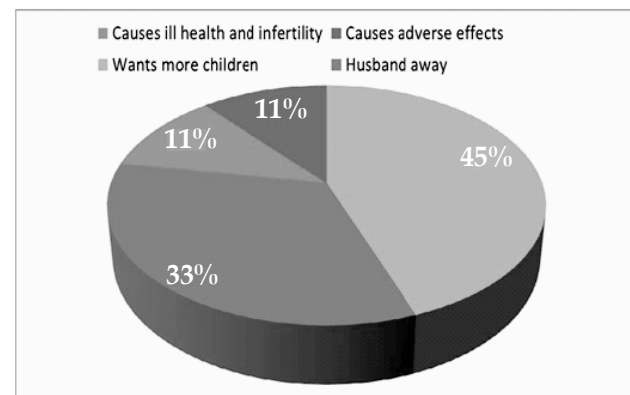


Figure 3 The reason for discontinuing the family planning method

DISCUSSION

Bangladesh is frequently referenced as a prototype for developing nations seeking to establish robust family planning initiatives and with good reason. With one of the world's most sturdy and effective national family planning programs, the nation saw a 40 percent

increase in contraceptive prevalence in just 33 years, from 7.7 percent in 1971 to 48 percent in 2004. As demonstrated by the drop in the overall fertility rate from 6.87 to 2.14 per woman and the drop in the maternal mortality rate from 570 to 173 per 100,000 live births during this period, Bangladesh has made significant progress in improving the health of mothers and children. But lately, Bangladesh's advancement has stalled. The nation's use of contraception has only gone up by six percentage points, from 48 to 54 percent, over the last 19 years (From 2004 to 2022).⁵

Among 188 participants of the current study, the mean age was found to be around 30.5(±4.53) years which was a little higher than 25.53 (± 6.34) the mean age found in a study conducted among the married Rohingya refugee women of reproductive age.⁶ The most common age group in the present study was 25-34 (45.74%) years however, in another similar type of study conducted in Rangpur division, the common age group was found to be 20-24 (31.6%).⁷ Majority of participants of the current study had completed their study up to SSC level (32%) while the women of Rangpur area were found to be less educated as their education status was most commonly Secondary incomplete (41.6%).⁷ Close proximity was found while distributing the participants according to their occupation, in present study, majority (99.3%) were housewives which is similar to the study conducted in Rangpur where majority of the participants were housewives (94.8%) as well.⁷ Commonest family type was found to be nuclear family (46.81%) which is quite similar to the results of a study conducted in west Bengal, India where nuclear family was the commonest type as well (65%).⁸ Maximum participants had at least two children (35.1%) which is also the scenario in West Bengal where maximum participants had at least two children (60%).⁸

The prevalence of using contraceptive methods was found a quite impressive 69% which is close to the findings of a study conducted from evidence of BDHS 2014 data where the prevalence was 62.4%.¹ Oral contraceptive pill was the most common method of contraception used by the participants with a whopping 71% rate, which is similar to the findings of an evidence based study.⁴ Birth spacing (49.23%) and family completion (33.85%) were the two most popular reasons for using contraception and this finding coincides with a study on prevalence and determinants of contraceptive method use among Bangladeshi women of reproductive age.⁹ Although majority of the

participants gave history of not suffering from any adverse effects (55.63%) among the few having adverse effects, the commonest was headache, nausea, back pain which was found to be similar to a qualitative explorative study conducted in Kitwe district of Zambia.¹⁰ There was very few participants who were willing to adopt permanent method of contraception as majority (93.62%) of them denied to it, this finding coincides with a systemic review study conducted in 2017 as that reported a decline in the use of long acting and permanent methods over the last two decades.⁴ Those who do not use any contraceptive methods reported that they want more children (38%) and afraid of side effects (14%). A cross sectional study performed among the Rohingya refugee women in Bangladesh showed some interesting reasons for the women regarding not using contraceptives as they identified husband's disapproval (40%) and to keep bearing children until they get a son (58%) to be the main reasons.⁶ As for those who discontinued using contraception gave their reason to be wanting more children (45%) and husband away (33%). This result is quite identical with an qualitative explorative study conducted in Kitwe district of Zambia as the main reasons for discontinuing contraceptive methods were the desire to get pregnant and the fear of unpleasant side effects, including excessive bleeding or prolonged menstruation, headache, dizziness, lower abdominal/back pain and weight gain.¹⁰

LIMITATIONS

Some proportion of different species in different sociodemographic groups are not available. In addition the study was of short duration of time with small sample size and it was a cross sectional study design.

CONCLUSION

70% of the study population uses contraceptive device and the common is OCP (71%). About 1/3rd of the population not using contraceptives was due to their desire to have more children. However the percentage of contraceptive use was more among the middle class population and the common adverse effects were headache, nausea and vomiting.

RECOMMENDATION

To find out the lack of awareness of contraceptive use about different contraceptive methods which can be ascertained by a nationwide survey.

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AUTHORS CONTRIBUTION

Conception and design - MEH, SRJ
Data collection - MEH, MTZ, SD, AA
Analysis and interpretation of data - MEH, SRJ
Manuscript preparation - MEH, MTZ, SRJ, SD, AA.

DISCLOSURE

All the authors declared no conflicts of interest.

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Clinical Profile and Outcome of Dengue Patients Admitted to Pediatric Department at Marine City Medical College and Hospital, Chattogram

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GRAPHICAL ABSTRACT

Clinical Profile and Outcome of Dengue Patients Admitted to Pediatric Department at Marine City Medical College and Hospital, Chattogram

Cohort	Results	
<p>Study design : Hospital based cross sectional observational study</p> <p>Sample Size □ - □106</p> <p>Sex :</p> <p>Male □ - □ 51</p> <p>Female □ - □ 55</p> <p>Age range □ - □ 0-12</p> <p>Residence</p> <p>Urban □ - □ 86 (81%)</p> <p>Rural □ - □ 20 (19%)</p> <p>Seasonal variation</p> <p>September □ - □ 52 (49%)</p>	<p>Notable clinical features</p> <p>Fever > 5 days □ 79 (74%)</p> <p>Hypotension □ 40 (38%)</p> <p>Oliguria □ 30 (28%)</p> <p>Skin Rash □ 49 (46%)</p>	<p>Common Lab abnormalities</p> <p>Thrombocytopenia □ 78 (74%)</p> <p>Anaemia □ 48 (45%)</p> <p>NSI Ag □ 56 (52%)</p> <p>PCV increased □ 49 (42%)</p> <p>CXR Bronchopneumonia □ 36 (34%)</p>
	<p>Outcome</p> <p>□ Cured □ - □ 64 (60%)</p> <p>□ Improving □ - □ 26 (25%)</p> <p>□ Not improving □ - □ 15 (14%)</p> <p>□ ICU referral □ - □ 01 (0.94%)</p>	

Conclusion: No paediatric age is immune. Half of children developed skin rash, anaemia and high PCV. Fever >5 days and thrombocytopenia were present in three-fourth of patients. In half of admitted patients had NSI positive Ag. Bronchopneumonia, oliguria and Hypotension were present in more than one-third of patients. However timely standard care decreased mortality.

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ABSTRACT

Background: Dengue fever, caused by the mosquito-borne dengue virus and transmitted by Aedes mosquitoes, with five virus serotypes. Dengue affecting over 130 countries, caused a significant outbreak in Bangladesh in 2019, with over 100,000 hospitalizations and 129 deaths. A 2023 outbreak focused on pediatric cases, prompting a need for detailed clinical profiling due to hypothesized increased severity and atypical manifestations in children during the outbreak. The study aims to investigate the clinical profile and outcome of dengue patients admitted to the pediatrics department at Marine City Medical College and Hospital, Chattogram, Bangladesh.

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Materials and methods: A cross sectional observational study was conducted in the Department of Pediatrics at Marine City Medical College and Hospital in Chattogram, Bangladesh between December 2022 to February 2023. The study used purposive sampling to examine 106 children aged 0-12 years with dengue fever. All patients underwent detailed history taking, Physical examination and hematological profiling. Children aged 0-12 years with dengue fever, features and warning signs were included. Patients with no probable dengue-like features as well as did not have supportive lab evidence were excluded.

Results: The most affected children were aged 6-12 (49.23%), with a higher prevalence in urban areas (81.13%). Male participants constituted 51.89%. Notable symptoms included fever <5days (74.53%), vomiting (39.62%) Hypotension (37.74%) and bleeding manifestations (9.43%) indicated potential symptoms. Laboratory findings positive results for Dengue diagnostic tests (52.83%) showed abnormalities in urine analysis (63.89%), and complications like anemia (45.28%) and thrombocytopenia (73.58%). Outcome measures revealed that 60.38% were discharged with advice (Cured), 24.53% were discharged on request (Improving), 14.15% were discharged with risk bond (Not cured), and 0.94% were referred to ICU. Associated diseases included bronchopneumonia (33.96%), UTI (21.70%), Rickettial fever 5.66%, AWD 4.72%, Enteric fever 3.77% and dengue shock syndrome (1.89%).

Conclusion: This study on 106 paediatric dengue patients reveals a higher vulnerability in children aged 6-12 years, particularly in urban areas. The early diagnosis, timely referred to the tertiary level hospital and initiation of intervention can prevent the complication which may leads to lower mortality rate in paediatrics age group.

Key words: Clinical profile; Dengue; Outcome; Pediatric patients.

INTRODUCTION

Dengue fever is a mosquito-borne tropical disease caused by the dengue virus.¹ The onset of symptoms typically occurs within a period of 3 to 14 days after infection.² These symptoms may manifest as a high fever, headache, vomiting, muscle, and joint pains, along with characteristic skin rash.^{1,2} The recovery period generally spans two to seven days.¹ Dengue is transmitted by various species of female mosquitoes, primarily from the *Aedes* genus, particularly *Aedes aegypti*.^{1,2} The virus is characterized by five serotypes, with infection by one type conferring

lifelong immunity to that specific type but only short-term immunity to the others.^{1,3,4} Subsequent infection with a different type increases the risk of severe complications.¹ Diagnostic tests, including the detection of antibodies to the virus or its RNA, are available to confirm the diagnosis.² An estimated 500,000 individuals with severe dengue infection require hospitalization annually and 90% of them are children <5 years of age. Without proper treatment, the case fatality rate in severe dengue exceeds 20%, but with timely intervention, it can be reduced to <1%.⁵ Children with dengue exhibit varying clinical presentations worldwide, with fever being the most common symptom irrespective of type and severity. However, there is variation in other symptoms and signs associated with fever. Over the past 60 years, the dengue virus has spread to over 130 countries, resulting in nearly 10,000 deaths and 100 million symptomatic cases annually.^{6,7} More than 50% of the global population is at risk of dengue transmission, with the majority in Asia, followed by Africa and America.⁸ It stands as one of the leading causes of death among children in Southeast Asia.⁶ In Bangladesh, the first recognized dengue outbreak occurred in the capital city, Dhaka, in 1964.⁹ Subsequently, sporadic dengue cases were reported until 2000, when the first major epidemic occurred across major cities and towns in Bangladesh.¹⁰ In 2019, the most extensive and deadliest outbreak of dengue in the history of Bangladesh took place, with over 100,000 people hospitalized and 129 recorded deaths.¹¹ The unofficial number of cases and deaths might be higher due to the poor health reporting system in the country. The high mortality was suspected to be associated with a high incidence of Dengue Shock Syndrome (DSS) and secondary dengue infections.¹² In 2023, a similar outbreak of dengue occurred in Bangladesh, and it affected children. We hypothesized that increased severity and atypical clinical features suggestive of multi-system involvement among children with dengue characterized the ongoing outbreak. This study aimed to investigate the clinical profile and outcome of dengue patients admitted to the pediatrics department at Marine City Medical College and Hospital, Chattogram, Bangladesh.

MATERIALS AND METHODS

This cross-sectional study was carried out and examined 106 children at the Department of Pediatrics within Marine City Medical College and Hospital, located in Chattogram, Bangladesh. The study spanned

three months, commencing from December 2022 to February 2023. Participants were selected using purposive, convenient sampling methods. Thorough clinical assessments and necessary investigations were conducted on the enrolled patients. Children of any age upto 12 years living in or travelled from dengue endemic area and having probable dengue like features were included. Patients with no probable dengue-like features and children with pre-existing liver diseases were excluded. Informed written consents were taken from guardians.

The dataset encompassed information such as demographical characteristics (Age, gender, etc.) signs and symptoms (Clinical manifestations, including fever, headache, myalgia, arthralgia, body ache, purpura, respiratory complaints, and various bleeding signs). A comprehensive diagnostic evaluation was conducted at our hospital, encompassing various investigations such as CBC, dengue NS1 antigen, dengue IgM and dengue IgG. Additionally, assessments were made for prothrombin time, serum albumin and USG abdomen. Statistical analysis was applied to interpret the data using the Statistical Package for Social Science (SPSS) on Windows. Continuous parameters were expressed as mean±SD, while categorical parameters were represented as frequency and percentage. Necessary permission was taken from the proper authority before start the study.

RESULTS

According to the demography of children in Table 1, most of the 49(46.23%) children were aged 6-12 years and the second most 32(30.19%) children were from the age group 2-5 years, and 25(23.58%) children were aged under two years. More than half of the participants were male (51.89%) and the rest of the children (48.11%) were female. There is a higher prevalence in urban areas (81.13%) than in rural regions (18.87%) of the study area (Table I). In this study, 49.06% of cases occurred in September, whereas 28.30% and 22.64% occurred in August and July (Figure 1). A significant proportion experienced fever for less than five days (74.53%), while other prevalent symptoms included vomiting (39.62%), abdominal pain/joint pain (20.75%), and anorexia/headache/body ache (41.51%). Notably, bleeding manifestations were observed in 9.43% of cases. Blood pressure showed a notable presence of hypotension (37.74%), were also noteworthy, indicating potential complications. Skin survey revealed petechial in 46.23% of cases, providing valuable insights into the diverse clinical presentation

and severity of Dengue cases in the pediatric population under study (Table II). Among the 28 participants, 21.43% exhibited the UGC of W/A with Ascites and organomegaly and 78.57% showed an absence. Urine analysis revealed abnormalities such as Puscell in 63.89% of cases, while most showed average results (66.67%). Positive results for diagnostic tests like ICT for Salmonella (80.0%) participants was 5, NS1 Ag for Dengue (52.83%) participants was 106 and ICT for Dengue (43.86%) whereas participants was 57, indicate the presence of Salmonella infection and Dengue virus. Hematological parameters reveal a high incidence of anemia (45.28%), a decrease in neutrophils (69.81%) and thrombocytopenia (73.58%). Abnormalities in chest X-ray findings, such as opacity (30.19%) and effusion (3.77%), signify potential complications. Prothrombin time increase (20.75%) (Table III). Based on the study outcome, 60.38% of the children were discharged with advice (Cured), 24.53% were discharged on request (Good), 14.15% were discharged on risk bond (Not Cured), and only 0.94% were referred to the Intensive Care Unit (ICU) (Table IV). Regarding dengue-associated diseases among the study participants, most children had bronchopneumonia (33.96%) UTI in 19.81%, Rickettsial Fever 5.66%, AWD (4.72%) Enteric Fever 3.77% and dengue shock syndrome in 1.89%. Other associated diseases were about 4.70% (Table V).

Table I Demographical characteristics of the study childrens (n=106)

Age group (Years)	Frequency (n)	Percentage (%)
<2	25	23.58
2-5	32	30.19
6-12	49	46.23
Sex		
Male	51	48.11
Female	55	51.89
Residency		
Urban	86	81.13
Rural	20	18.87
Month		
July	24	22.64
August	30	28.30
September	52	49.06

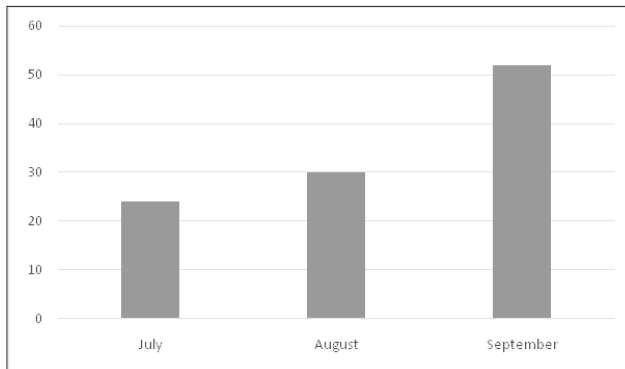


Figure 1 Monthly Distribution of Patient Number

Table II Distribution of participants by signs and symptoms of dengue (n=106)

Variables	Frequency (n)	Percentage (%)
Symptoms		
Fever <5days	79	74.53
Fever >5days	27	25.47
Vomiting	42	39.62
Nausea	13	12.26
Abdominal pain, Joint pain	22	20.75
Anorexia, Headache, Body ache	44	41.51
Bleeding manifestation	10	9.43
Loose motion	7	6.6
Cough	45	42.45
Convulsion	5	4.72
Others	9	8.49
Blood Pressure		
Hypotension	40	37.74
Normal	66	62.26
Urine output		
Good	76	71.7
Less	30	28.3
Skin Survey		
Normal	57	53.77
Petechial Rash	49	46.23

Table III Distribution of participants by UGC and laboratory findings

Variables	Frequency (n)	Percentage (%)
UGC of W/A-Ascites c organomegaly (n=28)		
Present	6	21.43
Absent	22	78.57

Variables	Frequency (n)	Percentage (%)
Lab Findings		
S. albumin (n=6)		
Normal	4	66.67
Decrease	2	33.33
Urine R/E (n=36)		
Normal	24	66.67
Puscell	21	58.33
ICT for Salmonella (n=5)		
Positive	4	80.0
Negative	1	20.0
Ns1 Ag for Dengue (n=106)		
Positive	56	52.83
Negative	50	47.17
ICT For Dengue (n=57)		
Positive	25	43.86
Negative	32	56.14
CBC-HB% (n=106)		
Anemia	48	45.28
Normal	58	54.72
D.C-Neutrophil		
Normal	32	30.19
Decrease	74	69.81
Platelet		
Normal	28	26.42
Decrease	78	73.58
PCV		
Normal	28	26.42
Increase	45	42.45
Decreases	33	31.13
Chest X-ray		
Opacity	32	30.19
Effusion	4	3.77
Normal	70	66.04
Prothrombin Time (n=40)		
Normal	18	16.98
Increase	22	20.75

Table IV Outcome measures and complications of study cases (n=106)

Outcome	Frequency (n)	Percentage (%)
D c Advice	64	60.38
DOR	26	24.53
DORB	15	14.15
Referred in ICU	1	0.94
Cured		
Good		
Not Cured		
ICU referred		

Table V Distribution of participants by dengue e associated diseases (n=106)

Dengue Associated Disease	Frequency (n)	Percentage (%)
Bronchopneumonia	36	33.96
UTI	21	19.81
Rickettsial Fever	6	5.66
AWD	5	4.72
Enteric Fever	4	3.77
Dengue Shock Syndrome	2	1.89
Others	5	4.70

DISCUSSION

This study provides valuable insights into the recent Dengue epidemic's impact on pediatric patients. The research sheds light on various aspects of Dengue, including age distribution, clinical presentations, complications, and outcomes. The predominance of Dengue cases among children aged 6-12 years, 46.23% of the study children, aligns with similar observations in previous studies, suggesting a higher susceptibility in this age group to severe Dengue infection.^{13,14} In our study, this urban-centric pattern aligns with the known association between Dengue transmission and urban environments, emphasizing the role of population density and water storage practices. More than 81% of the study population belonged to urban areas in this study (Table I). The monthly distribution of cases, with a peak in September (49.06%), corresponds to the established seasonal pattern of Dengue, with increased transmission during the post-monsoon period. This temporal trend underscores the significance of heightened surveillance and preventive measures during specific times of the year. Such variations highlight the dynamic nature of Dengue epidemiology and the need for region-specific analyses. The male-female ratio was almost similar, where 51.89% of children were female, and the rest of 48.11% of children were male (Table I). This means that, in the given data, there are about 1.078 males for every female.

In contrast, the previous study showed similarity as the study's identification of shock as the primary presentation of severe Dengue infection in 4.72% of cases contrasts with rates reported in the previous study.¹⁵ The revised classification based on the 2011 WHO guidelines reflect the ongoing efforts to refine diagnostic criteria, emphasizing the importance of staying updated with the evolving understanding of Dengue pathophysiology.^{13,16} Bleeding manifestations,

observed in 10(9.43%) cases, present a lower incidence than previous study.¹⁷ The poor correlation between the tourniquet test, bleeding, and thrombocytopenia underscores Dengue's complexity of bleeding patterns.¹⁸ Secondary dengue infections' association with severe outcomes echoes the findings of Wichmann et al. highlighting the critical role of immune responses in dengue pathogenesis.¹⁴ The study's acknowledgement of the poor correlation between thrombocytopenia, bleeding, and plasma leakage adds nuance to our understanding of Dengue's pathophysiological complexities. The discussion on management strategies, including platelet transfusion criteria, provides a targeted approach in severe cases. Identifying typical manifestations such as coryza, splenomegaly, hemophagocytic syndrome, and myositis reflects the diverse clinical spectrum of Dengue, as seen in studies by Faridi et al.¹⁹ Hepatic dysfunction, GI complications, and co-infections are discussed, emphasizing their potential to modify Dengue's clinical presentation. In our study, we found that bronchopneumonia was the most commonly associated disease (33.96%) and the second most common was UTI (19.81%) in the study children (Table V). More than 60% of the study patients were discharged with advice, and just one patient needed to be referred to ICU. Identifying factors associated with poor outcomes, including acute respiratory distress syndrome, acute kidney injury, fluid-refractory shock, myocarditis and disseminated intravascular coagulation, adds granularity to understanding Dengue's impact on pediatric patients.²⁰ The mortality rate of 2.3%, lower than in previous studies is attributed to increased public awareness, improved health-seeking behaviour, and timely interventions, underlining the positive impact of community engagement in Dengue management.^{13,15}

LIMITATIONS

This study's findings are limited by its single-center design, which may not fully represent the diversity of Dengue cases in pediatric populations across other regions or healthcare settings. Additionally, the reliance on retrospective data collection may introduce biases and inaccuracies, affecting the generalizability of the results.

CONCLUSION

In conclusion, this study highlights the varied clinical presentation and outcomes of 106 pediatric dengue patients in a recent outbreak. The findings emphasize

the vulnerability of children, particularly those aged 6-12 years, consisting 49.23% of the total, to severe Dengue, with urban areas most affected (81.13%). The study underscores the importance of early diagnosis, timely intervention and region-specific preventive measures to mitigate severe outcomes. While the mortality rate was lower than in previous studies, the presence of complications such as shock and co-infections indicates the need for continued vigilance and improved clinical management to reduce morbidity and mortality in pediatric dengue patients.

RECOMMENDATIONS

Overall, this research enhances our understanding of Dengue in pediatric populations and informs future public health strategies.

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AUTHORS CONTRIBUTION

Conception and design - MSU, BRM
Data collection - MSU, BAS, MNAS, IJ, ST
Analysis and interpretation of data - MSU, MTM
Manuscript preparation - MSU, BRM, MNAS, IJ, ST, MTM, BAS.

DISCLOSURE

All the authors declared no conflicts of interest.

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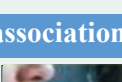
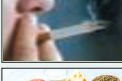

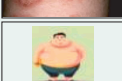
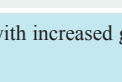
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Evaluation of Physiological, Psychological and Lifestyle Factors Associated with Hair Graying among Physicians: A Multicenter Study

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GRAPHICAL ABSTRACT

Evaluation of Physiological, Psychological and Lifestyle Factors Associated with Hair Graying among Physicians: A Multicenter Study

Cohort	Results
Study design : Cross sectional descriptive study Sample Size □ - □325 Male □ - □190 (58.5%)  Female □ - □135 (41.5%)  Age < 25 □ - □07 (9%) Common scalp region affected Male : Frontal and temporal  Female : Frontal and parietal 	Significant association with Graying of hair ❖ ≥ 25 years  ❖ Lack of exercise  ❖ Oil use  ❖ Stress / Depression No Significant association □ Smoking  □ More protein intake  □ Skin disease  □ BMI > 25 
Conclusion: Increase in age, oil use, lack of exercise and psychological stress are associated with increased graying of hair while dietary habit, BMI, skin disease and smoking has no significant association.	

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ABSTRACT

Background: Hair graying or Canities is a natural process of aging. Everyone develops gray hair with advancing age. So, it can't be considered as a disease. Besides aging, certain other factors can influence hair graying. The aim of the study was to investigate the physiological, psychological and lifestyle-modifying factors associated with hair graying among physicians.

Materials and methods: A descriptive cross sectional study was conducted on 400 physicians who answered a survey on hair graying from December 2022 to February 2023 in BGC Trust Medical College and Hospital and Chattogram Maa-O-Shishu Hospital Medical College.

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The sex, age of onset of hair graying, genetic history of hair graying among parents, presence of skin disease, smoking and alcohol history, psychological condition, concurrent medical diseases, dietary habits, exercise habits, history of oil used on scalp were taken into account. The data collectors approached the participating physicians after receiving their verbal consent. The participants then filled up the questionnaire. After collecting the questionnaire the data were input into IBM SPSS (Version 24) and analyzed by Pearson's Chi square. Pearson correlation coefficient was used to find relation between hair graying and presence of co-morbidities.

Results: In this study, a total of 400 samples were included out of which 215(53.8%) were male and 185(46.3%) were female participants. Hair graying was highest in the age group of 30 – 40 years. 85(26.1%) had history of seborrhoeic dermatitis. 205(63.07%) suffered from psychological stress. 18(5.53%) consumed 2 serving fruits and 3 serving vegetables daily. 88(27.07%) did exercise >150 min weekly. 28.61% accepted that they had been suffering from hair graying after "COVID-19". Hair graying was common among those with blood group "B" positive 140(43.07%).

Conclusion: The study concludes that the hair graying was more in male compared to female participants. Stress is a contributory factor of hair graying. 28.61% stated that their hair started graying post "COVID – 19". Blood group "B" was the most prevalent blood group in our study.

Key words: COVID-19; Hair graying; Seborrhoeic dermatitis.

INTRODUCTION

Skin tone and hair color play a significant role in overall appearance, social and sexual communication.¹ It is a natural age related component. Hair graying or canities is a part of aging which typically starts around 34.29.6 years (In whites) and 43.9 10.3 years (In blacks). Premature Hair Graying of Hair (PGH) is said to occur before age of 20 years (In Caucasians), 25 years (In Asians) and 30 years (In Africans).²

DOPA oxidase positive follicular melanocytes are the primary site of pigment production. Hair color depends on eumelanin content of hair, the more the eumelanin content, the darker is the color of hair.^{3,4} Family history, smoking and obesity were found to be associated with premature hair graying.⁵ According to a theory, hair growth after stress-induced telogen effluvium may provide the appearance of accelerated graying in people who have already started to do so.⁶

In Asians premature hair graying is less evident, may be due to the presence of higher levels of integral lipids, fatty acids, cholesterol and wax esters than Caucasians and African-Americans do. Additionally, the thicker lipid layer on Asian hair makes it more resistant to UV deterioration. Around the fourth and fifth decades of life, lipid levels start to decline with aging, this decline appears to be more prominent in women than in males.^{7,8}

The present study focused on age independent hair graying instead of premature hair graying. We sought to investigate the association between hair graying and various physiological, psychological and lifestyle factors among physicians.

MATERIALS AND METHODS

This cross sectional study was carried out in B.G.C.Trust Medical College and Chattagram Maa-O-Shishu Hospital Medical college, from December 2022 to February 2023. Physicians from Interns to Professors who gave consent were included in this study. Those who were absent during data collection and who refused to give consent were excluded.

The ethical clearance of the study was taken from Institutional Ethical Review Board of Chattagram Maa-O-Shishu Hospital Medical College and BGC Trust Medical College. Verbal Consent was taken from the participants prior to data collection. A total of 400 physicians answered the questionnaire from both the institutions.

A detailed history regarding the age of onset of graying, family history of hair graying, smoking and alcohol intake, psychological condition, co-morbidities, dietary history, exercise history were recorded.

Scalp area of onset of graying was recorded by dividing the areas into frontal, parietal, occipital and temporal. History of use of type of oil were recorded. Data were analyzed using computer based on Statistical Package for Social Science (SPSS) 24 version.

Ordinal variables were assigned to a numerical scale for data analysis, smoking history (1= never smoker, 2=former smoker and 3= current smoker) alcohol intake (Male: 1= <14 drinks per week, 2 = 14 drinks per week, 3= >14 drinks per week and for females 1= <7 drinks per week, 2 = 7 drinks per week, 3= >7 drinks per week) dietary history of vegetarians (1= <2 serving of fruit and three serving of vegetable daily, 2= 2 serving of fruit and three serving of vegetable daily) and non-vegetarians (1=65 gm meat per day, 2= >65 gm per day) exercise (1= non exerciser, 2= <150 minutes of moderate aerobic exercise per week, 3 = 150 – 300 minutes of moderate aerobic exercise per week).

Presence of stress, anxiety and depression in those with hair graying was measured by Depression Anxiety Stress Scale (DASS21) scale.

RESULTS

A questionnaire was distributed and completed by a total of 400 physicians. Among them 215 (53.8%) were male and 185(46.3%) were female. The numbers of physicians with hair graying were 325. The incidence of hair graying was 81.25%.

Among 325 cases, 135 (41.5%) were female and 190 (58.5%) were male. The onset of hair graying was prevalent among physician's aged between 30 to 40 years (27%) and premature hair graying i.e. graying before 20 years was 7% displayed in (Figure 1).

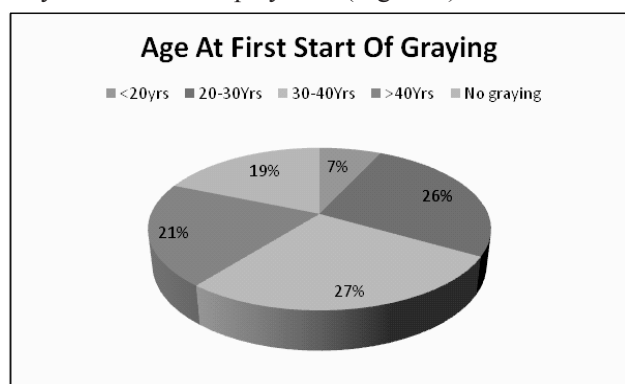


Figure 1 Distribution of age at onset of hair graying

Among the physicians with hair graying, 142 (43.7%) physicians suffered from obesity (BMI=30.0- 34.9) and 124 (38.15%) were overweight (BMI = 25-29.9).

Among those who were smoker 30 (9.23%) physicians with hair graying were current smokers and 8(2.46%) were former smokers.

17 (5.23%) physicians with gray hair drank <14 drinks of alcohol per week and were all males. p-value was 0.043 which was <0.05. So, hair graying showed a statistical significance with alcohol intake.

211(64.92%) of physicians with hair graying were non-exercisers, 26 (8%) of physicians with hair graying did exercise <150 minutes per week and 88 (27.07%) did exercise for 150 -300 minutes. Non-exercisers showed a significance with hair graying (p=0.027).

Among those who applied oil on scalp, 168(51.6%) of physicians with hair graying were coconut oil users, 26(8%) used olive oil, 16(4.9) used mustard oil, 5(1.53%) used fenugreek oil, 6(1.8%) used castor oil and 103(31.6%) didn't use any oil described in (Table I).

Table I Demographic and lifestyle pattern of physicians with hair graying

Variables	Graying Hair n=325(%)	Chisquare Value	p Value
Gender			
Male	190 (58.5)	15.478	0.000
Female	135 (41.5)		
BMI			
<18.5	8 (2.46)		
18.5-24.9	13 (4)		
25-29.9	124 (38.15)	8.465	0.076
30-34.9	142 (43.7)		
>35	38 (11.69)		
Smoker			
Current smoker	30 (9.23)		
Former smoker	8 (2.46)	2.622	0.105
Never smoked before	287 (88.30)		
Alcoholic			
<14 drinks per week	17 (5.23)		
14 drinks per week	0	4.097	0.043
>14 drinks per week	0		
Non drinker	308 (94.76)		
Exercise			
NonExerciser	211 (64.92)	9.156	0.027
Exercise <150 min weekly	26 (8)		
Exercise >150 min weekly	88 (27.07)		
Oil			
Coconut oil	168 (51.69)		
Olive oil	26 (8)		
Mustard oil	16 (4.92)	14.920	0.037
Fenugreek oil	5 (1.53)		
Castor oil	6 (1.84)		
None	103 (31.69)		

Regarding the skin conditions, 85 (26.15%) physicians with gray hair had history of seborrhoeic dermatitis.

Considering the dietary habits, 18 (5.53%) physicians with hair graying took 2 serving of fruit and 3 serving of vegetable daily, 22 (6.76%) of physicians with hair graying took <2 serving of fruit and 3 serving vegetable daily, 114 (35.07%) physicians took 65 gm of meat daily and 171 (52.61%) took > 65gm meat daily. In our study, preference of meat consumption >65 gm daily was significantly higher in physicians with hair graying. 93(28.61%) of physicians with hair graying had onset of hair graying after being affected with "COVID-19". Among those with gray hair, 31 (9.53%) physicians suffered from depression, 17.23% from anxiety and 45.84% from stress. Stress showed significant relationship (p=0.000) with hair graying shown in (Table II).

Table II Disease condition, dietary factors and psychological conditions related to hair graying

Characteristics	Graying Hair n=325 (%)	Chi square Value	p Value
Skin disease			
Seborrhoeic Dermatitis	85 (26.15)		
Psoriasis	10 (3.07)		
Skin Cancer	2 (0.61)		
No skin disease	228 (88.61)		
Dietary habit			
2 serving fruits and 3 serving vegetables daily	18 (5.53)		
<2 serving fruits and 3 serving vegetables daily	22 (6.76)	1.856	0.601
65 gm of meat daily	114 (35.07)		
> 65gm meat daily	171 (52.61)		
Psychological Condition			
Depression	31 (9.53)		
Anxiety	56 (17.23)	29.229	0.000
Stress	149 (45.84)		
None	89 (27.38)		
COVID-19			
Graying after COVID	93 (28.61)	22.658	0.000
Graying before COVID	232 (71.38)		

133 (40.92%) physicians with gray hair had paternal history of premature hair graying shown in (Figure 2).

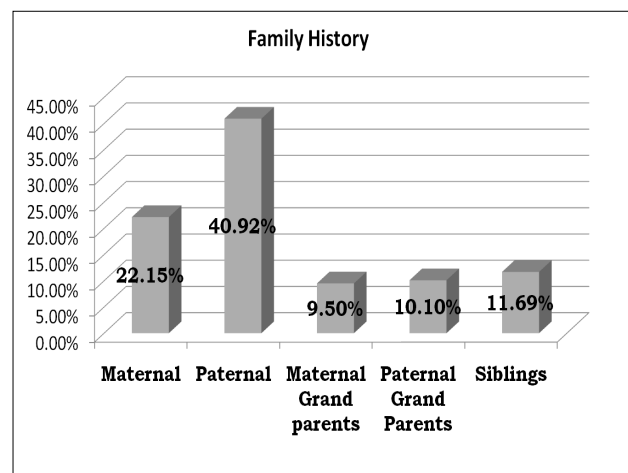


Figure 2 Family History of premature hair graying in physicians with gray hair

Among 190 male physicians with gray hair, 19.70% admitted that their temporal area of scalp grayed first followed by parietal, frontal and occipital.

Among 135 females with gray hair, 19.40% of female physicians admitted that their frontal area of scalp grayed first followed by parietal, temporal and occipital shown in (Figure 3).

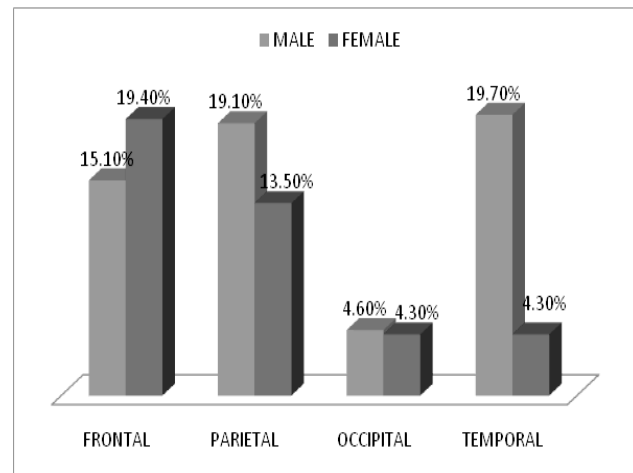


Figure 3 Distribution of Gray Hair with Scalp region

In this study, participants with hair graying had blood group B+ ve 140 (43.07%) prevalently. None of the blood groups exhibited a significant value with hair grayingshown in (Table IV).

Table IV Distribution of blood grouping among hair graying

Blood Group	Hair graying present	Hair graying absent	Chi Square Value	p Value
B+ ve	140 (43.07)	30	0.236	0.627
O+ ve	84 (23.86)	25	1.723	0.189
A+ ve	64 (19.69)	13	0.218	0.640
AB+ ve	29(8.920)	7	0.012	0.910
			Fisher Exact test Value	
AB- ve	2 (0.61)	0		1
A-ve	3 (0.92)	0		1
O- ve	3 (0.92)	0		1

*As participants with AB - ve, A- ve and O -ve without hair graying were '0' Chi square test couldn't be done. Fisher exact test was done for these blood groups as participants were less than 5.

169 out of 325 physicians stated that they suffered from certain co morbidities. 64(37.86%) of physicians with hair graying suffered from Hypertension, 36(21.30%) suffered from Diabetes Mellitus. There existed a negative co-relation between co-morbidities and hair graying and the value was $r = -0.042$. p value was not significant showed in Table V.

Table V Correlation between Co-morbidities and Graying hair (n =169)

Co - morbidities	Graying n=169(%)	Pearson Correlation Coefficient(r)	p Value
Diabetes Mellitus	36 (21.30)		
Hypertension	64 (37.86)		
Liver	2 (1.18)		
Hypothyroid	4 (2.36)	r = - 0.042	0.573
# Malignancy	3 (1.77)		
Alzheimer	2 (1.18)		
\$ Other	28 (16.56)		
Diabetes Mellitus and Hypertension	30 (17.75)		

\$ Other refers to Chronic heart diseases, Coronary artery diseases, Cerebrovascular diseases, Peripheral artery disease, previous history of Tuberculosis.

Malignancy refers to Hodgkin lymphoma and Melanoma.

DISCUSSION

This study revealed that the incidence of gray hair was more among males compared to that of females. The age of onset of graying of hair around 20 to 30 years was 26% and around 30 to 40 years was 27 % and above 40 years was 21% which is more or less similar to a study done in Korea. Interestingly there was also similarity found in the onset of scalp area of graying that is, frontal area grayed first in female whereas temporal area grayed first in male.⁹

40.92% of physicians with gray hair had paternal history of early hair graying followed by maternal history (22.15%). There was no significant association between gray hair and family history, but significance with family history was found in another study.¹⁰

Hair graying was more among obese (43.7%) and overweight (38.15%) revealed in the present study which was also found in study in Korea.¹¹

Erdogan et al. demonstrated that hypertension showed a significant relationship with hair graying. In the current study, physicians with hypertension did not exhibit significance with hair graying.¹²

149 (45.84%) of physicians with stress showed a significant correlation with hair graying. Stress is one of the factors associated with hair graying found in other studies.^{13,14}

211 (64.92%) of physicians with gray hair were non-exercisers and conveyed a greater significance with hair graying which was also revealed in other similar study.¹⁴ 171 (52.61%) physicians those who consumed > 65 gm meat daily, followed by 114 (35.07%) physicians those who took 65 gm of meat daily were more prone to hair graying. 18 (5.5%) physicians with gray hair consumed 2 serving fruits and 3 serving vegetables daily. A catalase-rich food like spinach in one's diet has been proposed as a natural remedy for diminishing the graying of hair. In addition, there are now commercially accessible nutritional supplements that contain catalase in its pure form, along with tyrosine, or consist of plant extracts that purportedly enhance catalase activity.¹⁵ As Bangladeshis are more inclined to non-vegetarian diet, it was not possible to make a comparison with pure vegetarians. So, it can be assumed that vegetables and regular fruits intake has a remarkable impact on delaying hair graying.

LIMITATION

As it is a multicentered study, more centers could be included. Only physicians of two centers were included, so the result of the study may not be representative of the general population.

CONCLUSION

Obese and overweight had higher rate of early hair graying. Hair graying started at the age of 30-40 years in 27% of participants. Non exercisers had early hair graying. Coconut oil users on scalp were more in this research. Hair graying was less among those who consumed 2 serving of fruits and 3 serving of vegetables daily. Hair graying was more in those who consumed >65gm of meat daily. Male had parietal and temporal area and female had frontal and parietal area of hair graying onset. Graying was more among hypertensive patients. Participants with Blood group B positive were more in this research.

RECOMMENDATION

Hair graying can be influenced by genetic factors in addition to various other physiological, psychological and lifestyle modifying factors. Further study with larger samples and from general population is required to confirm these findings.

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AUTHORS CONTRIBUTIONS

Conception and design - HRB

Data collection - HRB, HB, SRC

Analysis and interpretation of data - HRB, SRC, MA, RH

Manuscript preparation - HRB, SRC, MA, RH.

DISCLOSURE

All the authors declared no conflicts of interest.

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Delayed Diagnosis of Cerebral Tumour in a Patient with Chronic Kidney Disease : A Rare Case Report and Literature Review

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ABSTRACT

Background: Glomerulonephritis (GN) especially Membranous Nephropathy (MN) and Minimal Change Disease (MCD) have sometimes association with solid tumours of Gastrointestinal Tract (GIT) Lung, prostate, lymphoma and leukemia especially in elderly male patient. When sudden deterioration of renal function occurs in a patient with Chronic Kidney Disease (CKD) at earlier age between 18 years to < 60 years, clinician usually tries to find out Prerenal cause, Rapidly Progressive Glomerulonephritis (RPGN) or Acute Interstitial Nephritis (AIN).

Case Presentation: Here we report a case of 28 year old female patient presented with respiratory distress, marked ascites, generalized scaly skin lesions, dysphagia, marked weight loss with sudden increase in azotemia. Renal biopsy could not be done because of small size kidney and uremia. The common secondary cause like lupus was suspected clinically but could not be confirmed. The ascites fluid study revealed normal and CXR P/A and CT chest showed bilateral consolidation. However some of tumour markers were significant for which GIT and liver screening were done with no positive result. Her neurological examination was normal and she was conscious with Glasgow-coma score of 15/15. She was treated with steroid empirically. Her skin lesions disappeared, ascites gradually decreased, lung lesion was also being cleared slowly and azotemia was also partially corrected. She was empirically treated with anti tubercular therapy. She became clinically stable and

patient took discharge from hospital on request. But after 3 days the patient developed left hemiplegia at home. For our utter surprise she was diagnosed as a case of high grade cerebral glioma which was beyond our suspicion during clinical course in hospital.

Conclusion: The clinical symptoms and progression of Chronic Kidney Disease (CKD) can sometimes mimic the signs of a brain tumor, potentially leading to delayed diagnosis and treatment of Space - Occupying Lesions (SOL).

Key words: Ascites; Cerebral glioma; Chronic Kidney Disease; Deterioration of renal function; Lung consolidation.

INTRODUCTION

Though CKD in elderly population is mostly due to Hypertension (HTN) and Diabetes (DM) in younger population it is due to Glomerulonephritis (GN) and Focal Segmental Glomerulosclerosis (FSGS) in one third of the cases.¹ CKD patients in India are of two decades younger than European population and present with small kidneys and sometimes unclear etiology.² Though A recent meta-analysis done by researchers in Bangladesh showed quite higher prevalence (22.48%) and more female preponderance (Female vs male 25.32% vs 20.31%) of CKD in Bangladesh but data of Chronic kidney disease of uncertain etiology in Bangladesh is unknown.³

Besides pre renal failure, AIN and RPGN or acceleration of DM/HTN, the cause of renal progression due to Brain tumour is unusual. Sudden deterioration of renal function in a stable CKD patient associated with tumor occurs due to tumor lysis syndrome or chemotherapy drugs or radiation or paraneoplastic syndrome.^{4,5} There are also reports that Animal model bearing tumors may develop features of glomerulopathy and progression of renal failure in CKD patient.⁶

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Most of the time focal or generalized neurological symptoms does not have temporal relation with features of glomerulonephritis or renal failure. When suspicion of malignancy arises due to clinical or biochemical (Biological markers of solid tumour) abnormalities, we try to evaluate causes of GIT or Respiratory tract or haematological system.⁷ We hardly suspect brain tumour. Hence there is a significant delay in the diagnosis of brain tumor early. This failure of suspicion may lead to early mortality before any treatment of brain tumor.⁸

Our objective is to present an unusual case of cerebral glioma in a young female patient with CKD who followed an unusual clinical course simulating flare of systemic disease like tuberculosis or SLE but ultimately succumbed due to cerebral glioma. The pathogenesis is not clearly defined.

CASE PRESENTATION

A 28 year old Bangladeshi female was hospitalized (Marine City Medical College and Hospital, Chattogram, Bangladesh) in April 2022, with the complaints of respiratory distress, generalized scaly skin lesion, difficulty in food intake due to oral ulcer, weakness, no documented fever and significant weight loss. She was a diagnosed case of HTN, DM, Hypothyroidism with CKD. She was having fluctuating S. creatinine since 2019 with hypercholesterolemia.

Physical examination revealed moderate anaemia, enlarged thyroid gland, ascites, no organomegaly and no palpable peripheral lymph nodes. Her bowel and bladder habit was normal.

Her haematocrit was 24.3% and ESR was 14. She had hypoalbuminaemia (2.67gm/dl), hyperuricemia (12.6 mg/dl), mild proteinuria with 15-20 pus cells in urine, 24-h urine protein (577.5 mg/day) high LDH (1080U/L), CA125 (315U/ml), CEA (16.21ng/ml) decreased C3 (0.625g/L) normal C4. Her ANA, Anti dsDNA and Anti smith Ab result were negative. Her upper GI endoscopy, colonoscopy and ascetic fluid study revealed no abnormalities. FNAC of right thyroid swelling was suggestive of nodular Goiter, CXR showed suggestion of Pulmonary edema (Bilateral) / Pulmonary Tuberculosis. CT abdomen showed marked ascites and bilateral mild pleural effusion, evidence of sub-acute small bowel obstruction and right lower lobe consolidation.

After admission, patient was treated with Injection

Methylprednisolone followed by oral prednisolone and other medications as required. Gradually patient's skin condition improved but she developed AKI with Uremic encephalopathy. Patient was treated conservatively and her condition improved (Both physically and biochemical markers. As per patient's clinical condition and investigation reports anti TB drug was given empirically.

Few days later the patient presented with the complaints of weakness in left upper limb followed by lower limb. Gradually patient's conscious level deteriorated, she had seizure attack for twice within short gap. She had CT of brain which showed irregular marinate cystic/marinated SOL having marked perilesional vasogenic oedema. So we started treatment with Mannitol to reduce her cerebral edema. In the meantime her MRI of brain with Magnetic Resonance Spectroscopy (MRS) revealed high grade glioma in right fronto parietal junction with intralesional haemorrhage. Consent was taken from guardian regarding publication of imaging, biochemical and clinical features of patient.

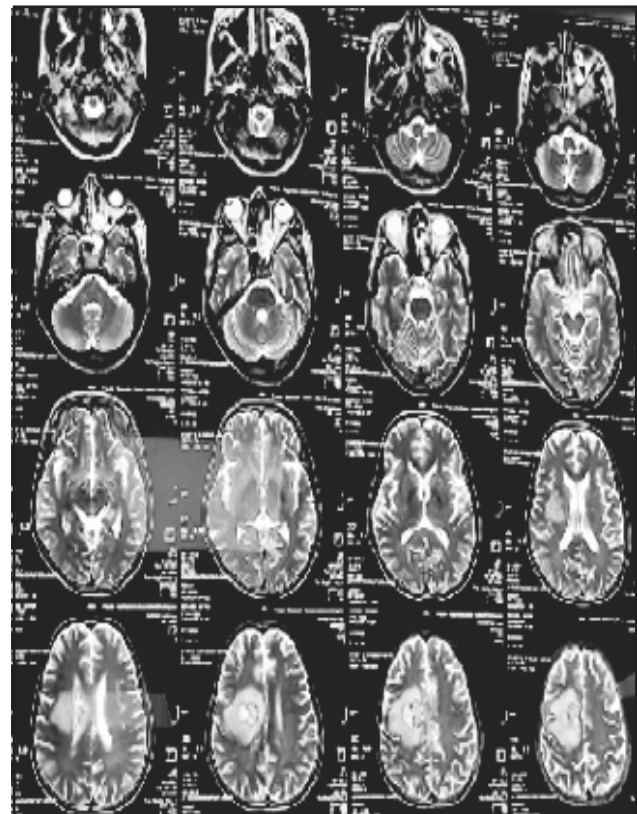


Figure 1 CT of brain of patient

DISCUSSION

Early symptoms of brain tumour are very much nonspecific and the patients present multiple times to different disciplines of medicine before they are subjected to specific investigations for Space Occupying Lesion (SOL) of brain.⁹ Here we present a case of cerebral glioma in a patient of CKD who presented with superadded Acute Kidney injury (AKI). Various impressions like generalized tuberculosis, SLE and even intra-abdominal malignancies were suspected and Patient initially improved with steroid and antitubercular therapy. But until she developed seizures and hemiplegia, she was not investigated for brain SOL. Unfortunately at that time she was diagnosed as high grade glioma and was unfit for any intervention or chemotherapy. Literature review showed that duration of sign-symptoms before diagnosis varies between 7.2 weeks to 52 weeks.¹⁰ Gender variation and mean age varies, also socioeconomic, occupational and environmental factors have no influence.^{11,12} Though in these studies average age varies between 40.2 to 44.2 yrs, our patient is only 28 years house wife hailing from an urban area, brought up in a middle class family with duration between sign-symptoms and diagnosis being less than a week. However in other series even 17 yrs old male was found to develop glioma and male female ratio was found to be 1.5:1.¹³ Whether comorbidity like CKD of unknown aetiology may delay early diagnosis or glioblastoma causes paraneoplastic syndrome is unknown.¹⁴ Literature review showed that glioma in young adult is rare (5.9% of primary brain tumours) and survive longer than those of elderly but our patient died earlier, whether it is due to coexistent CKD it is unknown.¹³ Though there are many case reports of glioma in young adults including efficacy of various intervention but the case report of glioma in CKD is scarce in literature. Even glioma may mimic clinical features of some diseases prevalent in specific location.¹⁵ We also delayed in diagnosing glioma in our case. We tried to exclude generalized Tuberculosis or solid malignancy or SLE in this context which are common in a developing country like Bangladesh, but did not do investigation like MRI to exclude glioma.

CONCLUSION

Clinical features and progression of CKD may masquerade clinical expression of cerebral tumour which may cause delayed treatment of SOL especially in a developing country resulting in early death of patient.

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AUTHORS CONTRIBUTION

Conception and design - PKD

Data collection - IN

Analysis and interpretation of data - PKD, RKS, IN

Manuscript preparation - PKD, RKS, IN.

DISCLOSURE

The author declared no conflicts of interest.

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Information to Authors

Marine City Medical College (MCMC) started its historical and memorable journey in the year 2013. MCMC is one of the famous and reputed Medical College among the Private Medical Colleges in Bangladesh. It is situated in port city, Chattogram. The aim of the MCMC is to attain a standard level in Health & Medical education at home and abroad.

Marine City Medical College is affiliated under Chittagong Medical University & approved by the Ministry of Health & Family Welfare, Government of People's Republic of Bangladesh. A very good number of academicians, researchers and skill professionals are performing in this institute.

Marine City Medical College inaugurated to publish a double blinded, peer reviewed scientific journal from April 2022.

The "Marine City Medical College Journal (MCMCJ)" is a half yearly published eg. April & October accorded with a view to translation of current research into clinical practice. It is the official publication of the Marine City Medical College.

MCMCJ publishes article of authors from any part of the globe, but has a special interest in publishing research articles of authors from Bangladesh and of relevance to developing countries. It publishes Editorial, Original (Research) article, Special article, Review article, Short communication, Case report and Letters on new findings of Medical Science.

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Manuscript (Papers) are submitted to the Managing Editor or authorised persons or by Email at any time. Papers accepted for publication are subjected to peer review and editorial revision. Manuscript should be typed in English (Font size and style: 10, Times New Roman) on one side of white bond paper of A4 size with margins of at least 2.5 cm, using double space throughout. With full title (Title should be concise and informative) accompanied by a cover letter signed by Principal and Co-authors including name, academic degrees, designation, the departmental and institutional affiliation. Complete address, Cell number including Email address of Corresponding author should be mentioned. Not more than 6 (Six) authors will be accepted for all manuscripts.

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(Includes aim or Objectives) Methods (Includes patient population, procedures and data analysis) Results and Conclusion. The abstract should contain the data to support the key findings or conclusions of the study and this should be self explanatory without references to the text. the first time an abbreviated term is used it should be spelled out in full form and follow with the abbreviation in parentheses for example:- CHD (Coronary Heart Disease). Please do not cite any references in the abstract.

3 (Three) to 10 (Ten) key words may be provided below the abstract.

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- Materials and methods (Length range 250-300 words)
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Single digit numbers used in the text should be in words except datas and reference numbers. Maximum length of text may be with in 2000-2500 words (Excluding references). The total number of reference should not be less than 15 (Fifteen) for the original article.

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- Conclusion
- Disclosure

Maximum length of the text may be with in 1000-1500 words (Excluding references). The total number of reference should not be less than 10 (Ten).

Letter

Letter should be brief and to the point with in 500-600 words only.

It is noted that standard abbreviations should be used whenever. The full form for which the abbreviations stands followed by the abbreviation in parenthesis should precede the use of the abbreviation in the text except for standard ones like 45^oc, 35mg/L etc in all types of text.

References

Regarding references please follow the Vancouver style (Uniform requirements for manuscripts submitted to biomedical journals prepared by the International Committee of Medical Journal Editors (ICMJE guideline <http://www.icmje.org>).

Reference citations in the text should be numbered in arabic numerals at the end of the sentence eg [1,2] consecutively in order in which they are mentioned in the text.

Book references should have the name of the authors, chapter title, editors, Book name, the edition, place of publication, the publisher, the year and the relevant pages.

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The first six authors of a work should be named.

Examples

Book reference : Bucholz RW and Heckman JD. Rock wood and Green's Fractures in Adult. In : Kinzler KW, editors. 8th ed. Philadelphia : Lippincott Williams & Wilkins. 2020;3:2639-2688.

Journal reference : Riddel V, Watkinson J, Gazet M. Thyroidectomy : Prevention of bilateral recurrent nerve palsy. British Journal of Surgery. 2021;57(2):8-12.

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Table

- All tables should be numbered using Roman numerals (I, II).
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The persons involved with all the following

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