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Contents

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Central Medical College Journal
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FROM THE DESK OF EDITOR IN CHIEF

In Bangladesh, from 03 January 2020 to 16 March 2023, 2,037,947 confirmed cases of COVID-19 with 29,445 deaths, reported to WHO. As of 13 February 2023, a total of 354,990,838 vaccine doses have been administered. COVID cases are decreasing day by day, but the consequences are continued as multi organ complications. Multi-organ effect of COVID-19 survivors may have a variety of long-term effects on their organs with a lot of names based on organ manifestations. As we are still in pandemic, and at a relatively early stage of a new disease, it is too early to tell what COVID-19 survivors are likely to experience in long periods.

Some researchers commented as SARS, many people will suffer post-viral chronic fatigue syndrome. Why does COVID-19 cause ongoing health problems? Organ damage could play a role. People who had severe illness with COVID-19 might experience organ damage affecting the heart, kidneys, skin, brain and problems with disregulated immunity. More studies will shed light, why these stubborn health problems persist in some peoples.

In the receding time of COVID-19 the members of editorial committee of this journal working hard to regularise the issues of our journal. I am thankful to the reviewers for their efforts to improvise the articles submitted by the authors. We are diehard to improvise the quality of this Journal also.

Prof. (Dr) Md. Mahabubul Islam Majumder
Editor-in-chief
Central Medical College Journal

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EDITORIAL

PROPER TIMING AND QUALITY SLEEP MAINTAIN HEALTHY LIFE

Sleep is the State of unconsciousness from which a subject can be aroused by appropriate stimuli. Depending on EEG criteria - during each night we go through 2 types of sleep that alternate with each other, SWS (Slow-Wave Sleep) and REM (Rapid Eye Movement) sleep. SWS sleep is an exceedingly restful type of sleep. It is typically exemplified in the first hour of sleep that follows a prolonged period of sleep deprivation. With decrease in peripheral vascular resistance (10-30% decreases in BP), decrease in respiratory rate and Basal Metabolic Rate (BMR). Sometimes dreams, even nightmares, occur during SWS sleep. However, dreams are more characteristic of REM sleep. REM sleep also called Paradoxical Sleep. In this type of sleep the person makes rapid movements by his eyes, in spite of the fact that he is sleeping. In a normal night of sleep, episodes of REM sleep lasting 5 to 30 minutes usually appear on the average every 90 minutes. REM sleep is not as restful as SWS. When the person is extremely sleepy, each episode of REM sleep is short and it may even be absent. Conversely, as the person becomes more rested through the night, the durations of the REM episodes increase. In a young adult SWS (NREM sleep) occupies 75-80% of a night sleep time & REM sleep occupies 20-25% of the sleep time. This cycle is repeated at intervals of about 90 minutes throughout the 8 hours or so of night sleep.

The excitatory areas of the upper brain stem, the reticular activating system, simply fatigued during the waking day and became inactive as a result. This was called the passive theory of sleep. An important experiment changed this view to the current belief that sleep is caused by an active inhibitory process. It was discovered that transecting the brain stem at the level of the midpons creates a brain whose cortex never goes to sleep. In other words, a center located below the midpontile level of the brain stem appears to be required to cause sleep by inhibiting other parts of the brain. Complex pathways between the reticular formation of brainstem, diencephalon and cerebral cortex are involved in the onset and maintenance of sleep. Raphe nucleus is situated in lower pons and medulla. Activation of this nucleus results in non-REM sleep. It is due to release of serotonin by the nerve fibers arising from this nucleus. Serotonin induces non-REM sleep. Activation Locus Ceruleus of Pons c produces REM sleep. Noradrenaline released by the nerve fibers arising from locus ceruleus induces REM sleep. Melatonin (released from Pineal Gland) plays a role in day-night alternation of sleep. Alternating “Sleep-Wake Cycles” are under marked Circadian Control. Darkness (e.g., at night) stimulates the Pineal Gland to secrete the hormone melatonin .Melatonin inhibits the RAS & thereby induces SWS. Daylight falling on the retina stimulates the Suprachiasmal Nucleus (SCN) of hypothalamus. SCN inhibits melatonin secretion by the Pineal Gland & thereby it inhibits sleep and promotes wakefulness. Circadian rhythm also dictates your natural bedtime and morning wakeup schedules. Once one get used to going to bed and waking up at the same time each day, his or her brain adapts to this schedule.

Most experts recommend that adults get at least 7 hours of sleep per night. In an adult person daily requirement of sleep is about 6to 9 hours, its vary with age, in case of new born its about 15 - 20 hours, children 10 -15 hours, in old age 5 - 6 hours. Early to bed and wake up in the early morning matches our biological sleep pattern. The best time to go to sleep at night is a time frame in which one can achieve the recommended sleep for age group. Irregular sleep pattern may cause circadian rhythm off-balance. This can result in periods of daytime sleepiness. It is a sign of not getting enough sleep at night, and also one might experience accidents, irritability and forgetfulness. Not getting enough sleep on a regular basis can also lead to more long-term health consequences including hypertension, diabetes, heart disease, obesity, depression.

Overall, it’s best to go to bed earlier in the night and wake up early each day. Still, this type of sleep schedule may not work for everyone. It’s far more important to make sure to get enough good quality sleep. One can ensure this happens by going to bed and waking up at the same time every day. Talk to a doctor if you’re having trouble falling asleep at night, or if you continue to experience daytime sleepiness despite sticking with a consistent bedtime schedule. This could indicate issues with sleep quality, which could warrant further investigation and report required a lot of sleep disorder.

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INSTRUCTIONS FOR AUTHORS

Scope of The Journal

The Journal of Central Medical College is a peer-reviewed journal and is published twice a year. It publishes original papers, reviews concerned with recent practices, case reports of exceptional merits and images in clinical medicine. Authors are invited to submit articles in all the fields of medicine, with a wide spectrum of coverage including clinical medicine, basic sciences, epidemiology, diagnostics, therapeutics, public health and standards of health care in relation to the concerned speciality. Review articles of current interest and a high standard of scientific value are considered for publication.

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Two typed copies (hard copies) of the article and one soft copy on a CD-ROM processed in MS Word (*.doc format only) should be submitted to the Editor-in-Chief. Alternatively, manuscripts may also be submitted electronically through Email: cemec05@yahoo.com. Manuscripts must be accompanied by a covering letter signed by all authors stating that the data have not been published elsewhere in whole or in part and all authors agree publication of their article in Journal of Central Medical College. If the work has been conducted abroad, the article must be accompanied by a certificate from the head of the institute where the work has been done. Authors need not to pay for publication.

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All submitted manuscripts are primarily reviewed by the editors of the journal and then undergo through a double-blind peer review process and finally editors make their decisions about publishing papers in the journal. Manuscripts of rejected articles are not returned, but the principal author or the author for correspondence is informed of rejection of the article. Ethical aspects are considered in the assessment of the paper. The decision on the priority of publication is strictly determined by the editorial board.

The editorial board reserves the right to edit and if necessary, shorten any material accepted for publication and to crop/trim any illustration to conform to the style of the text. The editorial board does not subscribe to the views expressed in the article written by the author or authors and published in this journal.

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Procedure of studies on humans should be in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975 (revised in 2000, available at http://www.wma. net/e/policy/17-ce.html). The ethical standards of experiments must be in accordance with the guidelines provided by the COMMITEE FOR THE PURPOSE OF CONTROL AND SUPERVISION ON EXPERIMENTS ON ANIMALS (CPCSEA) for animals and ICMR for humans.

A statement on ethics committee permission and ethical practices must be included in all research articles under the 'Materials and Methods' section. Evidence for approval by a local Ethics Committee be supplied by the authors on demand.

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The journal considers manuscripts prepared in accordance with the guidelines laid down by the international Committee of Medical Journal Editors.

The text should be typewritten in 12-point in Times New Roman font, double spaced on one side of the paper and not larger than ISO A4 (210 x 297 mm) with a 3cm margin and pages should be numbered consecutively.

Abbreviations and symbols must be standard and SI units should be used throughout. Whenever possible, drugs should be given their approved generic names. Acronyms should be used sparingly.

The level of English should meet the journal's standard. Please check for grammatical and spelling errors, and poorly constructed sentences, and refine the language carefully. Authors not fluent in English are advised to have their manuscript checked by a colleague with a good command of the language.

Manuscript Should Contain

a) Title page
b) Abstract (structured)
c) Introduction
d) Materials and Methods
e) Results (with tables and figures, where required)

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f) Discussion

g) Acknowledgement (if any)

h) Conclusion

i) References

Title page

The title page should bear the names of the author(s) and the name and address of the institution or laboratory where the work has been carried out, in addition to the title of the paper. The full address of the principal author or the author to whom proofs will be sent should be given including e-mail account number. A short (running) title of not more than 45 characters should be given.

Abstract

The abstract should not exceed 250 words and should state concisely what was done, the main findings and how the work was interpreted. The abstract should be structured having background, objectives, materials and methods, results and conclusion. Abstracts of case reports and review articles may not be structured. Below the abstract, three to five appropriate key words relevant to the article should be mentioned.

Introduction

Introduction should contain brief review of the subject, state the purpose of the article and summarise the rationale for the study or observation and should contain strictly pertinent references.

Materials and Methods

1. Selection criteria of the subjects (patients or laboratory animals, controls) should be described clearly, including eligibility and exclusion criteria and a brief description of the source population.
2. Regarding technical information, methods, apparatus (manufacturer's name and address in parentheses), and procedures are to be described. Give references to established methods, including statistical methods; provide references and brief descriptions for methods that have been published but are not well known; describe new or substantially modified methods, give reasons for using them, and evaluate their limitations.
3. All drugs and chemicals used, including generic name(s), dose(s), and route(s) of administration are to be described.
4. Reports of randomised clinical trials should present information on all major study elements, including the protocol, assignment of interventions (methods of randomisation, concealment of allocation to treatment groups), and the method of masking (blinding), based on the CONSORT statement.
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Results

Results should be presented in the text in logical sequence with tables and illustrations (where necessary) and should be described without any comment. All the data in the tables or illustrations should not be repeated in the text; only important observations should be emphasised or summarised. Do not duplicate data in tables and figures. Tables and figures should be inserted in the text where those are referred to.

Tables should be self-explanatory, as few as possible and should present only essential data. Explanatory matters should be placed in footnotes. Explain in footnotes all non-standard abbreviations used in the table. For footnotes use the following symbols, in this sequence: *, , $, , **, , it, Each table should have a title or caption with Roman numbers. Do not use internal horizontal or vertical lines.

All photographs, graphs, diagrams should be referred to as figures and should be numbered consecutively in the text in Arabic numerals. All illustrations must be in JPEG format at a resolution of 300 dots/inch (DPI) or higher. Photomicrographs should have internal scale markers and should include in the legend the original magnification and the stain used. Subject/patient must not be identifiable on the photograph. If this is unavoidable, written consent from the subject or legal guardian must be obtained.

Discussion

This section should present comprehensive analysis of the results in the light of any previous research. Emphasise the new and important aspects of the study and the conclusions that follow from them. Do not repeat in detail data or other materials given in the Introduction or the Results section. Include the implications of the findings and their limitations, including implications for future research. Relate the observations to other relevant studies. State new hypotheses when warranted, but clearly label them as such.

Acknowledgement

Contributions by any person or department or institution, but not justifying authorship, may be acknowledged. Nature of support, such as general support by a departmental chair, technical help, financial and material support, should be specified.

Conclusion

The conclusion of the article in few words at the end.

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References

References should follow the Vancouver format. In the text, references should appear as numbers starting at 1. At the end of the paper these should be listed (double spaced) in numerical order according to the order of citation in the text. All authors should be quoted for papers with up to 6 only should be quoted followed by et al. Abbreviations for title of medical periodical should conform to those used in the latest edition of Index Medicus. The first and last page numbers for each reference should be provided. Abstracts and letters must be identified as such. Authors must check references against original sources for accuracy. Examples of references are given below.

Articles in Journals

a. Standard Journal Article:

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Authors

The person who mainly did the research work and wrote the paper is the first or prime author of any research paper. Other persons who made substantial contributions to the work are also listed as co-authors. It is not ethical to enlist or to be enlisted as co-authors in a research article without having substantial contribution in the research -work. Those who just helped with the experiments, commented on the protocol or manuscript or helped in collection of data etc. can be acknowledged.

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Original Article

Prevalence of Iron Deficiency Anaemia in Ischaemic Stroke

Hasan AA[1], Azad AK[2], Das P[3], Chowdhury NH[4]

Abstract

Background:
Iron Deficiency Anaemia has been proposed as a risk factor for developing ischemic stroke. In long-term follow-up studies, and it is also known to increase the risk of death. Very little is known about the prevalence of Iron Deficiency Anaemia (IDA) in Bangladeshi stroke patients. We aimed to determine the prevalence of IDA among admitted patients of acute ischemic stroke in a tertiary care hospital in Bangladesh. ***Materials and methods:*** *In this cross-sectional study, 75 patients with acute ischemic stroke were selected purposively from the Neurology & Medicine Department of Comilla medical college hospital from February 2021 to May 2021. Traditional risk factors for stroke, stroke type and severity at admission were recorded for each patient. Anaemia is defined as haemoglobin <12gm/dl in women & <13gm/dl in men. IDA was defined as serum ferritin level <20 µgm/L in males and <40 µgm/L in females.* ***Results:*** *Mean age was 65.8 (±11.4) years. Sixty percent of patients were male. Hypertension was the most prevalent risk factor present in 73.3% of the cases, followed by diabetes mellitus (49.3%), smoking (28.0%), ischaemic heart disease (25.3%), and dyslipidemia (21.3%). Small vessel strokes were the most common, accounting for 48% of all the patients, followed by large vessels getting affected in 38.7% of the cases. Prevalence IDA was 24%. (95% confidence interval: 14.9%-35.3%). However, the proportion of IDA among patients with severe stroke was 84.6% compared to 11.3% in non-severe strokes (p=0.001).* ***Conclusion:*** *Prevalence of IDA in acute ischemic stroke is significant and it is associated with severe stroke in our hospital.*

Keywords: *Ischaemic stroke, iron deficiency anaemia.*

Introduction: A cerebrovascular accident (CVA), or stroke, is the rapid loss of brain function due to a disturbance in the blood supply to the brain. According to the latest report from the Centers for Disease Control and Prevention, mortality from stroke was the fourth leading cause of death in the United States in 2008. Stroke was a leading cause of severe long-term disability.[1] Nearly half of older stroke survivors were noted to experience moderate to severe disability.[2] Care for stroke survivors has been estimated to cost $18.8 billion in health care expenses within the United States during 2008, in addition to $15.5 billion as a result of lost productivity and premature mortality.[3] There are many established risk factors of stroke: hypertension, diabetes mellitus, dyslipidemia, etc.[4,5] However, the cause of stroke in about 30% of the cases remains undetermined, especially in young adults.[6]

Therefore there is a need to focus on discovering other risk factors. Anaemia is implicated as an important risk factor in the development of cerebrovascular and cardiovascular diseases. The focus was mainly on sickle cell anaemia and not on non-sickle anaemia. Anaemia is the most common blood disorder and proved to be highly related to cardiovascular diseases and cerebrovascular accidents.[7-11] Recently, iron deficiency anaemia (IDA) has been proposed as a stroke risk factor.[12,13] Iron deficiency decreases the amount of haemoglobin which in turn compromises the oxygen-carrying capacity of the blood. Anaemia is a hyperdynamic state which increases blood flow and

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turbulence leading to endothelial injury favoring thrombosis. Secondary reactive thrombocytosis in IDA also makes blood hypercoagulable.[14]

Bangladesh is a country where the stroke is the third leading cause of death. WHO ranked Bangladesh's mortality rate due to stroke as number 84 in the world. The reported prevalence of stroke in Bangladesh is 0.3%, although no data had been recorded.[15] In one study by ICDDRB found that most anaemia in rural Bangladesh was as high as 60%, but only half of the anaemic children were iron deficient.[16] IDA is an established risk factor for ischaemic stroke in children. Hence, if IDA can be established as a risk factor for stroke in adults, many major cerebrovascular events can be prevented. Therefore, IDA as a possible cause of stroke should be studied. Extensive literature search reveals to date, no such study was done. One case report had been reported as a probable cause of stroke due to IDA in 2008 by Boshak et al.[17] We aimed to investigate the prevalence of IDA in ischaemic stroke patients admitted to a tertiary hospital of Bangladesh.

Materials and methods:

A total of 75 subjects with first-ever stroke consecutively admitted to the Department of Neurology of Comilla Medical College Hospital was recruited for the study from February 2021 to May 2021. Inclusion criteria were age between 30 and 90 years and patients presenting with the first-ever stroke. Diagnosis of stroke was made based on findings from Neuroimaging (either of CT or MRI). Patients with intracerebral haemorrhage, subarachnoid and subdural haemorrhage, post trauma features, history of the previous stroke, previously diagnosed cases of sickle cell anaemia and other haemoglobinopathies were excluded from the study.

A structured questionnaire was used to collect information on demographic variables, stroke severity (with the help of the National Institute of Health Stroke Scale [NIHSS]), stroke subtype using TOAST criteria, vascular risk factors, and stroke workup. Patients were labeled as hypertensive if systolic blood pressure was greater than 140 mm Hg or/and diastolic blood pressure was greater than 90 mmHg during admission in the hospital or if the patient was on antihypertensive drugs at the time of entry. We classified the patient as diabetic if self-reported fasting glucose level was 120 mg/dL or more or if the patient was on hypoglycemic agents or insulin. Patients having serum high-density lipid of 100 mg/dL or less and/or serum low-density lipid of 100 mg/dL or more and/or fasting serum cholesterol of 200 mg/dL or more were labeled as having dyslipidemia. Smokers were the patients who had smoked ten or more cigarettes for ten or more years. Electrocardiogram was used to check for atrial fibrillation.

Complete blood count was done using Wheisman Auto Haematology Analyzer (Model - AC-310) ,Random blood sugar, S. Creatinine, Iron Profile [S. Iron, S. Ferritin, Total Iron Binding Capacity(TIBC)] were conducted using the methodology & reference range of department of clinical pathology Comilla Medical College Hospital. IDA was defined as serum ferritin level <20 µgm/L in males and <40 µgm/L in females.[18]

Patients or their next of kin were briefed about the purpose and nature of the study. Written consent was obtained from the patients or their next of kin in case of incapacitation of the patients. Ethical approval was obtained from the Ethical Review Committee of Comilla Medical College. Upon receiving the patients' consent or their nearest relative's consent, qualified medical personnel, not below senior medical officer and assistant register, examined and interviewed the patient or the patient's attendant about past medical and personal history and recorded the variable of interest.

Standardized Data Collection Form was used in recruiting patients. Data were managed using Statistical Package for Social Science (SPSS) for Windows Version 23. The presentation expressed data as mean ± SD and number (percent) as appropriate. Chi-squared tests were performed, where applicable, to calculate the statistical difference between corresponding groups and/or association between groups. value <0.05 was taken as the level of significance.

Results:

The results are showed in table and graph Data were presented as frequency (percentage) if not mentioned otherwise.

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Table 1: Sociodemographic characteristics of the patients with acute ischemic stroke (n=75)

Variables		Frequency	Percentages
Age, years			
	Mean ±SD	65.8±11.4	
	Range	38-90	
	≤60 years	28	37.3
	>60 years	47	62.7
Sex			
	Male	45	60.0
	Female	30	40.0
Occupation			
	Housewife	45	60.0
	Business	12	16.0
	Service	9	12.0
	Others	9	12.0
Education			
	Illiterate	24	32.0
	Primary	27	36.0
	Secondary	20	26.7
	Graduate	4	5.3
Socioeconomic class			
	Lower	21	28.0
	Middle	54	72.0

The mean age of the stroke patients was 65.8 years, and most patients (60%) were male. Most patients (62.7%) were more than 60 years of age. Most patients were illiterate (32.0%) or had education up to the primary level (36.0%). Most of the patients (72.0%) were from the middle socioeconomic class.

Table 2: Risk factors of stroke patients with acute ischemic stroke (n=75)

Risk factors	Frequency	Percentages
Hypertension	55	73.3
Diabetes mellitus	37	49.3
Smoking	21	28.0
Ischemic heart disease	19	25.3
Dyslipidemia	16	21.3
History of stroke	7	9.3
Renal impairment	7	9.3
Valvular heart disease	2	2.7
Atrial fibrillation	2	2.7

Hypertension was the most prevalent risk factor present in 73.3% of the cases, followed by diabetes mellitus (49.3%), smoking (28.0%), ischaemic heart disease (25.3%), and dyslipidemia (21.3%).

Table 3: Risk factors of stroke among family members of the patients with acute ischemic stroke (n=75)

Risk factors	Frequency	Percentages
Family history of Diabetes mellitus	18	24.0
Family history of Hypertension	13	17.3
Family history of Ischemic heart disease	10	13.3
Family history of stroke	10	13.3

About one-third of the stroke patients had a family history of diabetes.

Table 4: Types of stroke of the patients with acute ischaemic stroke (n=75)

Stroke characteristics		Frequency	Percentages
Stroke type			
	Small vessel	36	48.0
	Large vessel	23	30.7
	Cardioembolic	4	5.3
	Unknown	12	16.0
Stroke severity			
	Severe stroke	13	17.3
	Nonsevere stroke	62	82.7

Small vessel strokes were the most common, accounting for 48.0% of all the patients, followed by large vessel stroke in 30.7% of the cases. Cardioembolic stroke was present in 5.3%, while the cause was unknown in 16.0% of the stroke cases. Thirteen patients (17.3%) had a severe stroke (NIHSS score greater than 14).

Table 5: Hemoglobin and iron profile of the patients with acute ischaemic stroke

Parameters	Level	Frequency	Percentage
Hemoglobin			
	Normal	39	52.0
	Below normal*	36	48.0
Serum iron			
	≥50 µgm/dl	45	60.0
	<50 µgm/dl	30	40.0
Serum ferritin			
	Normal	57	76.0
	Below normal**	18	24.0
Total iron binding capacity			
	≤355 µgm/dl	58	77.3
	>355µgm/dl	17	22.7

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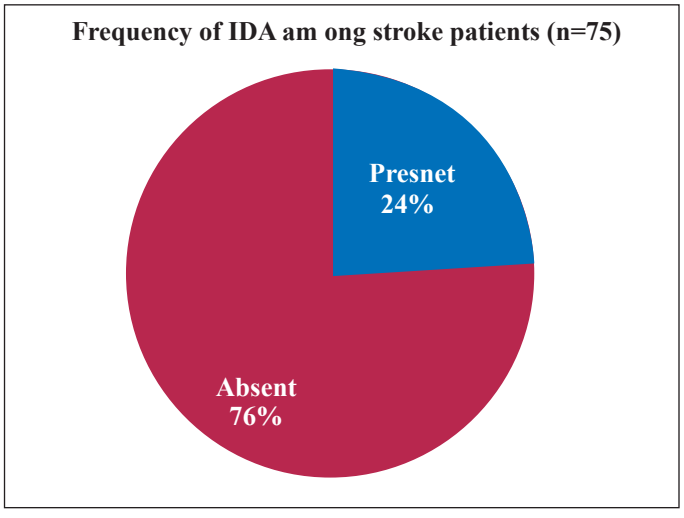
Anaemia statuses of the patients were determined by measuring hemoglobin and iron profile. About half of the patients were (48%) anaemic.
* <12 g/dl in women and <13 g/dl in men **<20 µgm/L in males and <40 µgm/L in females

Figure 1: Prevalence of IDA among patients with acute ischaemic stroke.



We identified that out of 75 patients with acute ischaemic stroke, 18 (24%.0; 95% confidence interval: 14.9%-35.3%).

Table 6: Association demographic factors and IDA in stroke patients

Variables		IDA absent	IDA present	P value*
Age				
	≤60 years	21 (75.0)	7 (25.0)	**0.876**
	>60 years	36 (76.6)	11 (23.4)	
Sex				
	Male	31 (68.9)	14 (31.1)	
	Female	26 (86.7)	4 (13.3)	
Economic class				
	Lower	18 (85.7)	3 (14.3)	**0.219**
	Middle	39 (72.2)	15 (27.8)	
Education				
	Illiterate	20 (83.3)	4 (16.7)	
	Primary	20 (74.1)	7 (25.9)	**0.784**
	Secondary	14 (70.0)	6 (30.0)	
	Graduate	3 (75.0)	1 (25.0)	

Iron Deficiency Anaemia was detected in a higher proportion among patients' ≤60 years, male patients, patients with middle socioeconomic class, and patients with secondary educational level compared to their counterparts. However, none of these differences was significant statistically.
Data were presented as frequency (percentage). *P values were obtained from the Chi-square test.

Table 7: Association between IDA and other risk factors of ischaemic stroke

Risk factors	IDA absent	IDA present	P value*
Hypertension	44 (80.0)	11 (20.0)	0.179
Diabetes mellitus	27 (73.0)	10 (27.0)	0.545
Smoking	18 (85.7)	3 (14.3)	0.219
Ischemic heart disease	12 (63.2)	7 (36.8)	0.129
Dyslipidemia	10 (62.5)	6 (37.5)	0.154
History of stroke	5 (71.4)	2 (28.6)	0.769
Renal impairment	7 (100.0)	0 (0)	0.118
Valvular heart disease	1 (50.0)	1 (50.0)	0.425
Atrial fibrillation	1 (50.0)	1 (50.0)	0.425

Traditional risk factors had no significant association with the presence of IDA.
Data were presented as frequency (percentage). *P values were obtained from the Chi-square test.

Table 8: Association IDA with stroke type and severity

Stroke characteristics		IDA absent	IDA present	P value*
Stroke type				
	Small vessel	20 (87.0)	3 (13.0)	
	Large vessel	25 (69.4)	11 (30.6)	0.499
	Cardioembolic	9 (75.0)	3 (25.0)	
	Unknown	3 (75.0)	1 (25.0)	
Stroke severity				
	Severe stroke	2 (15.4)	11 (84.6)	0.001
	Nonsevere stroke	55 (88.7)	7 (11.3)	

The proportion of patients with IDA was higher in patients with large vessel strokes (30.6%) than patients with small vessel stroke (13%), but the difference was not significant statistically. IDA was more common in patients with severe stroke at admission than those with non-severe stroke (84.6% versus 11.3%, p=0.001).
Data were presented as frequency (percentage). *P values were obtained from the Chi-square test.

Discussions:

Understanding the risk factors for ischemic stroke occurrence must be the priority for targeted preventive measures. Risk factors associated with ischemic stroke are age, male population, hypertension, diabetes mellitus, smoking and alcohol use. IDA has been suggested to be associated with stroke, but few cases have proven it thus far. In the present study, the prevalence of IDA among patients with acute ischaemic stroke was 24%. Anaemia is a

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common disease in about 10% of people age ≥ 65 years 7 its prevalence increase with age.19 Ischemic stroke is frequently accompanied by anaemia, previous studies have confirmed an average prevalence rate of 15-20%.[20-24] and a maximum prevalence of 30%.[25] IDA is the most typical type of anaemia, accounting for nearly half of all anaemia cases worldwide. Most of the patients with anaemia are asymptomatic, so that the actual incidence might be higher than reported. The incidence of IDA is very high in developing countries.[26]

In a study conducted by Chellan and his colleague, results showed that more than 95% of children, adolescent girls and pregnant women suffer from anaemia.[5] The association of stroke and IDA has been explained based on three physiological mechanisms: hypercoagulable state, thrombocytosis, and hypoxia.[12]

The possible reason for the IDA as a risk factor for stroke could be a decrease in haemoglobin level in the blood would compromise the oxygen-carrying ability of the blood flow resulting in low oxygen delivery to the brain, causing hypoxia and subsequently increase the risk of cerebrovascular or cardiovascular diseases. Another possible mechanism that may explain the association between IDA and stroke is secondary thrombocytosis. This mechanism is supported by findings of the association of thrombotic and embolic ischemic stroke with IDA. Cases of carotid thrombus associated with IDA and thrombocytosis have been reported in adults.[27-29] Anaemic patients need more blood to flow to the brain to compensate for the lack of oxygen. Therefore increase in blood flow can cause endothelial damage, causing a cascade of thrombus formation.[6] In the study done by Dubyk et al., they supported the role of IDA as a risk factor for stroke in elderly patients.[14]

In our study of 75 patients with stroke, 24% were anaemic due to IDA. This study thus suggested an association between IDA and ischemic stroke. However, there are various associated comorbid conditions with stroke. A study conducted by Ellie Choi et al. showed that blood transfusion might be considered adjuvant therapy in treating stroke patients.[28] In the case presented by Mehta et al., the ischemic stroke patient showed marked improvement after receiving a blood transfusion.[12]

The mean age of the stroke patients, around sixty-five years, is consistent with previous findings from a stroke registry study in Bangladesh.[30] Most of the patients from a stroke registry in the USA presented with stroke at 71 years.[31] The lower percentage of female stroke patients being registered implies either a low prevalence of stroke among females or lower access of female stroke patients to the tertiary care hospital.

In this sample, atherosclerosis in the small vessel was responsible for most of the stroke cases. The majority of these patients had dyslipidemia. Hypertension and diabetes were other risk factors that were present in them. Dyslipidemia, hypertension, and diabetes are important risk factors for stroke, as reported previously.[30,32] Proportion of two important risk factors, diabetes and hypertension, are more common among stroke patients in Bangladesh, as revealed in a previous study.[30]

Understanding social and demographic characteristics in stroke patients is important to understand the population at risk and address the risk factors. The present study aims to present the sociodemographic picture of patients with ischemic stroke in a developing country like Bangladesh. The study shows higher incidences of stroke in males than females, with most cases in the age group more than 60 years. Hypertension was found to be the commonest risk factor. Understanding these variables will help to formulate preventive action plans for specific risk factors and targeted population groups.

Limitations: This study has several limitations. First, the sample size was small. All the patients were selected from a public tertiary hospital conveniently. Data on the nutrition practices of the patients were not available, and we were not able to explore causal mechanisms for the development of IDA. Finally, the study's cross-sectional design was not appropriate to define a causal relationship between two variables.

Conclusions: From the present study, it can be concluded that IDA is common in patients with acute ischaemic stroke, and there is significant association between the severity of the ischemic stroke and IDA.

Conflict of interest: There is no conflict of interest.

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Recommendations: Early detection of anaemia will help to decrease the incidence of stroke cases. Patients found to have IDA should be more aggressively screened and managed for the possible underlying bleeding source and /or iron deficiency status, to reduce the risk of subsequent ischemic stroke. While a thorough neurologic evaluation is not often considered in patients presenting with signs and symptoms of severe anaemia, vigilance regarding focal neurologic deficits should prompt suspicion for ischemic stroke in patients with significantly low hemoglobin levels. However, more studies should be conducted with a larger sample size from different centers in a case-control design to establish a definite relationship between ischemic stroke and IDA.

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Original Article

Association of Vitamin-D Receptor Gene Single Nucleotide Polymorphism (FokI) with COPD

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Abstract

Background: *Vitamin D receptor gene (VDR) polymorphism and its association with various diseases have been previously investigated. But the association of vitamin D receptor gene polymorphism with COPD has not been investigated yet.* ***Objective:*** *To assess the association between vitamin D receptor gene polymorphism (FokI) and COPD.* ***Methods:*** *This cross sectional study was carried out in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from March 2019 to February 2020. For this study, 15 (fifteen) pulmonologists diagnosed COPD patients with age 40 to 80 years (post-bronchodilator FEV1/FVC<0.70 and FEV1<80% predicted) and 15 (fifteen) apparently healthy age-matched individuals (for comparison), were selected. The single nucleotide polymorphism of vitamin D receptor gene (FokI) of all subjects was assessed by PCR-RFLPs. Data were expressed as mean ± SD and percentage. Statistical analysis was done by independent sample 't' test and chi-square test. In the interpretation of the results, ≤0.05 level of probability (p) was accepted as significant.* ***Results:*** *The frequency distribution of FokI genotype was 13.33% (FF), 73.34% (Ff), 13.33% (ff) and 13.33% (FF), 80% (Ff), 6.66% (ff) COPD patients and healthy subjects, respectively. Associations of FokI [FF (OR 1,95% CI 0.12-8.21, p=1.00); Ff (OR 0.68,95% CI 0.12-3.78, p=0.66); ff (OR 2.15,95% CI 0.17-26.67, p=0.54)] VDRSNP with COPD was statistically non-significant. Conclusion: The present study reveals that the FokI of VDR SNP is not associated with COPD.*

Keywords: *Vitamin D receptor gene, Single nucleotide polymorphism, FokI.*

Introduction: Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. It is a complex disease associated with the multifactorial background of long-term exposure to noxious gases and particles, combined with a variety of host factors, including genetics, airway hyper-responsiveness and poor lung growth during childhood1. It has been found that different genes are associated with COPD. Among them, alpha1- antitrypsin (AAT) deficiency is one of the most common genetic causes of COPD. This enzyme deficiency occurs due to Taq-1 polymorphism of AAT, Z-isoform of AAT, and mutation of serpin family A member 1 (SERPINA 1). In addition, Single nucleotide polymorphism (SNP) of matrix metalloproteinase 9 (MMP9), the promoter region of tumour necrosis factor-alpha (TNFα) gene and SERPINA3werealsoassociatedwith COPD[2-6].

As COPD is a chronic inflammatory respiratory ailment, so, immunomodulation would be one of its major causative factor[7-9]. Recently the immunomodulatory role of vitamin D has been explored[10-14]. This immunomodulatory characteristic acts via vitamin D receptor (VDR), which alters genomic signaling[12,15-19]. So, the main regulator of vitamin D signaling is the VDR[20], which is present in numerous tissues, including kidney, heart, muscle, breast, colon, prostate, brain and immune cells,

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making itself a natural target of modulation in disease pathogenesis, including a variety of cancers[21], metabolic syndrome[22,23], renal transplant[24] and dermal disorders[25]. In addition, polymorphisms of the VDR gene have been found to be associated with immune-mediated diseases characterized by an imbalance in helper T- cell development[9], such as Crohn's disease[26] and tuberculosis[27].

VDR gene is located on 12q13.11 possessing 11 exons with a length of 5.6 kb[28]. This VDR gene has more than[3] 470 single nucleotide polymorphisms (SNPs), a number of which modulate the uptake of 1,25 (OH)2D[29]. Among them, the common SNPs are ApaI[30], BsmI[31], TaqI[32] and FokI[33].

These SNP s have been found to be associated with the efficacy of antiresorptive treatments in postmenopausal women (with BsmI)[34], essential hypertension (with FokI)[35], metabolic syndrome (with FokI)[23], prostate cancer (with ApaI)[36], Leprosy (with FokI and ApaI)[13], lumbar spine pathogenesis (with BsmI, ApaI and TaqI)[37] and multiple familial sclerosis (with TaqI)[38]. Moreover, in the perspective of respiratory ailments, both FokI and ApaI VDR SNPs were found to be associated with asthma[11,39,40] and FokI VDR SNP was found to be associated with tuberculosis[41,42]. In addition, ApaI was associated with osteoporosis[43] and FokI along with BsmI were associated with skeletal muscle strength in COPD patients[44]. To the best of our knowledge, different diseases were found to be associated with VDR polymorphism. However, as far as we searched, no study was available on the association of VDR SNP with COPD. Therefore this study aimed to investigate the association of one common VDR SNP (FokI) with COPD.

Materials and Methods Data collection

This cross-sectional study was conducted from March 2019 to February 2020 in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), after getting protocol approval from the Institutional Review Board (IRB) of BSMMU. For this study, 15 male (age 40 to 80 years) COPD patients (Study group) were diagnosed by a Pulmonologist with spirometric evidence of COPD (presence of a post-bronchodilator FEV1/FVC <0.70 and FEV1 <80% predicted) and enrolled by purposive sampling from Out-Patients Department (OPD) of the National Institute of the Diseases of Chest and Hospital (NIDCH). For comparison, 15 age, BMI and smoking status matched apparently healthy males (Comparison group) were selected by personal contacts. Written informed consent was taken from all the participants after detailing the study procedure. With all aseptic precautions, 5ml of venous blood was drawn from the ante-cubital vein.

DNA extraction

DNA extraction was done by ReliaPrep™ Blood gDNA isolation kit (Promega, Wisconsin, USA) and assayed for purity and concentration by spectrophotometry (absorbance at 260 nm and 280 nm).

FokI polymorphism

PCR amplification of the VDR gene was done in 25µ l reaction mixtures containing primers for FokI polymorphism45. The PCR amplification conditions were initial denaturation at 94°C for 5 minutes followed by 35 cycles at 94oC for 30 sec, 58°C for 30 sec, 72°C for 1 min and final extension at 72°C for 7 minutes. The primers for FokI polymorphism were 5 ′- GATGCCAGCTGGCCCTGGCACTG-3′ and 5′-ATGGAAACACCTTGCTTCTTCTCCCTC-3′45. The PCR product (272 bp) was digested with 1.0 unit FokI restriction enzyme (New England Biolabs Inc, USA) in a heat block at 25°C for 20 minutes. The products of restriction enzyme cleavage were analyzed on 1% agarose gels and were visualized under UV light after staining with ethidium bromide (Figure 1, Table 1). FokI VDR SNP resulted in fragments of 272 bp, 198 bp and 74 bp. Thus for FokI, FF resulted in one fragment of 272 bp, ff in two fragments of 198 and 74 bp, and Ff exhibited all three fragments (272bp,198bp,74bp).

Table no. 1: Primer sequence and PCR conditions for genotyping of FokI VDR.

Location	Locus	Alleles	PCR primer	PCR product (bp)	Restriction enzyme	RFLP products (bp)
Exon2	rs2228570	C/T	F: GATGCCAGCTGGCCC TGGCACTG	272	FokI	272
			R: ATGGAAACACCTTGC TTCTTCTCCCTC			198
			* Initial denaturation: 94°C for 5 min; 35cycles: 94°C for 30s, 58°C for 30s, and 72°C for 1min; and final extension: 72°C for 7min			74

PCR- Polymerase chain reaction; RFLP-Restriction fragment length polymorphism; bp- Base pair.

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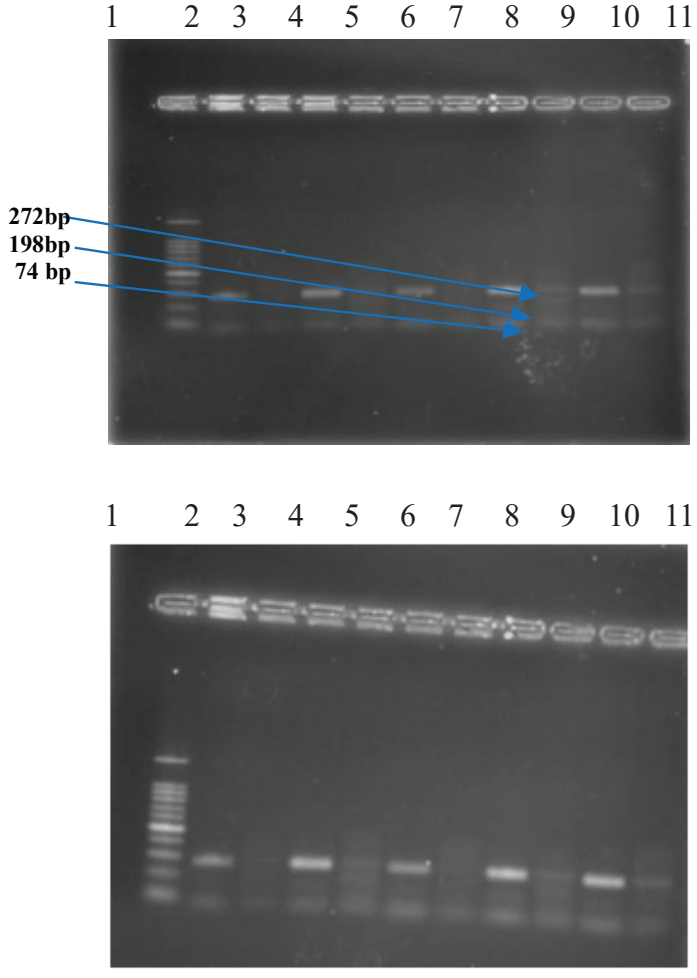

Figure 1: Restriction fragment length polymorphism digestion of FokI in 1% agarose gel stained with ethidium bromide with 100 bp ladder in the first Lane, in lanes 2, 4, 6, 8, 10 shows PCR products; in lanes 3, 5, 7, 9, 11 shows digested products in gel picture. FokI digestion – FF/272 (major homozygous), Ff/272, 198, 74 (heterozygous), ff/198,74 (minor homozygous).

Statistical analysis

The data were expressed as mean with standard deviation (mean ± SD) and frequency distribution in percentage. The data were statistically analyzed by SPSS statistical package, version 22.0 (IBM, SPSS Inc., Chicago, IL), using the Chi-square test. Allelic frequencies of VDR gene polymorphisms were determined by Hardy-Weinberg equilibrium. In the interpretation of the results, ≤0.05 level of probability (p) was accepted as significant.

Results

The baseline characteristics of all our study subjects are presented in Table 2. The distribution of FokI VDR genotype and allele frequency is shown in Table 3. The FokI genotype, frequency distribution was 13.33% (FF), 73.34% (Ff), 13.33% (ff) and 13.33% (FF), 80% (Ff), 6.66% (ff) COPD patients and healthy subjects, respectively. The associations of FokI FF (OR 1, 95% CI 0•12-8.21, p = 1.00); Ff (OR 0•68, 95% CI 0•12-3.78, p=0•66); ff (OR2.15, 95% CI0•17-26.67, p = 0•54)] VDR SNPs with COPD were statistically non-significant.

Table no. 2 : Baseline characteristics of COPD patients and healthy subjects (N=30)

Characteristics	COPD patients (n=15)	Healthy subjects (n=15)	p-value
Age (years)	60.46 ±6.31 (40-80)	56.00 ±7.80 (40-80)	0.096^{ns}
Body mass index (BMI) (kg/m^2)	22.76 ±4.26 (16.90-33.70)	21.96± 2.30 (18.80-25.91)	0.531^{ns}
Duration of smoking (pack year)	14.07 ±5.41 (4-30)	17.16 ±5.17 (4-30)	0.121^{ns}
FEV1/FVC(%)	57.60±10.61 (39-68)	80.60 ±6.38 (72-92)	0.000***
FEV1(% of predicted value)	44.88 ±10.98 (28.30-63.60)	83.26 ±10.51 (70-100)	0.000***

Data were expressed as mean ± SD; Figures in parentheses indicate ranges; Statistical analysis was done by Independent sample t-test; N = Total number of subjects; n = number of subjects in each group; Pack year = (number of cigarettes smoked per day/20) X no. of years smoked; FEV1 = Forced expiratory volume in the first second; FVC = Forced vital capacity; ns = non-significant; *** = statistically significant (p<0.001)

Table no 3: Genotype and allele distribution of FokI VDR SNP in study subjects (N = 30)

SNP	COPD patients (n = 15)		Healthy subjects (n = 15)		OR(95%CI)	χ^2 value (p value)
	no	%	no	%		
FokI						
FF	2	13.33	2	13.33	1 (0.12-8.21)	χ^2=0.00, p=1.00
Ff	11	73.34	12	80	0.68 (0.12-3.78)	χ^2=0.18, p=0.66
ff	2	13.33	1	6.66	2.15 (0.17-26.67)	χ^2=0.37, p=0.54
F	15	50	16	53.34	1.14 (0.41-3.14)	χ^2=0.06, p=0.79
f	15	50	14	46.66	0.87 (0.31-2.41)	χ^2=0.06, p=0.79

VDR = Vitamin D receptor; SNP = Single Nucleotide polymorphism; OR = odds ratio; CI = confidence interval

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Discussion

It is well known that the VDR gene is located on chromosome 12q13.11[28,46] encoding the VDR protein by exon II to IX. In addition, it has been reported that exon VII to IX involves the binding of VDR to vitamin D[47]. It has also been observed that variations in the 3′ UTR sequence often affect mRNA stability, the efficiency of protein translation and alter protein levels. Among the four common VDR SNPs, FokI is located in exon 2 at the 5' end of the VDR gene[10,13,32,47,48,49,50,51,52]. However, it is due to the nucleotide substitution of T to C within the first codon of exon 2 (ATG to ACG, giving rise to the allelic conversion of "f" to "F")[52]. Therefore, this FokI polymorphism may affect the activity of VDR and subsequent downstream effects of vitamin D[53], including its immunomodulatoryrole[50,51]. FokI VDR SNP was found to be associated with essential hypertension, metabolic syndrome, acromegaly, leprosy, hepatocellular carcinoma, multiple sclerosis, urolithiasis and skeletal muscle strength in COPD patients[13,22,23,29,35,44,47,54]. From the perspective of respiratory ailments, FokI VDR SNP was found to be associated with asthma and tuberculosis[39,41,42]. However, in our study, neither the genotype nor the allele of FokI VDR single nucleotide polymorphism was associated with COPD. Similarly, in a Turkish study regarding the global COVID condition, was found no association between FokI polymorphism of the VDR gene with COVID-1955. It may be explained as respiratory diseases showing the similarity of genetic involvement.

Conclusion

The results of the present study elucidate that FokI VDR SNP is not associated with COPD. There were a few limitations in our study. First, the intake of vitamin D and environmental exposure to ultraviolet radiation of our study population could not be assessed. Second, as a genetic association study, the results were based on a small number of samples. For further research, a similar type of study should be done, including information on vitamin D intake and environmental exposure to ultraviolet radiation in a large number of COPD patients.

Conflict of interest

There is no existence of a conflict of interest in this study.

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Original Article

Contraceptive Practices and Awareness of Emergency Contraceptive Pills among Rural Women of Reproductive Age

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Abstract

Background: *Regular contraceptive use and emergency contraception are tools to prevent population explosion. Objective: To assess the contraceptive practices and awareness of emergency contraceptive pills among rural women of reproductive age. Methods: The cross sectional study is conducted over 3months (December 2021 to February 2022) among 345 women of reproductive age (15-49 years) who living with their husbands in selected rural residence at Mostafapur village under Sadar Upazilla in Cumilla district. Women who were pregnant, had a child younger than 2 years, or had any physical & psychological disorder were excluded. Participants are selected by convenience sampling technique, data are collected by face to face interview with a semi-structured questionnaire to assess socio-demographic characteristics, contraceptive practices and awareness of emergency contraceptive pills. Data are analysed by SPSS software. Results: In this study, majority (48.7%) of the participants are in the age group 25-34 years. Most of them are housewives (92.2%) and 33.0%has secondary education. The mean (±SD) monthly family income of the participants is 25463.77 (±15971.158) tk and 58.3% of the participants has 1-2 children. About the current practice of contraceptive method, 52.2% of the participants practice and OCP is the widely used method (58.3%), 44.40% take decision by both husband and wife. About reasons for using contraceptives, majority (38.3%) of them use due to spacing of birth and 27.2% cases do not use due to husband disapproval. Regarding awareness of ECPs, 55.9% of them aware of and Norpill is the widely heard method (20.7%). 27.4% of the participants' source of information is frommedia: TV/Radio. About correct time of taking ECPs, 33.60%of them have no knowledge. Regarding conditions where ECPs are to be taken, majority 39.7% of them have no knowledge. About benefits of taking ECPs, majority (79.30%) of them know it can prevent pregnancy. Conclusion Contraceptive practices and awareness of ECPs are not satisfactory among rural women. So national wide campaign program should be conducted to improve this field.*

Keywords: *Contraceptive practices, Rural women of reproductive age, Emergency contraceptive pills.*

Introduction: In Bangladesh, population explosion is the major problem, which emphasis on the awareness and practice of contraceptive methods both rural as well as urban people. Contraception is one of the major determinants of fertility levels. As majority of people still live in rural areas thus this populations are the major part of any program to find out the real situation of our country. The history of successful family planning in Bangladesh started in the early 1960s, when Bangladesh was an eastern province of Pakistan[1].Family planning services in Bangladesh are still developing and there are some advances in the health indicators but the need for family planning which cannot be met still stands out as an important health problem[2].

Family planning is defined by WHO as, "a way of thinking and living that is adopted voluntarily, upon the basis of knowledge, attitudes and responsible decisions by individuals and couples, in order to promote the health and welfare of family groups and

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thus contribute effectively to the social development of a country"[3]. Contraceptive use plays a significant role in controlling fertility, particularly in reaching the replacement level of fertility. In Bangladesh now population is 159,453,001 (July 2018 est.). TFR in Bangladesh is 2.15 children born/woman (2018 est.) and CPR is 62.3% (2014 est.)[4]. Contraception is unique among medical interventions for effective means of FP and fertility control and therefore very important in promoting maternal and child health[5].

Many women, during the reproductive period are aware about family planning using different methods in the form of Oral Contraceptive Pills (OCP), or intrauterine devices (IUDs), or safe periods or other methods[6-8]. Ideally, family planning programs should offer a wide range of methods and appropriate counselling, so that users can make an informed choice and easy access to quality follow-up services since these factors are associated with method satisfaction, continuation and switching. Evidence from different studies has a number of programmatic implications, including better monitoring and evaluation of program activities, improved effectiveness in meeting the needs of users, and more generally, improved ability of governments to achieve goals set for total fertility, and for maternal and child health services[9].

Emergency contraception (EC) refers to postcoital contraceptive methods that are used after unprotected sexual intercourse, to prevent unwanted pregnancy[10]. Unwanted pregnancy is a significant public health issue and poses a major challenge to the reproductive health of women. The World Health Organization estimated nearly 21,600,000 unsafe abortions took place in 2008, almost all in developing countries with restrictive abortion laws[11]. According to the Bangladesh Demographic and Health Survey (BDHS) 2014, women still have 11% of children more than they desire in Bangladesh and an estimated 1.194 million induced abortions performed in Bangladesh, and most were unsafe. EC is globally considered as a means to avoid unwanted pregnancy, unsafe MR, and unsafe abortion in the context of Bangladesh[12].

Emergency contraceptive pills are mostly hormone-based regimens consisting of combination of ethinyl estradiol with levonorgestrel and levonorgestrel alone. Previously ECPs were considered to be effective only within 72 hours after unprotected intercourse but recent studies have indicated some ECPs are effective for upto 120 hours[10]. Although success of the family planning program and practice of contraceptives in Bangladesh has been widely acclaimed, many challenges still remain. Several demand-and supply-side strategies can help to overcome these challenges. At the same time, a renewed commitment from government bodies to implement and monitor such strategies, as well as to maintain ongoing collaboration with independent organizations is needed[13].

Unmet need varies with increasing age and area of residence. Women aged 15–19 had 10% more unmet need than women aged 45–49 (17 and 7%, respectively). Similarly, rural women had a higher unmet need than urban women (13 and 10%, respectively)[14].

The present study deals with one of the most important issue of our country. So, mass media, adult-education, and school curriculum need to be used to motivate people to value children irrespective of their sex, to highlight the benefits of small family size, and the important role of girls in the family as well as in the society. Inter-spousal communication should be encouraged during family planning counselling of couples to influence men's desired family size and contraceptive method use[13].

METHODS AND MATERIALS

The cross-sectional study is conducted over 3months (December 2021 to February 2022) among 345 women of reproductive age (15-49 years) who were living with their husbands in selected rural residence at Mostafapur village under Sadar Upazilla in Cumilla district. Women who were pregnant, had a child younger than 2 years, or had any physical & psychological disorder were excluded. Participants are selected by convenience sampling technique; data are collected by face to face interview with a semi-structured questionnaire to assess socio-demographic characteristics, contraceptive practices and awareness of emergency contraceptive pills. Data are analysed by SPSS software. Descriptive analysis was done by mean, frequency, standard deviation, percentage in table.

ETHICAL IMPLICATIONS:

Permission was taken regarding data collection from local administrative authority. Each participant was

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informed about the study, assured and informed written consent was taken. All participants were treated equally, secretly and with respect. All participants were assured that all information would be kept confidential and would not be used for any other purpose except research following standard guideline. The purpose of the study was explained to the participants without any distortion.

LIMITATIONS OF THE STUDY:

The main limitation is the small sample size and the representativeness of the sample. Validity of responses provided by participants on a sensitive issue like emergency contraceptive pills cannot be guaranteed. Some of the rural women were reluctant to participate in the interview because there was no monetary benefit, but their information could have enriched our research report.

RESULT:

Socio-demographic characteristics:

The socio-demographic characteristics are shown in Table 1. Majority of the women 168(48.7%) were age group between (25-34) years with the mean age of 29.86± 6.792. 114(33.0%) had Secondary education, 12(3.50%) were completely illiterate and the same 12(3.50%) got informal education. Regarding occupation, 318(92.2%) were house-wives, 181 (52.5%) had an income between 5000- 20000 taka and 201(58.3%) had less than 2 children.

Table 1: Socio-demographic characteristics of the respondents (n=345)

Variable	Frequency	Percentages (%)
Age (Years)		
15-24	78	22.6
25-34	168	48.7
35-49	99	28.7
Educational status		
Illiterate	12	3.50
Informal education	12	3.50
Primary	28	8.10
Secondary	114	33.00
S.S.C/Equivalent	101	29.30
H.S.C/Equivalent	50	14.50
Graduation/Equivalent	21	6.10
Post-graduation/Equivalent	7	2.00
Occupational Status		
Housewife	318	92.20
Service	17	4.90
Student	7	2.00
Business	3	0.90
Monthly income (in taka)		
5000-20000	181	52.5
20001-40000	115	33.3
40001-60000	40	11.6
60001-80000	9	2.6
Number of children		
None	15	4.3
1-2	201	58.3
3-4	120	34.8
5-6	8	2.3
7-8	1	0.3

Contraceptive practices:

Table – 2 shows information regarding contraceptive practices. Among the total participants, majority i.e. 180 (52.2%) of the practiced contraceptives and rest 165 (47.8%) did not practiceOut of total contraceptive practicing participants (n=180), maximum 105(58.3%) used OCP followed by condom 39(21.7%) and only 9(5.0%) undergone tubal ligation. In 80(44.40%) cases both the husband and wife took the decision regarding the choice of contraceptive use. 95(38.30%) of the participants were using contraceptives for birth spacing followed by 84(33.90%) to complete their families and in 52(27.20%) cases women didn't use any contraceptive method due to husband's disapproval (n=165).

Table 2: Contraceptive practices

Variable	Frequency	Percentages (%)
Current practice of contraceptive method		**(n=345)**
Yes	180	52.2
No	165	47.8
Method of contraception used		**(n= 180)**
OCP	105	58.3
Condom	39	21.7
Injection	21	11.7
Implant/Norplant	3	1.70
Copper-T	3	1.70
Tubal ligation	9	5.00

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Deciding member for use of particular method		**(n=180)**
Self	49	27.20
Husband	31	17.20
Both	80	44.40
Health worker	20	11.10
Reasons for using contraceptive*		**(n=180)**
Complete their families	84	33.90
Spacing of birth	95	38.30
Improvement of health	21	8.50
Economical problem	7	2.80
Husband approval	41	16.50
Reasons for not using contraceptives*		**(n=165)**
Husband disapproval	52	27.20
Economical problem	05	2.60
Religious belief	20	10.50
Fearing side effect	45	23.60
Son preference	21	11.00
Family pressure	07	3.70

*Multiple responses

Awareness of emergency contraceptive pills (ECPs): Table – 3 presents participant's awareness of emergency contraceptive pills. 193(55.9%) had awareness on ECPs, among the participants who are aware of ECPs, 62(20.70%), 57(19.00%), 54(18%) had heard the name of Norpill, Emcon and Peuli respectively (n=193). 87(27.40%) said they got information from TV/Radio, 82(25.80%) from health personnel and relative & friends. About 64(29%) knew ECPs should be taken within 72 hours and only 9(4.1%) knew within 5 days of unprotected sex. About 70(29.90%) said they would take ECPs in case of failure to follow regular methods, 45(19.20%) and 9(3.80%) choose the options that ECPs can be taken in case of condom breakage and after rape respectively. Regarding benefits of ECPs, the participants had greater recognition to prevent pregnancy, 175(33.1%), knew that ECPs can not cause abortion. 192(79.30%), 161(30.5%) knew ECPs cannot prevent HIV/AIDS.

Table 3: Awareness of emergency contraceptive pills (ECPs)

Variable	Frequency	Percentages (%)
Heard/ aware about ECPs		**(n=345)**
Yes	193	55.9
No	152	44.1
Heard about trade names*		**(n=193)**
Emcon	57	19.00
I-pill	43	14.30
Norpill	62	20.70
Norix	45	15.00
Peuli	54	18.00
Don't know	39	13.00
Source of information*		**(n=193)**
Media: TV/Radio	87	27.40
Health personnel	82	25.80
Family planning worker	41	12.90
Relatives & friends	82	25.80
Husband	26	8.20
Correct time of taking ECPs*		**(n=193)**
Within 72 hours	64	29.0
To be taken daily	52	24.0
When menstrual cycle is missed	22	10.0
Within 5 days' sexual activity	9	4.1
Don't know	73	33.00
Conditions of taking ECPs*		**(n=193)**
After rape	9	3.80
When condom breaks	45	19.20
Forget to take pill	70	29.90
Undue pressure from husband	16	6.80
Don't know	93	39.70
Benefits of taking ECPs*		**(n=193)**
Can prevent pregnancy	192	79.30
Cannot prevent HIV/AIDS	161	30.5
Can not cause abortion	175	33.1
***Multiple responses**		

Discussion:

Contraceptive practices and awareness of emergency contraception was studied among rural married women of reproductive age group (15-49) years. In the present study most of the studied women (48.7%) were in the age group 25-34 years with a mean value 29.86±6.792 years. 114(33.0%) women had Secondary education and 52.5% had an income between 5000- 20000 taka. Majority 318 (92.2%) were house-wives which is almost similar to a study conducted by in Mangalore, India which reported that 69.5% of the studies population were housewives[13].The parity among 58.3% women was

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1-2 with a mean (±SD) of 2.22 (±1.114) which is inconsistent with another study in Karachi[11]. Now family planning method has been reached to every rural area with the help of our government as well as private sector and peoples are now more conscious about planning a family. So, now majority of family prefer to 1-2 children. The study showed that 52.2% of participants practiced contraception which is lower as compared to another study in Mangalore which showed user proportion of contraceptive 71.25%[13]. Regarding type of contraceptive methods in users, OCP was the most common method of contraception which was used by 58.3% of the participants which is almost similar to another study conducted by among currently married women in Bangladesh[12]. Our study reveals that about half of the couples (44.4%) took decisions by themselves which is almost similar (41.45%) to another study conducted in Mumbai, India14.38.3% of the participants used contraceptives for spacing of birth followed by 33.9%to complete their families, 16.5% used due to husbands approval which do not correlate with another study done in Bangladesh that showed 5.71% and15.71% women used contraceptives for birth spacing and due to husbands approval respectively[15]. Regarding reasons for not using contraceptives, 27.2% of the participants did not use contraceptives due to husband's disapproval which does not correlate withanother study in Bangladesh (7.43%)15. 23.6% said they didn't use contraceptives fearing of side effects which is higher than other studies in Bangladesh and Nagpur, India that is 18% and 2.1% respectively[15, 16].

This study reveals information related to awareness of emergency contraceptive pills. majority i.e. 55.9% participants heard about ECPs which is higher than among currently married women in Bangladesh (14%) and lower than among college students in south India (85.5%)12,17. In this study, 27.40% of the participants got information from media: TV/Radio which is lower than a study conducted in India where 77.9% of college student's source of information was television[17].

The correct time frame for contraceptive use was seen to be lower in comparison to previous studies. 29.0% knew ECPs should be taken within 72 hours of unprotected sex which is lower than study conducted in Ghana 85%10 and higher than a study in Lao 7.9%18. 4.1% participants knew ECPs should be taken within 5 Days of sexual activity which is inconsistent with a study conducted among college students in India 54.4 %[17]. This may be due to lack of knowledge of family planning and contraceptive methods among rural women. 39.7% of the participants had no knowledge regarding correct time of taking ECPs, which is almost similar to women who were aware of ECPs in Ghana (50.0%)10. 9(3.8%) knew ECPs are to be taken after rape which is lower than the study in Ghana (17.4%)10. Regarding benefits of taking emergency contraceptive pills, 192 (79.30%) of the participants knew emergency contraceptive pills can prevent Pregnancy which is a bit lower than the study in Lao which reported 88.6% women knew emergency contraceptive pills can prevent Pregnancy[18].

CONCLUSION:

In this study it is observed that the level of contraceptive practices and awareness of emergency contraceptive pills are relatively low. So, this study provides information that further evaluation is needed in this field specially about awareness of emergency emergency contraceptive pills to achieve our goal of population stabilization in Bangladesh. Efforts should be focused on providing health education through personal communication, films, posters, newspaper articles, folk dramas, radio & television programs and group meetings regarding contraceptive practices and awareness of ECPs to the rural women. Inter-spousal counselling to adopt contraceptive methods and discourage of preference for son through campaign programs and awareness rising activities should be implemented at community and national level.

CONFLICT OF INTEREST:

There is no conflict of interest among the authors.

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Original Article

Iatrogenic Fistula after Gynecological Operation in a Tertiary level Hospital

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Abstract

Background: *Genitourinary fistula constitute a social calamity for the women in the developing countries.The most common cause being obstructed labor, as my study is on fistula due to iatrogenic cause, the most common cause is gynecological surgery. This study has been designed to find out the general information about iatrogenic genitourinary fistula and its outcome.* ***Method:*** *A cross-sectional descriptive study was done on 42 women suffering from urogenital fistula admitted in fistula corner in the department of Obs. & Gynae, Rajshahi Medical College Hospital from March to September 2015. A detailed history was taken to find out the casual factor. All the result had noted in pre-designed history sheet. The data has analyzed by SPSS version II and percentage were calculated.* ***Results:*** *Among 42 of total genitourinary fistula 19 cases of iatrogenic fistula were isolated after proper searching of detailed history. Among the 19 patients 11 (57.90%) patients developed fistula following total abdominal hysterectomy, 4 (21.05%) following laparotomy, 03 (15.79%) following vaginal hysterectomy with anterior colporrhaphy, and 1 (5.26%) patient developed fistula following repair of complete perineal tear. Among 11 patients with total abdominal hysterectomy, 06 were suffering from pelvic inflammatory diseases, 03 patients with fibroid uterus and of the rest 02 patients 01 with endometriosis and 01 patient with dysfunctional uterine bleeding. It was found in majority of the cases (68%) fistula developed within10 days. Among the iatrogenic genitourinary fistulas vesicovaginal type was found to be the most common (84.21%) in this study.* ***Conclusion:*** *The etiology of urogenital fistula is preventable. By utilizing basic principal of surgery, all types of urinary fistula can be repair.*

Keywords: *Urogenital fistula, Vesicovaginal fistula, Vaginal hysterectomy, Total abdominal hysterectomy.*

Introduction: An abnormal communication between urinary and genital tract termed urogenital fistula. The commonest type of genitourinary fistula is vesicovaginal. The close embryo-logic development and anatomic proximity of the urinary and genital organ predisposes the urinary tract injury during surgical procedure in the female pelvis.[1] Fistula is commonest in developing countries because of the higher incidence of obstetric complication. In contrast in the developed countries, 90% of vesicovaginal fistulae (VVF) are caused by gynecological procedures.[2] Hysterectomy is the most common procedure that comprises 75% of fistulae. Injury usually occurs when surgery is done in a hurry by a person with lack of knowledge & proper procedure, without adequate skill in complicated cases and in adverse situation (e.g. without adequate light or exposure). The vast majority of fistulas following hysterectomy are noted to be high in the vaginal vault above theinter-ureteric ridge and coinciding with the vaginal apex scar. The gynecological ureteric injury occurred during Wertheim's operation, when the

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ureter was accidentally transected near the uterine vessels.[1] The earliest evidence of a VVF was found in 1923, when Derry examined the mummified body of Henhenit, a lady in the court of mentuhotep of the 11th dynasty who reigned around 2050 BC. These dissections revealed a large VVF in a markedly contracted pelvis. However, not until 950 AD. The term fistula (previously called rupture) had not used until 1597, when luiz de mercads first coined the term.[1] In 1663 von Roonhuysen, in his text book on operative gynecology, described a vesicovaginal repair in the lithotomiy position. Marison Sims in 1852 however, was the first who had repeated success in fistula repair that depends on timing of repair. James Marison Sims overcome a mountain of obstacles to build the first "Fistula Hospital" in New York, United states of America on 5th may 1855. After 120 years 24th may 1975, Reginald and cathrin Hamlin built the second fistula hospital in Addis Ababa, Ethiopia. This is now the only fistula hospital in the world. Genitourinary fistula is a devastating condition affecting the physical and psychological health of women. With advance obstetric care these fistulas are rare in industrialized world, but they continue to pique women in the third world. Globally about 3.5 million women are living with genitourinary fistula, a miserable condition. 2An incidence of 1-2 per 1000 delivers has estimated worldwide, with an annual incidence of up to 50,000 to 100,000. However, the accuracy of this estimate on colposcopic examination is unknown given that these are almost no reliable data on the magnitude of obstetric fistula at the country level. In Bangladesh 1.9 percent women are suffering from vesicovaginal fistula (BIRRERTH).[3] According to UNFPA & Engender Health, the number of women living with fistula is estimated to be 1.69 per 1000 over married women.The etiology of genitourinary fistula broadly categorized into congenital and acquired. Congenital fistula is extremely rare. Acquired fistula is divided into obstetrical, surgical, post radiation, extension of disease process, foreign body, chemical burn, accidents. The etiology of urogenital fistula is dependent on the availability and adequacy of obstetric care, malignancy rate and types of previous pelvic surgery that a women was undergone. While proximate causes of fistulas are physical injuries, the larger causes are social i.e poverty, lack of education, child bearing at too early age and lack of medical care. In many rural areas, girls are married off just after between 12 and 15 years of age. These girls become pregnant which leads to many unwanted conditions including mortality and long-term morbidity like obstetric fistula. Medical facilities are not trusted, or may be used only as a desperate last resort when damage is already for advanced.3 In developing countries, obstetric traumas are more likely to be the cause, where as in developed countries, gynecological procedures are main contributors.[4] The urinary tract is at risk of injury during pelvic surgical operations due to its proximity to the female genital system.[5] These complications although rare can result in morbidity and even morality for the patients, which can create anxiety and psychosocial concerns for the patients and their spouces.[6] In developing countries like Bangladesh, obstetrical injury is the main cause of genitourinary fistulas and it usually gives rise to complicated fistulas but iatrogenic fistulas are seen and are due to frequently reflects lack of experiences of the young surgeons, most of whom did not have sufficient and methodic tutoring during their obstetrics & gynecologic training. This study has been designed to critically analyze the different aspect of iatrogenic fistula with the hope that findings as this studies may help to develop the awareness among the health provider about the fistula.

Method:

From March to September 2015, 19 patients with iatrogenic genitourinary fistula were admitted in Rajshahi Medical College Hospital having complains of continuous dribbling of urine. A detailed history was taken & through examination was done in each case. All patients had their fistula confirmed by vaginal examination using sim's speculum. The fistula was visualized noting its number, size, anatomical location & surrounding tissue morbidity. For differentiatingthree swab test was done; not only confirms VVF, but also differentiates it from uretero-vaginal and urethra-vaginal fistula. It is done by placing three large plegets of cotton wool. Three swab in vaginas, one above another and to run methylene blue solution in to the bladder. If only the lowest swab stains, the fistula is urethral, if middle or upper swab stain the fistula is vesicle. If none of the swab stains but the upper one is wet, the fistula is ureteric.[7] When this was difficult a pre-operative examination under anesthesia was done and similar information was obtained.Fistula due to obstructed

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labor or caesarean section was excluded from this study. Surgery was done in 19 patients, repair was done vaginally in 14 patients & rest of had abdominal repair. All vaginal repair was done in exaggerated lithotomy position. The method of repair was varied with the location & type of fistula patients required labial graft and one patient required urethral reconstruction. Bladderand vaginal wall was sutured by delayed absorbable poly glycolic acid suture, all patients were given prophylactic post-operative antibiotics and had indwelling catheters for a minimum period of 3 weeks. They were discharged 2 to 3 days after removal of catheter with advice that they should abstain from sexual intercourse for 3 months.Surgery was considered to be successful if patient can hold urine and there is no leakage of urine in between the act of voiding after removal of catheter and before discharge from the hospital. The data was processed and analyzed with the help of SPSS versionII software program. Result was compiled in chart and diagram and conclusion was drawn.

Result:

Total 42 patients with genitourinary fistula were admitted,among them 19 cases of iatrogenic fistula were isolated. Fistula due to iatrogenic causes includes total abdominal hysterectomy, laparotomy and repair of complete perineal tear which is about 6.17% to total genitourinary fistula. The most common cause of fistula included prolonged and obstructed labor in over 94% case. Previous surgery was done in union level to tertiary care Centre. The fistula developed following operation in union level 02 (10.5%), in upazilla level 04 (21.5%), district level 10 (52.6%) and tertiary Care Centre 03 (15.8%). Age distribution and socioeconomic status was described in table 1. Various level of surgeons were involved in the surgical procedure described in table 2. Causes of the fistula was shown in table 3. The development of fistula was noticed from 10 days to more than 30 daysdescribed in table 4. Vesicovaginal fistula was the predominant type in this study.Position of the fistula wasdescribed intable 5. Size of the fistula was ranged from less than 2 cm to more than 4 cmshown in table 6. Various methods was applied for repair the fistulasdescribed in table 7. All patients were repaired locally. Theapproach of surgery was shown in table8. Among 19 patients repair was done successfully 17 cases and the success rate was 89.47%. Only 02 patient in when repair was unsuccessful due towound infection shown in figure 3. Religion and education level of patients with genitourinary fistula was described in figure 1 and 2 respectively.

Table 1: Baseline characteristics of the patients:

Variable	No	%
Age		
<30	01	5.27
31-40	04	21.05
>40	14	73.68
Sociodemographic status		
Rural	16	84.21
Urban	03	15.79
Total	**19**	**100**

Most of the patients were in >40 years age group (73.68%).
Rural patients were more (84.21%).

Table 2: Competency of Surgeon.

Level of surgeons	No	%
Consultant	02	10.5
Trained MO	05	26.3
General Practitioner	12	63.1
Total	**19**	**100**
Most the surgery 63% was done by general practitioner.		

Table 3: Causes of the fistula.

Name of Cases		Number of patients	%
Total abdominal hysterectomy	Total	11	57.89
	PID	06	
	Fibroid uterus	03	
	Endometriosis	01	
	DUB	01	
Laparotomy		04	21.05
Vaginal hysterectomy		03	15.78
Complete perineal tear		01	5.26
Total		**19**	**100**

Most of the fistula (57.89%) was developed following total abdominal hysterectomy.

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Table 4: Duration of developing fistula.

Time (days) after surgery	Number of patients	%
Within 10 to 20 days	13	68.42
Within 20 to 30 days	04	21.05
More than 30 days	02	10.52

Majority of cases 13 (68%) fistula developed within 10 to 20 days.

Table 5: Position of the fistula.

Position of fistula		No of patients	%
Vesicovaginal		16	84.21
	High vaginal vault	11	57.087
	Mid vaginal vault	03	15.78
	Juxta-Cervical	02	10.52
Uretero-vaginal		01	5.26
Urethro-vaginal		02	10.52

Most common type was vesicovaginal found in 84% of cases.

Table 6: Size of the fistula.

Size (cm)	Total number	%
Less than 2 cm	12	63.15
2 cm to 4 cm	06	31.58
More than 4 cm	01	5.26

Most of the fistula 63%was less than 2 cm in size.

Table 7: Procedure of repair of the fistula.

Name of operation	Total Number	%
Flap splitting	15	78.94
Urethral reconstruction	02	10.52
Ureteroneocystostomy	01	5.26
Repair RVF	01	5.26

Flap splitting method was used in most of the cases 15(78.94%).

Table 8: Approach of surgery.

Route	Total number	Percentage
Abdominal	05	26.31%
Vaginal	14	73.68%

Most of the (73.68%) fistula were repaired through vaginal approach.

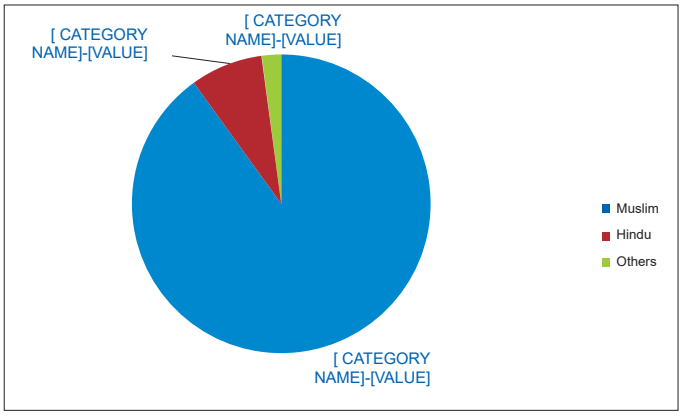

Figure 1: Pie chart shows Muslim patients were more (90%).

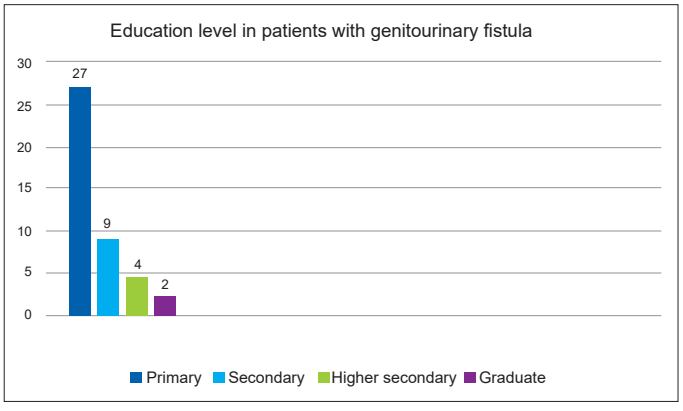

Figure 2: Bar diagram showing genitourinary fistula more in primary education level.

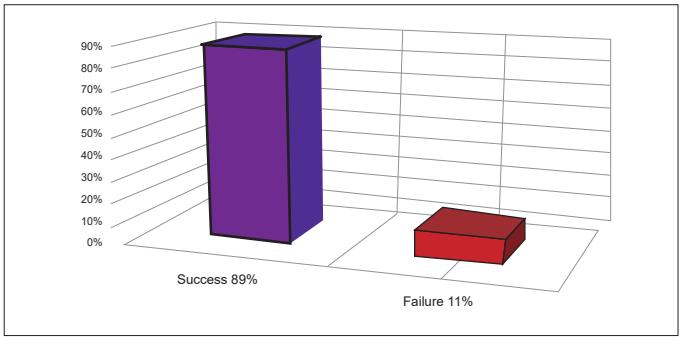

Figure 3:Outcome of iatrogenic fistula surgery.

Discussion:

Genitourinary fistula is a real misery for the women in the developing countries, the most common cause being obstructed labor, as my study fistula due to iatrogenic after gynecological operation, the most common cause is during the procedure of hysterectomy. After such fistulas develop, the lives of these women are disrupted unless they can gain access to curative surgical services, the constant uncontrolled dribble of urine makes the offensives to

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their husband & family members. Kochakarn W et al reported in 2000, and found 164 cases of 230 fistulae caused by Trans abdominal hysterectomy (TAH) (71.3%), 23 cases (10%) caused by Trans vaginal hysterectomy (TVH) and 08 cases caused by radical hysterectomy for malignancy[8]. Bai et al reported and overall incidence of urinary tract injury in pelvic surgery of 0.33%. The bladder is the most common organ to be injured, comprising 76% of the cases[9]. Lee, in series of 35000 hysterectomies, found more than 80% of genitourinary fistulas arise from gynecological surgery for benign diseases[10]. In this study we found 57.89% patients developed fistula following abdominal hysterectomy and 21.05% after vaginal hysterectomy with anterior colporrhaphy, which was almost similar to other studies. In approximately 10% of cases of vesicovaginal fistula, the associated etiology was obstetrical trauma. Radiotherapy & surgery for gynecologic disease each account for 5% cases[11]. An evaluation by Symmonds at the Mayo clinic over 30 years period showed that 85% VVF were related to pelvic operations, 755 were related to hysterectomy, 5% were obstetric & 10% occurred after radiotherapy.

These days more and more caesarean section was carried out and fistulas were encountered either vigorously with the finger & these maneuver frequently result in trauma to the bladder with haematoma formation that ends with sloughing and late vesicovaginal fistula formation. A few days of vesicovaginal & vesico-uretero-vaginal fistulas are also noted after lower segment caesarean section that resulted from unwary suturing of the lower segment and indvarent inclusion of the bladder wall and or distal end of the ureter[12]. The vast majority of fistulas following hysterectomy is noted to be high in the vaginal vault above the inter ureteric ridge coinciding with the vaginal apex scar. In additional to this type of supratrigonal fistula, a bladder neck fistula below the trig one may occur with anterior colporrhaphy or urethral surgery. This type of fistulas would be to found in the mid vaginal vault[13]. Vesicovaginal type of fistula was found to be the most common in this study which constitute about 84%, among them high vaginal vault fistula was 57%, mid vaginal vault about 15%, juxta cervical type is about 5.26%. Certain precaution to be taken to prevent urinary tract injury and post-operative fistula formation are a thorough knowledge of anatomy and common sites where urinary injury is likely to occur is essential. The patient at high risk should be identified and these are the cases with possibility of altered anatomy, fibrosisand direct extension of disease process as in cases of chronic PID, large fibroid, endometriosis, previous pelvic surgery, malignancy, previous irradiation and congenital abnormalities of urogenital system. Abnormal relation of the uterus and bladder caused by the uterine leiomyoma[14]. In this study abdominal hysterectomy were done up to PID at 31% cases, fibroid uterus at 15% cases, endometriosis & DUB at 5% cases. A fistula may appear a few months to several years after the radiation treatment is completed. Vesicovaginal fistula induced by radiation therapy are usually complicated and difficult to close for several reasons. The apex of the vagina the tissue surrounding the fistula is fixed, relatively avascular & fibrotic. Because the radiation induced obliterative endarteritis is progressive over a period of many months, the fistula may enlarge with continued ischemic and necrosis of more tissue[13]. The main concepts of repair have not change much since the recommendation of sims in 1852. The most important factor for successful repair of a fistula is adherence to basic principles, including pre-operative evaluation, good exposure of the fistula and excision of surrounding fibrous tissue tension free closure and adequate post-operative urinary drainage. A transvaginal versus transabdominal approach depends on the location of the fistula, relation with the ureteric orifice and time to repair after fistula formation. The transvaginal approach can be done earlier than the transabdominal approach, which has to be delayed until 3 months after hysterectomy turnover, the transvaginal approach has limitations in the case of a high fistula that is hard to approach or a fistula close to ureteric orifice. Many studies have claimed that the transvaginal approach is less invasive than the transabdominal approach. All patients in this study had undergone local repair, repair by the vaginal approach was favored unless the fistula was inaccessible vaginally. 73% of our patient were repaired through vaginal route and 26% cases transabdominally. This data almost similar to the study of C.R mange[14]. Vaginal approach was favored because it gives a less stormy post-operative recovery surgeons feel comfortable and gets the opportunity to use labial fat pad graft which was used in at 06 cases. Two third of the cases, flap splitting method was used, accounting for 78% and rest was corrected by

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ureteroneocystotomy[8]. Time needed for repair procedures takes only less than 02 hours in most cases, only 03 cases took up to 03 hours. Following repair procedure, catheter was kept in situ 21 days in most patients. Post-operativecomplicationswere negligible. 15 patients among 19 patients, did not develop almost any complication. 03 cases had variable forms of urinary tract infection which was controlled with antibiotics. Most troublesome complication was vaginal wound infection in 01 patient. Among 19 patients repair was done successfully in 178 cases and the success rate was 8915. The remaining 02 patients in whom was unsuccessful.

Limitations:

1. The duration of this study was only seven months and sample size was also small, only 19 patients; thus subject to bias in the sample of diseases seen.
2. As the study was single centered govt. hospital based, many patients of different community may missed that may affect in results of the study.

Author's Contributions:

All the authors were contributed in various parts of the publication from concept and design, acquisition of data, analysis & interpretation of data and drafting of the manuscript.

Declaration of Conflicts:

The authors declare that, there is no conflict of interest regarding the publication of this article.

Conclusion:

Naturally, UGF makes the patients embarrassed that they are unable to control their bodily functions, that they are constantly soiled and wet, and that they smell. Thus, UGFs have a profound effect on the patient emotional well-being that results from the social distress because of persistent leakage of urine and feces.

Recommendation:

Injury to the urinary tract may occur with gynecological surgery. It is important to have a detailed understanding and knowledge of pelvic anatomy or reduce the risk of trauma.

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Original Article

Pattern of suicide in Bangladesh: A retrospective study

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Abstract

Background: *The most important global cause of mortality is suicide.Global suicide rates have increased 60% in the last 45 years. Unnatural death is one of the indications of social and mental health in a society.It is often neglected by researcher, health professionals, health policy makers and the medical profession.Unnatural death by suicide relates to multiple factors eg. low socio-economic condition, dowry system, lack of education, failure of love, poverty etc. Shooting, hanging and stabbing are a hard way of committing suicide and typically a male choice.Poisoning and drowning are soft way of committing suicide and typically a female choice. This article was aimed to find out the pattern and demography of suicidal death.* ***Materials and method:*** *To find out the pattern of suicidal death, a retrospective data was collected from the records of Forensic Medicine Department in Sir Salimullah Medical College, Dhaka for the period of 1 year from January 2021 to December 2021.* ***Objective:*** *The objective of this study was to find out pattern and demography of suicidal death, its distribution according to age, sex, common method used by victims and in this way try to identify the causative factors and develop the preventive measures that are essential to reduce suicidal death.* ***Results:*** *The commonest methods of committing suicide were found hanging which was 60.3%, followed by poisoning 26%, burn 1.34%. Most of the victims (25%) were from the age group 1-15 years. Out of 328 cases 170 (52%) were male and 158 (48%) were female. Among them 196 (59.8%) were married and 132 (40.2%) were unmarried. Most common poison was Organo Phosphorus Compound (OPC).* ***Conclusion:*** *To reduce the number of suicide a well designed and comprehensive program is needed which will identify the causative factors and which might help in prevention of suicide.*

Introduction: Suicide usually means self destruction. Suicide occurs throughout the world.It can be defined as ruin or harm suffered by a person, society etc on account of his own action.Suicide may injure themselves in different ways, some bizarre in the extreme. Suicide is one of the forms of criminal offence in our country and it is also prevailing in other countries of the world.In every country suicide is considered a social stigma. The gradual increase in the trend of suicide in the modern world posses a great social and human problem. Whenever attempts to commit suicide and does any act towards the commission of such offence, shall be punished with simple imprisonment for a term and may extend upto 1 year or with fine or with both. This increasing trend of suicide can be minimized to a certain extent with the help of psychiatric experts and experts in social medicine.It also constitutes an important medico legal problem and hence all suspected cases of suicide should be thoroughly investigated by forensic pathologists, forensic scientists as well as other investigating agencies.Investigations are sometimes confused in complex and bizarre cases of suicide.[1]

Global suicide rates have increased 60%in the past 45 years. Over one million people die by suicide worldwide each year. The global suicide rate is 16 per 100000 populations. On average, 1 person dies by suicide every 40 seconds somewhere in the world. 1.8% of worldwide deaths are suicides.[2]

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Availability of specific means for suicide affects national patterns in the methods used. In the USA, firearms are used in most suicides, with risk of their being highest where guns are kept in household[3]. In general men tend to choose more violent means (hanging or shooting)[4] and woman less violent methods (eg. Self poisoning. In rural areas of many developing countries, ingestion of pesticides is the main method of suicide, reflecting toxicity, easy availability and poor storage. As many as 30% of global suicide deaths might involve ingestion of pesticides[5-6]. In our country the incidence of suicide is increasing day by day. Unfortunately we are considered as the 3rd world developing nation with high rate of birth, mortality and morbidity and the higher population growth rate.

Hanging goes in favour of being suicidal in nature.Both sexes are equally prone and incidence in both sexes are more or less same.[7] Suicide by road traffic injury has been investigated by Mohanti. The suicidal attempt can be made by aiming the vehicles or by smashing the car against an obstacle at the side of the road-a tree or utility pole. The car may be driven on to rail road tracks to be run over by an coming train. Leaps into the path of a moving car or from or over bridge into traffic have also been reported[8]. The cunning suicide perhaps with the intention to defraud an insurance company or through suspicion or an innocent person by way of revenge, may plan his death in a manner which suggest homicide. Higher population pressures directly and effects on countries low socio economic growth, lack of education, unemployment and poverty. As a result the number of suicidal deaths increases day by day. Although mortality of a man breaks down under certain conditions like social and economic insecurity, social stigma etc[9]. The causes of suicides are not only related with the victims but also associated with other factors. Now-a-days different papers publish the incidence of suicide with due importance though many cases are not reported due to social stigma, fear and prestige of the family. In fact, the suicidal death cases are much higher than the cases recorded by authority.

Materials and method

It is a retrospective study carried out in the department of Forensic Medicine in Sir Salimullah Medical College from January 2021 to December 2021. The various characteristics of the cases and their medicolegal aspects were collected from the relative of the victim, police papers, postmortem and chemical examiner's report from Forensic Medicine Department, SSMC.

Result

Total 378 cases were brought by different police stationof Dhaka city for post mortem examination to Forensic Medicine Department, Sir Salimullah Medical College. Out of them total number of suicidal death were 328.Among the suicidal victims 52% were male and 48% were female. 56% of these victims have committed suicide by hanging themselves. About 24% committed suicide due to poisoning 4.41% with fire on the body. 25% of those who commit suicide were under 15 years of age. About 38% were 16-30 years old, 22% were 31-45 years, 10% of 46-60 years and 5% over 60 years of age.

Table 1 : Shows the distribution of the case according to sex

Sex	No.of cases	%
Male	170	52%
Female	158	48%
Total	**328**	**100%**

Table 2: Shows the frequency of method used in suicidal death

Method	No. of cases	%
Hanging	183	56
Poisoning	78	24
Burn	21	6.34
Drowning	18	5.60
Firearm	16	4.41
Cut throat	12	3.65
Total	**328**	**100**

Table 3: Suicidal deaths according to marital status

Marital status	No.of cases	%
Married male	34	10.4
Married female	162	49.4
Un married male	55	16.8
Un married female	77	23.4
Total	**328**	**100%**

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Table 4: Suicidal deaths according to the age

Age	No.of cases	%
1-15	82	25
16-30	125	38
31-45	72	22
46-60	33	10
>60	16	05
Total	**328**	**100**

Table 5: Suicidal deaths according to cause

Cause of suicide	Number of cases	%
Poverty and family problem	185	56.40
Failure in exam and love affair	112	34.14
Drug addiction	10	3.05
Unknown	21	6.41
Total	**328**	**100**

Discussion

Suicide is increasing day by day. According to the Bureau of police research and development, number of suicides has been increasing continuously in Bangladesh than the previous year. Our study shows that out of 378 cases, there are 328 cases of suicide amounting to 86%. According to the police statistics from January to December 2021 among the suicidal victims 52% were male and 48% were female. This study showed that suicidal hanging is one of the major causes of unnatural death in our country. In our country suicidal death was observed in all age group, but majority were within 19-30 years age group.[10] This is the most active period of one's life and there are great fluctuation of emotions of this group. Young people get frustrated due to various reasons such as unemployment, poverty, failure in examination, failure of love, excessive mobile addiction etc. Suicide are constantly happening in different parts of the country due to such trivial reasons. From January to June, police across the country recorded suicide among teenagers and young people who did not buy mobile phone and had a little quarrel with parents. All these causes form the motivational factors to terminate their lives.

Suicides were not only diagnosed clinically but also circumstantial evidence given by the relative and investigating agencies. Our study shows hanging is one preferred means of committing suicide in this subcontinent followed by poisoning differs from the study of Sharma et al[11]. However death by hanging may be accidental or even homicidal. The condition is very rare. Suicide is increasing day by day. Suicides apart from hanging and poisoning may use some of the other methods such as stabbing, cutting, firearm and explosives, jumping from height, burn, suffocation by plastic bags, electrocution, road and railway injuries, drowning. Suicidal knife wounds may be incised and stab wounds are self inflicted either from victims of self destruction, from mental aberrations or by deliberately for some form of gain. Suicidal knife wounds are those, whose site and range are within the reach of the deceased suicidal cut throat usually has the trial of incision. Deliberate cutting of the wrist is rarely effective the sole method of suicide. In case of suicide by firearm there are certain site of selection which are predominantly over the throat, the wrist and the front of the chest. The weapons must be present at the scene[12]. There may a suicidal note left behind.

There should be a motive for committing suicide. We found that most of the victims were committing suicide by hanging is more prevalent among the females. This may be due to the fact that there are too many influencing or provoking factors like lack of family bonding, emotion, sentiment, poverty, dowry agreement, 2nd marriage of the husband, failure of love, pregnancy resulting from rape, failure in examination, eve teasing etc which eventually lead to suicidal attempts[13]. The incidence of sexual harassment and eve teasing in Bangladesh are rapidly increasing.The young or teen aged girls usually commit suicide in order to escape from sexual harassment or eve teasing. In recent years in India the researchers have documented the prevalence of physical, sexual and emotional abuse, association between violence and physical and mental health14. In our study majority were married. Marital disharmony was the commonest cause. In our country males are predominantly earning member of the family and husbands torture or harass the wives for various family problems including dowry. The female members have low frustration tolerance level and weak protective value in social institute like family especially in low socio economic condition. Due to repeated physical and mental torture, sometimes they go beyond the threshold level of self control and commit suicide. In case of male; poverty, lack of job, failure in the examination, illness, family

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problems, defamation, drug addiction like alcoholism are the main reasons for suicidal hanging. These causative factors are similar to those in India. A five year study (1998-2002) in Turkey also showed that hanging is the commonest method of suicide in Istanbul. A study in Lithuania has shown that a total of 8324 suicides were committed during 1993-1997 and 7823 between 1993-2002. Among all these registered suicides cases, hanging was the commonest method used to commit suicide[15].

Suicide by self emollition is indeed rare since most people, unless of unsound mind are well aware of the terrible pain which must follow this course. It was once a custom among certain religious group, for a widow to cast herself into the funeral pyre of her dead husband. It was an inhuman ritual and now it has been prohibited. Suicidal burning are still sometimes documented now a days. In autopsy series by Gupta 9.34% were burnt cases, number of female and male cases we 345 and 53 respectively.[16] Kitchen was the most frequent place of incidence. Circumstances of death were accidental, suicidal anhomicidal. Our study showed that suicide by burning was 6.34% where the commonest method of suicide in India was burning 38.8%. Suicide by burning is most prevalence in Northern India specially in Delhi. Suicidal electrocution is still uncommon. Organo phosphorus compound more commonly used suicidal poison. The number of cases due to dowry death has reached such a high proportion in recent years that the Government is trying to find ways and means of resolving the problem.

Abetment of suicide is an offence and punishable under the section 306 and attempt to commit suicide under section 309. Whoever attempts to commit suicide is liable to be punished with imprisonment of upto 1 year or with fine or both[17]. If the victim survived she/he could be charged of attempted suicide. Though the punishment is defined as such in the penal code, usually in such cases they are detained under probation and no punishment is given. Provocative suicide is also an offence under the section 305,306. Whoever provocates a person to commit suicide than the provocator is liable to be punished with an imprisonment of upto 10 years or fine or both. Abetment of suicide of child or insane person the punishment is 10 years imprisonment.[18]

Conclusion

Suicide is the form of criminal offence which is prevailing all over the world.Unfortunately it is also increasing day by day in our country. A well designed and comprehensive program is needed to identify the causative factors and prevention of suicide. To prevent suicide, status of mental health and social wellbeing should not be ignored. To improve the mental health status family bonding, proper education, sex education, self awareness and counseling may play important role. There should be proper employment facilities for the youth and involvement of young population in encouraging activities may reduce the rate of suicide in future.

Conflict of interest:

There is no conflict of interest.

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Original Article

Pyogenic granuloma: Clinicopathological and treatment scenario in Rajshahi Medical College Hospital.

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Abstract

Background: *Oral pyogenic granuloma is a soft-tissue lesion of the oral mucosa. This lesion has a tendency to recur after surgical excision.* ***Materials and Methods:*** *A total of 35 patients underwent surgical excision of pyogenic granuloma in the period from January 2019 to June 2022. Two surgical techniques were used to remove pyogenic granuloma: simple excision with root planing and modified excision with deep curettage.* ***Results:*** *Females (54%) were slightly more predominant than males (46%). The upper and lower jaws were almost equally affected by the lesion with more predilection toward the posterior region. The size of the lesion ranged from 0.5 to 3 cm in diameter with slow-growing rate. Rural residents were more affected (57%) than urban people. The lesion appears clinically as a small red mass with sessile base, and these clinical features were similar in pregnant and nonpregnant women. The recurrence rate was 14.8% and seen only in patients treated by simple excision. Histopathological feature was consistent with inflammatory hyperplastic lesion, and there was no radiographic evidence of bone resorption associated with the lesion.*

Conclusion: *Modified excision with deep curettage prevents the recurrence of the lesion after 1-year follow-up.*

Keywords: *Clinical features, etiology, pyogenic granuloma, recurrence, surgery*

Introduction: Pyogenic granuloma, which is a nonneoplastic soft-tissue lesion, occurs as a result of inflammatory reaction.[1] It is mostly affecting the gingiva and very rarely other sites of the oral cavity such as lip, tongue, and buccal mucosa.[2] Pyogenic granuloma is not considered as an appropriate term, as it does not occur as a consequence of granulomatous inflammation and does not contain pus material.[3] Previous studies suggested that soft-tissue injury due to infection was the main cause of this lesion.[4] Others, however, stated that the invasive stimuli of lowgrade intensity behind the development of pyogenic granuloma.[5] These include chronic irritation from dental calculus or retained roots and trauma. In addition, hormonal changes during pregnancy or puberty, and certain drugs such as cyclosporine could be the etiological factors of pyogenic granuloma.[6] Besides, certain cases of pyogenic granuloma have been reported in patients who underwent guided tissue regeneration[4] and dental implant.[7]

Pyogenic granuloma is usually seen in young adult females and most commonly occurring at the anterior gingiva of the upper jaw.[8] Clinically, this lesion presented as exophytic mass with smooth or ulcerative surface. Though, sometimes the lesion appears as a small erythematous papule on a pedunculated or sessile base.[9] The growing of pyogenic granuloma is slow and takes weeks to months to reach optimal size.[10] Therefore, the size of the lesion during presentation ranges from few millimeters to 4 cm in diameter. Although there are many treatment modalities of pyogenic granuloma, surgical excision is still the treatment of choice to eradicate this lesion.[6-

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Many researches showed that there was no recurrence following such a treatment modality.[10] However, the recurrence of the lesion was reported and rated between 5.8% and 16% after surgery.[12] The aim of this work is to study the clinicopathological aspect of pyogenic granuloma and to detect the recurrence rate after 1-year follow-up of two surgical techniques used to manage this lesion.

MATERIALS AND METHODS

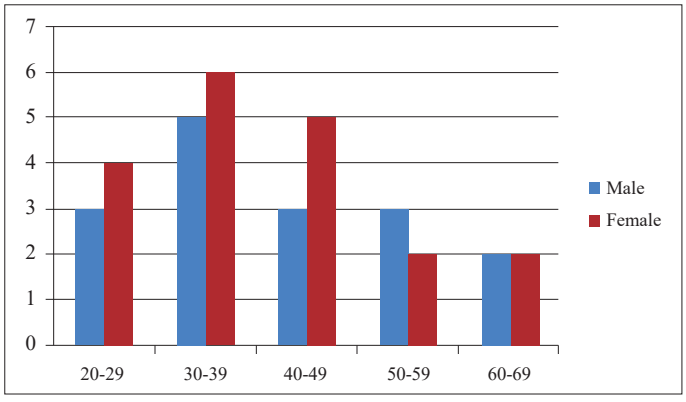
Successive patients who underwent surgical excision of pyogenic granuloma in the department of Oral & Maxillofacial Surgery, Rajshahi Medical College Hospital, during the period from January 2019 to June 2022 were studied. A consent form was taken from each patient before surgical procedure. Patients' information (age, sex, and resident) and features of the lesion (site – anterior or posterior/upper or lower jaw, size and duration of the lesion, clinical feature, and recurrence) were reported and analyzed. The etiology of the lesion whether local factors such as bad oral hygiene and occlusal trauma or systemic factors like hormonal changes as in case of puberty and pregnancy were recorded as well. A periapical view was taken for all patients to detect bone resorption.

The lesion was excised under local anesthesia for all patients. To detect the effect of surgical technique on recurrence rate of the lesion, patients were divided equally into two groups: in the first group, the excision was confined to the original lesion followed by root planing of the adjacent tooth and removal of the local causative factors, and in the second group, 2 mm of the normal adjacent tissue was excised with deep curettage until healthy bone and removal of the causative agents. For brevity, the first technique was described as simple excision with root planing and the second technique was modified excision with deep curettage. The excised specimens were kept in formaldehyde solution and sent for histopathological investigation. Patients were instructed to improve oral hygiene using toothbrushing and flossing. Chlorhexidine mouthwash were prescribed for 1 week. The treated cases were followed up for 1 year to detect any possibility of recurrence. This study was approved by the Ethical Committee of Rajshahi Medical College Hospital.

Results

A total of 35 patients with pyogenic granuloma were studied, in which 16 (45%) were male, and 19 (55%) were female. The ratio of male to female was 1:1.18. Six cases out of 19 were pregnant women. The mean age of the affected patients was 35.7(±12.5), with an age range of 20–70 years. The most frequent cases of pyogenic granuloma were seen in the age group of 30–39 years, as shown in Figure 1.

Figure: 1 Distribution of pyogenic granuloma according to age groups



Rural residents were more affected than urban people (57% and 43%). The upper and lower jaws were almost equally affected by the lesion, and the premolar–molar area of the upper and lower jaws was more predominant (36% and 64%) than the anterior part, as depicted in Table 1.Most of the cases presented clinically as a sessile lesion (72%). The size of the lesion ranged from 0.5 to 3 cm in diameter with duration ranging between 1month and 10 months. The majority of the cases were developed as a result of bad oral hygiene (78%) and the rest due to hormonal changes during pregnancy, as shown in Table 2. After 1-year follow-up, four cases were reported with recurrence in the group treated by simple excision and root planing, whereas no cases of recurrence had been reported in patients treated by modified excision with deep curettage.

Table 1: Distribution of the site of the lesion according to age groups

Age group	Jaw		Region	
	Upper jaw	Lower jaw	Anterior	Posterior
20-29	3	4	3	5
30-39	6	5	5	6
40-49	5	3	4	3
50-59	2	3	1	4
60-69	2	2	1	3
Total	18	17	14	21

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Table 2: Distribution of clinical features, etiology, and residents according to age groups

Age group	Clinical feature		Etiology		Residents	
	Sessile	Pedunculated	Local	Systemic	Rural	Urban
20-29	6	2	7	1	7	2
30-39	8	4	7	4	8	4
40-49	5	2	6	1	4	3
50-59	3	1	4	1	2	2
60-69	3	1	3	1	2	1
Total	25	10	27	8	23	12

Discussion

Oral pyogenic granuloma can be seen in all age groups from children to elderly people. The present study showed that the mean age of the affected patients with pyogenic granuloma was 35.7 years and the most affected age group was people in the fourth decade of life. Other studies stated that the peak incidence of pyogenic granuloma was seen in the second, third, and fourth decades of life.[3,5]

Adult females were slightly more affected by pyogenic granuloma than males, and the ratio of male to female was 1:1.15. The outcome of this work is similar to that of other studies, and this could be associated with female sex hormone and contraceptive medications.[10] The high-level estrogen and progesterone during puberty and pregnancy deteriorate the already established gingival inflammation by increasing dilatation and proliferation of blood vessels and releasing vasoactive mediators from the damaged mast cells.[8] It is thought that the expression of angiogenic factors such as basic fibroblast growth factor and vascular endothelial growth factor can be enhanced by trauma and female sex hormones which cause the development of pyogenic granuloma.[13] In the present work, six cases were pregnant women, and the surgical excision was carried out in the second trimester. This is to avoid the side effect of surgery on pregnancy.

Both the jaws were almost equally affected by pyogenic granuloma, and the premolar–molar region was more predominant than the anterior one, particularly the labiobuccal aspect of the marginal gingiva. This is because the posterior portion is more subjected to occlusal trauma and difficult to clean during toothbrushing. These findings are in agreement with previous study[10].

Clinically, most cases of pyogenic granuloma presented as painless red mass tends to bleed easily upon probation and a smooth surface attached at a sessile base. A similar feature was seen by Jafarzadeh et al.[4] but disagrees with that observed by Al-Khateeb and Ababneh[12] where the lesion was ulcerated and a part of the lesion had pedunculated base. Pyogenic granuloma of short duration tends to bleed easily because of high vascularity and less collagen fibers, while mature lesion contains more collagen and less vasculature.[4].

The role of oral hygiene and socioeconomic status (according to patient's income) of the patients in the evolution of pyogenic granuloma was obvious in the present study, as more rural residents suffered from this lesion compared to that of urban people. However, the sample size in the present work may be not enough to judge about the distribution of the lesion between rural and urban population.

The size of the lesion in this research ranged between 0.5 and 3 cm in diameter and small lesion developed within 5–20 days, whereas larger one took longer time (6–9 months). This indicates that the development of pyogenic granuloma is slow, and this phenomenon was reported by other studies.[14].

There are two techniques were used to manage pyogenic granuloma in this study. In the first group, simple excision (confined to the base of the lesion) was used followed by root planing of the adjacent tooth and removal of the causative agents such as dental calculus, overhanging filling, or retained roots. In the second group, surgical excision of the lesion with 2 mm of the adjacent normal tissue with deep curettage up to healthy bone and removal of the irritants was performed. This is to detect the effect of surgical technique on recurrence rate of the lesion.

Follow-up of the treated patients indicated that there was no evidence of recurrence in patients treated by modified excision with deep curettage. In contrast, the recurrence of the lesion was seen in 4 (14.3%) who treated by simple excision with root planing. The recurrence appeared with different intervals ranging between 10 months and 1 year. Although there were no huge differences between the two groups, this

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indicates that removal of 2 mm from the normal tissue and deep curettage may have an influence in the prevention of recurrence of the lesion. It has been postulated that recurrence is ascribed to incomplete removal of the lesion and persistent of the causative agents.[11] Therefore, 2 mm of the adjacent normal tissue was excised to ensure complete removal of the lesion.

Histopathologic examination of the excised lesion revealed pieces of rich vascular granulation tissue infiltrated with macrophages and other inflammatory cells consistent with that of pyogenic granuloma. In accordance with the study of Kamal et al.,[16] this study reveals that there was no radiographical evidence of bone resorption associated with the lesion.

Conclusion

Females in the fourth decade of life and rural residents were more prone to develop pyogenic granuloma. The posterior region of the upper and lower jaws, particularly labiobuccal aspect, was more affected by such a lesion. There is no difference in the clinical feature of pyogenic granuloma between pregnant and nonpregnant women. The majority of the cases occurred as a result of local factors such as deep pocket or retained roots. The size of the lesion was not exceeding 3 cm with slow-growing rate. Modified excision with deep curettage was successful to eradicate pyogenic granuloma with no recurrence after 1-year follow-up. Histopathologic investigation of the excised lesion was consistent with hyperplastic inflammatory lesion. Radiographically, there was no evidence of bone resorption associated with the lesion.

Conflicts of interest

There are no conflicts of interest.

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Original Article

Effectiveness of topical tacrolimus treatment in vitiligo patients

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Abstract

Background: *Vitiligo is an acquired, pigmentary skin disorder that is disfiguring and difficult to treat. Phototherapy and the application of topical corticosteroids are most commonly prescribed. However, these therapies are often not effective and the use of corticosteroids on the face may lead to cutaneous atrophy, telangiectasia, and ocular complications.* ***Objective:*** *To evaluate the effectiveness of topical tacrolimus treatment in vitiligo patients.* ***Materials and methods:*** *This prospective, randomized control trial study was conducted among the patients who sought health care in the Dermatology and Venereology out patient department of KYAMC, Enayetpur, Sirajgonj from August 2021 to July 2022. The study was conducted with a view to evaluate the efficacy of topical tacrolimus in vitiligo and to see the adverse effects of topical tacrolimus in the treatment of vitiligo.* ***Results:*** *This study shows 70 patients were enrolled them 32 were male and 38 were female. The mean age was 28.52±10.98 years. Monthly evaluations were performed. Maximum 61 patients (87.1%) achieved varying levels of repigmentation. 28 patients (40.0%) had reported up to 50% repigmentation. Sign and symptoms of erythema (8.6%) and burning (7.1%) were minimal.* ***Conclusion:*** *This study revealed that tacrolimus ointment may be an effective and safe option for the treatment of vitiligo. The ease of topical self-administration with minimal side effects makes this novel immunomodulatory agent a promising addition to the therapeutic armamentarium for vitiligo.*

Keywords: *Vitigo, topical tacrolimus.*

Introduction: Vitiligo is an acquired pigmentary disorder of the skin, characterized by the loss of function of melanocytes in the epidermis and well-circumscribed, asymptomatic pearly white macules varying in size and shape which tend to extend and increase centrifugally with time in an unpredictable way.[1] Segmental vitiligo has depigmented macules arranged in a dermatomal or quasi-dermatomal distribution, which does not cross the midline and is usually unresponsive to medical treatment.[2] Tacrolimus and topical corticosteroids are effective in treating vitiligo,[3] but there are not many studies conducted on segmental vitiligo.

Vitiligo is characterized by the progressive disappearance of melanocytes, resulting in depigmentation of the skin and/or hair. The etiology of vitiligo is unknown.[4] Genetic studies support a non-Mendelian inheritance, suggesting that vitiligo is a multifactorial, polygenic disorder. The autoimmune theory remains the most widely accepted. Vitiligo has frequently been reported in association with autoimmune disorders such as thyroid disease, diabetes mellitus and alopecia areata. Several studies have suggested that the presence of increased antimelanocyte antibodies and the imbalance of T-cell (CD4+/CD8+ and Tregs) subsets, along with their functional defects, may result in melanocyte destruction in vitiligo patients.[5] The disease affects both genders equally. It can appear at any age and the average age of onset is somewhat variable in different geographic regions. Vitiligo treatment remains a challenge. Therapeutic options for vitiligo include: topical and systemic corticosteroids, topical calcineurin inhibitors, calcipotriol, phototherapy, excimer laser, and surgical methods such as skin single-hair grafting,

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autologous cultured melanocyte or epidermal suspension transplantations. Topical corticosteroids are most commonly used drug to treat vitiligo but there are concerns over side effects due to long-term use. Steroid application causes skin atrophy, telangiectasia, hypertrichosis and acne. Tacrolimus and pimecrolimus are used as topical immunomodulators. They inhibit calcineurin action, thus preventing T-cell activation and the production of various inflammatory cytokines. Both have been used to treat other inflammatory and immunologic skin disorders, including vitiligo, with encouraging results.[6] Tacrolimus is a macrolide antibiotic produced by Streptomyces tsukubaensis with strong T-specific, immunosuppressant activity. The biological activity of tacrolimus takes effect after binding to the cytosolic 12- kd macrophilin FK506 binding protein (FK-BP). The tacrolimus/FK-BP complex inhibits calcineurin-mediated phosphorylation of the transcription factor, the nuclear factor of activated T-cells (NFAT). Hence, the expression of several inflammatory T-cell cytokines is inhibited.[6]

Vitiligo is an acquired depigmenting disorder characterized by loss of functional melanocytes. It is estimated that about 1-2% of population[7] suffers from vitiligo. The onset of vitiligo is usually in childhood or young adulthood. Men and woman are equally affected; all races are affected, in 50% of cases the age of onset fall within the first two decade of life. in Iraq the mean age of onset 17.9 years and in 60% of patients it develops before the age of 20 years, 25% of patients had family history of vitiligo.[8] Current treatment of vitiligo e.g. topical corticosteroid, topical tincture iodine 5%,[9] narrow band UVB[10] and PUVA are the most prescribed, corticosteroid applied to the face may lead to cutaneous atrophy, telangiectasia and ocular complication, narrow bad UVB requires expensive equipments and trained personnel and PUVA has been associated with risk of carcinogenesis, phototherapy and corticosteroid have limited effectiveness particularly on the face.[11] Immunomodulator such as Tacrolimus 0.1% and 0.03 %, and pimecrolimus cream 1 % are approved for treating atopic dermatitis in adult patients and pediatric patients over 2 years of age.(5) Tacrolimus (FK-506) is an immunosuppressive drug membered macrolide lactone discovered in 1984[12] from the fermentation broth of Japanese soil sample that contained the bacteria streptomyces tsukubaensis can be used as an alternative to topical steroids in many other forms of dermatitis. This ointment does not cause atrophy, telangectasiae or adverse ocular effects of topical corticosteroids which has limited application to the face and intertregnous areas.[11] Tacrolimus acts on T cells and mast cells inhibiting T cell activation and the production of proinflammatory cytokines such as tumor necrosis factor (TNF) whose level is higher in vitiligo lesional skin. Moreover, it prevents the release of proinflammatory mediators in mast cells by degranulation.[12]

MATERIALS AND METHODS

It was a prospective, randomized control trial study carried out in the Out Patient Department of Dermatology and Venereology, KYAMC, Enayetpur, Sirajgonj 2. Total 70 cases were included in this study from August 2021 to July 2021. Vitiligo was diagnosed by clinical assessment & wood's lamps examinations. Clinical assessment was done at baseline. Clinical assessment consists of examine all the treated lesions. Lesions of one palm sized area are considered as 1% of involvement. As the study was conducted by topical application of medicine, involvement less than 10% was included in the study. Disease activity was assess by taking history, disease was considered as active if the existing lesion increase in size or there is development of new lesions. History of spontaneously repigmenting vitiligo was excluded from the study. There is currently no quantitative tool for evaluating vitiligo treatment response using parametric methods.13 Repigmentation may starts on the hair follicle(typical perifollicular) or starts as homogenous pigmentation from the periphery of the lesions(perilesional).14 At the baseline repigmentation was considered as 0% means the lesion was completely depigmented or no pigmentary remnant. 1-25% pigmentation was considered as minimal, when only specks of pigment appeared. 26-50% pigmentation was considered as mild, when some pigmentation but depigmented area exceeded pigmented area. 51-75% pigmentation was considered as moderate, when there were some depigmentation but pigmented area exceeded depigmented areas. 76-100% pigmentation were considered as excellent, when the treated areas were either completely repigmented or there is only specks of repigmentation (Lepe et al 2003). Colored photographs of treated lesions were taken at the beginning of the study and subsequent monitoring of the efficacy of the treatment assess by comparing the treated lesions with baseline photograph.

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Topical tacrolimus 0.03% (Tacrol ointment) is applied twice daily for 24 weeks to the case group. The control group applied Vaseline only twice daily. Clinical assessment was done monthly for six months. The monthly assessment includes seeing the extent of repigmentation and depigmentation, and also monitoring the adverse effects such as pruritus, erythema, burning, stinging, anaphylactoid reaction. All data were checked and edited after collection. Then the data were entered into computer and analyzed with the help of SPSS windows version 25.

RESULTS

Table-1: Demographic characteristics of two groups (n=70)

Characteristic	Number of patients	Percentage (%)
Age in years		
≤20	7	10.0
21-30	33	47.1
31-40	18	25.7
41-50	12	17.1
Age (mean±SD)	28.52±10.98	
Sex		
Male	32	45.7
Female	38	54.3

Table 1 shows out of 70 patients maximum patients belong the age group 21-30 years 33 (47.1%), followed by age 31-40 years 18 (25.7%),41-50 years 12 (17.1%) and less than 20 years 7(10%). According to sex distribution female are more 38 (54.3 %) and male are 32 (45.7%).

Table-2: Koebner's sign between two groups (n=70)

	Number of patients	Percentage (%)
Present	19	27.1
Absent	51	72.9

Table 2 shows that Koebner's sign absent in maximum patients 51 (72.9%) and present only 19 (27.1%).

Table- 3: Distribution of side effects case (n=70)

Side effects	Frequency	Percent
Erythema	6	8.6
Burning	5	7.1
No side effects	59	84.3

Table 3 shows the pattern of side effects. The common side effects in most of the cases are erythema, 6 (8.6%), followed by burn 5 (7.1%). Maximum cases, 59 (84.3%) show no side effects.

Table- 4: Improvement of the body surface area before and after treatment of topical tacrolimus

	Mean±SD	P value
Before treatment (%)	6.84±2.91	0.001
After treatment (%)	4.25±2.13	

Table 4 shows the improvement of the body surface area before treatments are 6.84% and after treatment which is reduced to 4.25%.

Table-5: Percentage of repigmentation after tacrolimus use in case group and relationship with their site of lesion (n=70)

Percentage of repigmentation	Acral part No(%)	Non-acral part No(%)	Total No(%)
No Pigmentation	9(42.9)	0(00)	9(12.9)
1-25%	12(57.1)	5(10.2)	17(24.3)
26-50%	0(00)	28(57.1)	28(40.0)
51-75%	0(00)	14(28.6)	14(20.6)
76-100%	0(00)	2(4.1)	2(2.9)
Total	21(30.0	49(70)	100

Table 5 shows the percentage of repigmentation after use of tacrolimus. Among 70 patients 61 patients (87.1%) achieved varying levels of repigmentation and 9 patients (12.9) have no repigmentation.

DISCUSSION

Although medical and surgical options are available for the treatment of vitiligo, this condition remains one of the most daunting therapeutic challenges in dermatology. Sunscreens, cosmetics, topical

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and oral psoralens plus ultraviolet A, narrow-band ultraviolet B exposure and phenylalanine with heliotherapy are current medical approaches used to treat vitiligo. Surgical modalities include a variety of grafting and melanocyte transplant techniques. Each of this treatment options has achieved some success in the management of vitiligo. However, many patients are not successfully treated with the current therapeutic options due to a lack of efficacy, intolerance of side effects, concern about long-term effects or resistance of treatment.[15]

This study was conducted with a view to evaluate the efficacy of topical tacrolimus in vitiligo and to see the adverse effects of topical tacrolimus in the treatment of vitiligo. As there is no recorded study in this field, it happens to be the first time in Bangladesh. The present study findings were discussed and compared with previously published relevant studies.

This stud shows 70 patients were enrolled in this study as a case. Among them 32 were male and 38 were female. Mean age of this study group was 28.52±10.98 years which concurs with other similar studies.[1,16]

This study shows the mean involvement of the body surface area before treatment was 6.84%, which is reduce to 4.25% after treatment. It revealed that there is a strong association between tacrolimus use and repigmentation (P< 0.001). This is supported by many other studies.[16,17,18]

According to this study, 61 patients (87.1%) achieved varying levels of repigmentation. 28 patients (40.0%) had reported up to 50% repigmentation. This findings consistent with other studies accords the world.[1,5,6]

This study findings does not accord with the findings of Grimes et al where they found 41.3%.[14] and also differ from Silverberg et al findings of 61% for head/neck regions and 47% for trunk and/or extremities.[17] It is worthy mention that Grimes et al's study was performed by 0.1% tacrolimus upon the group of mean age 38.4 years with SD ± 10.26, and Silverberg et al.[17] study was performed upon children by 0.03 & 0.1% tacrolimus.

Excellent repigmentation was noted, 76-100%, in 2 (2.9%) patients. This result is largely differ other studies.[19,20] This result is also differ from Lepe et al, where they found tacrolimus produce more than 75% repigmentation, most of this on facial areas.[15,16,17] The probable causes of the difference is the concentration difference of tacrolimus 0.03% vs 0.1%.

The present study further documents the safety of tacrolimus for the repigmentation in vitiligo. Because of the need for an effective therapy with a positive benefit-risk profile, the results of the study are quite promising. Twice-daily tacrolimus 0.03% ointment therapy was well tolerated. Report of side effects from this study was only 20% & were transient and mild, no patient discontinue therapy due to adverse effects. 80% patient was free from any kind of side effects. Most common side effects were erythema and burning. This result is supported by various other studies.[12,16,14]

CONCLUSION

This study revealed that tacrolimus ointment may be effective and safe for the treatment of vitiligo. The ease of topical self-administration with minimal side effects makes this novel immunomodulatory agent promising to the therapeutic armamentarium for vitiligo.

Conflict of interest: None.

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Data availability statement
Data will be made available on request.

Ethical Approval
The ethical permission received from the ethics review committee of Khwaja Yunus Ali Medical College (KYAMC), Enayetpur, Sirajgonj, Bangladesh. Prior to data collection, patients were told about the project and consented, and anonymity was maintained throughout the study.

Consent for Publication: Not applicable

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Case Report

Management of ST Elevation Myocardial Infarction in a 17 years Girl in A Tertiary Care Hospital.

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Abstract

Background: *Worldwide, myocardial infarction (MI) is an important cause of death. Number of AMI among young adult is increasing day by day in Bangladesh. Acute MI occurs most commonly at an older age. However, the incidence of acute MI in adolescents is increasing. This is partly due to an increase in cardiovascular risk factors (e.g. smoking, unhealthy diet), which might lead to premature atherosclerosis. However, several non-atherosclerotic causes of MI in adolescents are also described in the literature, such as vascular spasm due to the use of cocaine, amphetamine etc. We may assume that acute MI is not considered to be the most likely cause of chest pain in adolescents. Therefore, the risk of a dramatic outcome in this patient category may be significant. Myocardial infarction (MI) in the young (age < 45 years) is a significant problem; however, there is a scarcity of data on premature coronary heart disease and MI in the adolescent patients. MI in adolescents (age between 10–19 years) is extremely rare.Premature AMI, particularly in the setting of obstructive CAD and/or female sex, is an aggressive disease with high rates of recurrence and mortality, attributed largely to suboptimal control of modifiable risk factors.1 Collet et al2 reported that 1 in 3 patients with premature (≤45 years of age) CAD, of whom the majority experienced AMI, had at least 1 recurrent event over a follow-up period of 20 years. Strong independent predictors for recurrent events were persistent smoking, diabetes, hypertension. We present a case of the 17-year-old girl with extensive ST-segment elevated anterior wall myocardial infarction and found to have complete thrombotic occlusion of proximal left anterior descending coronary artery.*

Keywords: *ST-elevation myocardial infarction, Young MI, Premature coronary artery disease, Acute coronary syndrome, Primary percutaneous coronary intervention, Risk factors.*

Introduction: Number of AMI among adolescence is increasing day by day in Bangladesh.The earlier age of AMI in South Asians can be largely explained by higher risk factor levels at younger ages. Acute myocardial infarction (MI) is rare in teenagers and young adults. The pathophysiology of their infarcts is varied, which not usually due to atherosclerotic plaque rupture except for those genetically predetermined or familial hyperlipidemias. There are many non-atherosclerotic causes of premature coronary artery disease like the coronary spasm, coronary embolization, coronary dissection, anomalous coronary origin, coronary aneurysm, antiphospholipid syndrome, myocardial bridges and very rarely hypercoagulable states.

The South Asian countries of India, Pakistan, Bangladesh, Sri Lanka, and Nepal account for about a quarter of the world's population and contribute the highest proportion of the burden of cardiovascular diseases compared with any other region globally.[3-5] South Asian migrants living in several countries have higher death rates from coronary heart disease (CHD) at younger ages compared with the local population despite apparently lower levels of conventional risk factors.[4-8] Deaths related to cardiovascular disease also occur 5 to 10 years earlier in South Asian countries

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than they do in Western countries.[9,10] This has raised the possibility that South Asians exhibit a special susceptibility for acute myocardial infarction (AMI) that is not explained by traditional risk factors.

Among individuals living in the United Kingdom, the earlier onset of CHD among South Asian migrants is not an artifact of differences in the population distribution because the higher incidence of CHD is most marked in those younger than age 40 years (about a 3-fold difference), whereas it is less marked in those older than 60 years (about a 1.5-fold difference) based on an analysis of UK mortality data.[8] Despite documenting the higher rates of earlier CHD in South Asians, few studies have been able to shed light on its reasons. Most studies do not include information on diet, physical activity, abdominal obesity, psychosocial factors or apolipoprotein levels, and do not have sufficiently large numbers of clinical events to reliably assess the comparative effects of the various risk factors at various ages in South Asians compared with other ethnic groups.

Within the 5 South Asian countries studied, Bangladeshis had the highest prevalence of most risk factors. Similar observations also have been made in migrant Bangladeshis living in the United Kingdom. Whether this is related to lower income and educational levels in Bangladesh compared with other South Asian countries is unclear and needs to be examined. The striking variation observed in the lower age of presentation of first AMI in South Asians, with Bangladeshis being the youngest and Nepalese the oldest, indicates that the onset of AMI could be delayed by modifying these risk factors.

It is important to consider an acute MI as a diagnosis in adolescents with chest pain. Acute MI can present with or without ST-segment elevations on the electrocardiogram: STEMI or non-STEMI [4,5]. Prior to acute MI, a phase of unstable angina pectoris may occur. Unstable angina pectoris means chest pain at rest, de novo or with a crescendo pattern. Unstable angina pectoris, STEMI and non-STEMI are part of the acute coronary syndrome[4,5]. It is important to realize that acute MI presents differently over time on an electrocardiogram. At first, there is a hyperacute phase with large symmetrical or peaked T waves. These are followed by convex ST-segment elevation, which represents a completely developed ischaemic phase. Finally, a chronically stabilized phase develops, in which negative T waves are replaced by positive T waves. A STEMI in adolescents may be the result of premature atherosclerosis or have an underlying non-atherosclerotic cause.

Case Report:

A 17 years old, poorly controlled known diabetic girl, height-5-1 inches, weight-48 kgs, admitted in CCU of Rangpur Medical College Hospital with 48 hours history of retrosternal, compressive chest pain, profuse sweating, shortness of breathing, palpitation, nausea, vomiting, pain radiate to left upper limb. She was drowsy, her pulse was non-palpable, BP was non-recordable. Immediately ECG was done, her 12-lead ECG shows ST elevation from Lead V1 to V6, heart rate-146 beat/mi, rhythm-regular, her serum troponin-I was-10.76ng/ml (Reference value<0.06ng/ml). She was diagnosed as acute extensive anterior MI with uncontrolled Type 2 diabetes mellitus & managed conservatively by standard protocol, comprising-oxygen inhalation, Ecosprin, inj-Pathedine, inj-Low-mollicular weight Heparin, B-Blocker, Atorvastatin, inj-Dopamin, Inj-Nor-adrenalin, ACE-inhibitor, Nicorandil, Ivabradin, Frusemide, subcutaneous regular insulin, etc. She was not thrombolysed by streptokinase due to delayed arrival in hospital. There was no history of premature coronary artery disease in the family or familiahypercholesterolemia (FH) and she denied any history of smoking and drug abuse, analgesic abuse, athletic training or vigorous physical exercise. There was no history of any previous episode of arterial or venous thrombosis. On examination, her BMI was 15.74 and there were no tendon xanthomas, no arcus senilis, no carotid or renal bruit. At CCU, her bed side echocardiogram was done on day of admission & found-global hypokinesia of LV except basal segment of postero-lateral wall, moderate LV systolic dysfunction (LV EF-34%), Trace TR, no pericardial effusion. After all initial management, at 9 days, she was referred to National Institute of Cardiovascular Disease (NICVD), Dhaka for further specific management.

On September 28, 2022, she got admitted in NICVD, Dhaka for coronary angiogram. During preparing her for coronary angiogram, she was found Covid-19 positive by rapid antigen test. Then she was isolated & treated conservatively for 8 days. After 8 days, she was again tested & found covid-19 negative, then she was transferred from covid isolation ward to cardiology unit for coronary angiogram.

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On 12.10.2022, after maintaining all standard protocol, her coronary angiogram was done by right sided radial route & found-LAD-Type 111 vessel & Proximal LAD had 90-99% stenosis, Diagonal-Normal, LMCA-Normal, LCX-Dominant vessel, normal, RCA-Non-dominant vessel, normal, PDA & PLB-Normal. During coronary angiogram, she suddenly developed cardiac arrest. Immediately CPR was started, IV Nor-adrenalin, IV Dopamine started, IV atropine given, cardiac anesthetic was called immediately, then promptly she was intubated & then she was put in Ventilator. Inspite of applying all life-saving medicine, her heart was non-responsive for about 7 minutes, then after applying repeated Intracardiac-Nor-adrenalin, her heart started beating. Then suddenly ventricular fibrillation developed & managed immediately by applying repeated DC Cardio version following standard protocol. Immediately she developed respiratory acidosis & managed by repeated IV Sodium bicarbonate injection, oxygen inhalation, etc. She was still then in cardiogenic shock. With all supportive measures, then immediately stenting was done at Proximal LAD, using one drug-eluting stents-Orsiro 2.75x30 mm (At 10 ATM), G. catheter was-EBU 6Fx3.5, G. Wire was-Asahi Rinato. Then after completion of CAG & PCI, she was sent to CCU for further management. At CCU, repeated ECG was done & found no further development of new MI. Immediately blood was sent for urgent Blood Gas Analysis, Serum Electrolyte, Serum Creatinine, RBS, Complete Blood Count & found respiratory acidosis, Hypokaelemia, Hyponatremia, Leukocytosis & managed accordingly. Next day, at CCU, bed sided Echocardiogram was done to see whether any pericardial effusion. Echocardiogram revealed no pericardial effusion, LV-Antero-septum, apex, mid to apical anterior wall was hypokinetic, moderate LV systolic dysfunction (LVEF-35-40%), good RV systolic function. Next day, she complaints of pain & swelling of right thigh & femoral access site with haematoma formation. We examined & found that she developed haematoma but her distal right leg pulse was normally present. Then we referred her to vascular surgery department for Duplex Study of right leg swelling & for its further specific management. Duplex Study report was found normal. Her pain & haematoma subsided with conservative management. Before discharged, we've completed a further echocardiogram & found-whole septum, apex, mid to apical segment of anterior wall of LV was found hypokinetic, mild LV systolic dysfunction with LV EF-47%, No Diastolic Dysfunction, No Pericardial Effusion, No pulmonary Hypertension. We further check her all vital & biochemical parameter & when found all normal, then we discharged her with all optimal drugs treatment, life style modification advices & further follow-up advices.

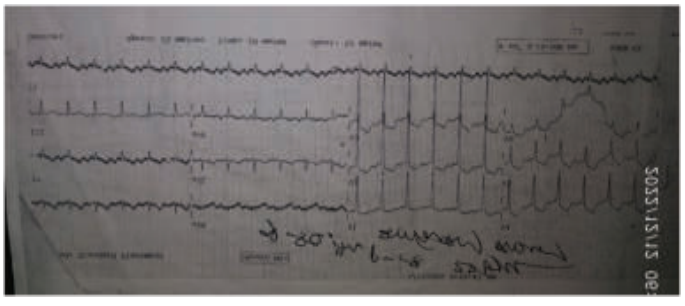

Figure 1: ECG on 21.09.2022.

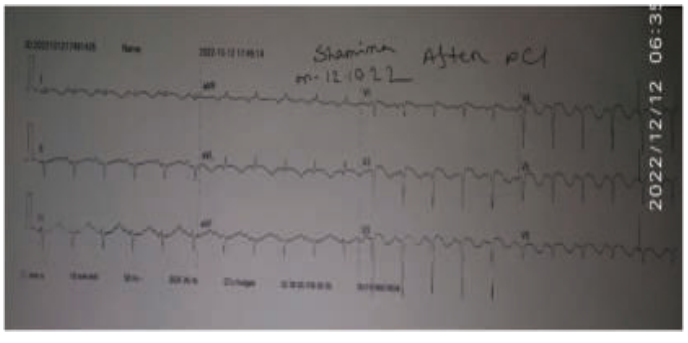

Figure 2: ECG on 12.10.2022 after PCI.

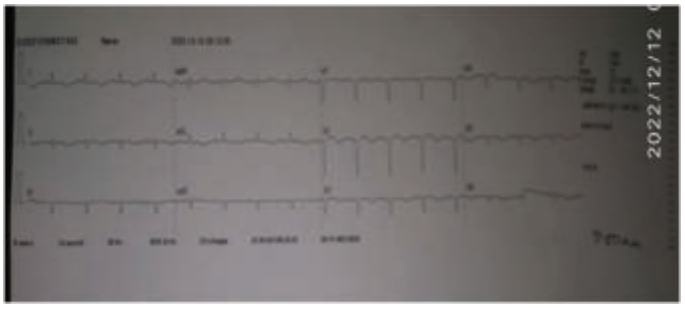

Figure 3: ECG on 16.10.2022.

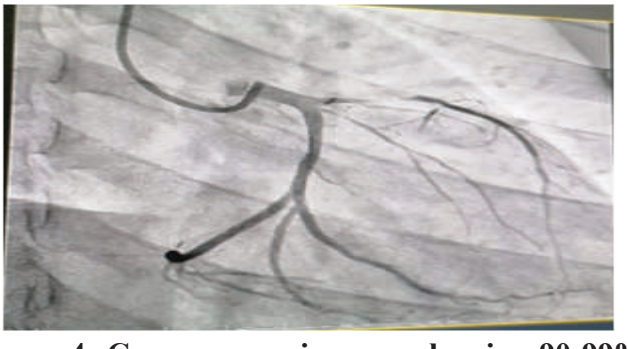

Figure 4: Coronary angiogram, showing 90-99% block at Proximal LAD before Stenting.

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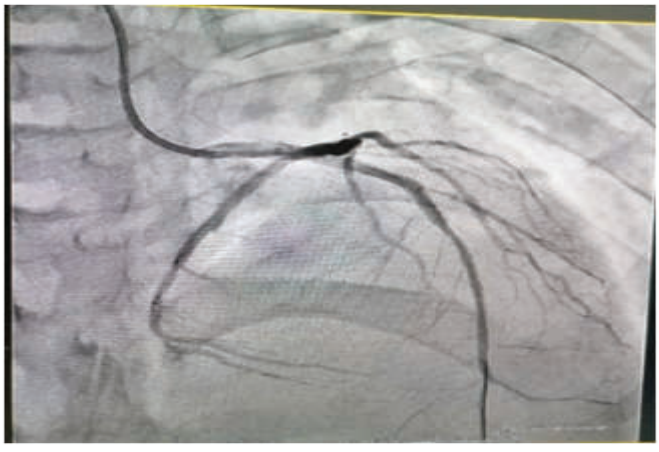

Figure 5: Coronary angiogram-after stenting at Proximal LAD.

Discussion:

Epidemiology

The prevalence of CAD varies considerably by populations, may be up to 10 folds.[3] South Asians are unduly prone to develop CAD.[4] Most notable features of CAD in this population are the extreme prematurity and severity; 2–4-fold higher prevalence, incidence, hospitalization and mortality; 5–10 years earlier onset of first myocardial infarction (MI) and 5–10-fold higher rates of MI and death before the age of 40 years.[4] The exact prevalence of CAD in Bangladesh is not known. Only a limited number of small-scale epidemiological studies are available. Probably the prevalence of IHD was first reported in 1976, which was 0.33%.5 More recent data indicates CAD prevalence between 1.85%6 and 3.4%7 in rural and 19.6% in an urban sample of working professionals.[8, 9] Despite marked disparity in values, there seems to be a rising prevalence of CAD in Bangladesh.

A recent study from rural Bangladesh demonstrated a dramatic increase in CVD from 1986 to 2006. The age-standardized CVD mortality rates increased by 30-fold (from 16 deaths per 100,000 to 483 deaths per 100,000) among males and 47-fold (from 7 deaths per 100,000 to 330 deaths per 100,000) in females.10 A nation-wide survey is needed to find out the current epidemiological aspects of CAD in the country.

Coronary artery disease (CAD) is an increasingly important medical and public health problem, and is the leading cause of mortality in Bangladesh. Like other South Asians, Bangladeshis are unduly prone to develop CAD, which is often premature in onset, follows a rapidly progressive course and angiographically more severe. The underlying pathophysiology is poorly understood. Genetic predisposition, high prevalence of metabolic syndrome and conventional risk factors play important role. Lifestyle related factors, including poor dietary habits, excess saturated and trans-fat, high salt intake, and low-level physical activity may be important as well. Some novel risk factors, including hypovitaminosis D, arsenic contamination in water and food-stuff, particulate matter air pollution may play unique role. At the advent of the new millennium, we know little about our real situation. Large scale epidemiological, genetic and clinical researches are needed to explore the different aspects of CAD in Bangladesh.

Among patients presenting with acute myocardial infarction (AMI), the proportion of young individuals has increased in recent years. Although coronary atherosclerosis is less extensive in young patients with AMI, with higher prevalence of single-vessel disease and rare left main involvement, the long-term prognosis is not benign. Young patients with AMI with obstructive coronary artery disease have similar risk factors as older patients except for higher prevalence of smoking, lipid disorders, and family history of premature coronary artery disease, and lower prevalence of diabetes mellitus and hypertension. Smoking cessation is by far the most effective secondary preventive measure. Myocardial infarction with nonobstructive coronary arteries is a relatively common clinical entity (10%-20%) among young patients with AMI, with intravascular and cardiac magnetic resonance imaging being key for diagnosis and potentially treatment. Spontaneous coronary artery dissection is a frequent pathogenetic mechanism of AMI among young women, requiring a high degree of suspicion, especially in the peripartum period.

Myocardial Infarction with Obstructive Coronary Arteries:

Pathology of atherosclerotic plaque in young individuals:

Premature atherosclerosis: Development of coronary atherosclerosis at a young age is correlated with the presence of conventional cardiovascular risk factors. Examples are smoking, hypertension, dyslipidaemia, overweight, inactivity and stress [1]. Smoking is one of the most important risk factors.

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Frequent exposure to cigarette smoke stimulates the release of catecholamines, which cause damage to the endothelial cells. This can lead to vascular intima dysfunction already at a young age. This process involves alternating low-level cholesterol deposition and platelet aggregation (plaque formation). The lipid core within this plaque formation may rupture. This results in release of vasoactive factors leading to acute vascular occlusion. Genetic predisposition also increases the risk of premature atherosclerosis, such as in the case of a mutation in the factor V Leiden gene or genetic hypercholesterolemia [7]. Treatment of acute MI due to premature atherosclerosis consists of protocolized revascularization by means of primary PCI, followed by cardiovascular risk management on risk factors.

Atherosclerosis is a progressive disease that starts during the early years of life. It can be considered a "childhood disease" with an "incubation period" of a few decades.11,12 Age-associated changes in the cardiovascular system accelerate atherosclerosis; hence atherosclerotic CAD is expected to be less extensive in young individuals. Indeed, angiographic studies in patients with CAD that used intravascular ultrasound-virtual histology have demonstrated that the burden of atherosclerosis is increasing day by day.

Myocardial Infarction with Nonobstructive Coronary Arteries:

Non-atherosclerotic causes: In MI of non-atherosclerotic causes the mechanism of coronary occlusion differs [1, 2]. This may result from various underlying disorders that are accompanied by unconventional risk factors in some cases, such as pregnancy and direct contact sports. For example, the occlusion can be induced by coronary spasms, embolization through coronary arteries due to endocarditis or secondary thrombus formation. Development of secondary thrombosis could be explained by the Virchow triad. This theory describes that development of thrombosis that can be triggered by three factors: stasis of blood flow, endothelial damage and hypercoagulability or abnormal blood composition. For example, patients with the nephrotic syndrome have an increased risk of developing thrombosis because of an increased coagulation state. Coronary spasms can also cause an increased risk of secondary thrombosis because these spasms induce minor damage to the vascular endothelium and activate coagulation. Both cocaine and binge drinking can cause coronary spasms.

We should address the pathophysiological process and subsequent diagnostic approach in adolescents with MI resulting from either premature atherosclerosis or of non-atherosclerotic causes. Insight into the potential operational mechanisms of the coronary artery incident may have a major impact on the clinical course following admission. We would like to underline that a personalized clinical approach remains of utmost importance in each patient treated by protocolized medicine. This is particularly true when acute MI occurs at a young age, since the underlying cause more frequently differs from the conventional atherosclerotic process in this patient category.

Acute MI in adolescents may be caused by premature atherosclerosis or have non-atherosclerotic causes (e.g. vascular spasms during the use of cocaine)[2]. We should address the pathophysiological process and the diagnostic approach in adolescents with MI resulting from either premature atherosclerosis or non-atherosclerotic causes. We would like to mention that our description of non-atherosclerotic causes extends beyond the current clinical conception of MINOCA (myocardial infarction in non-obstructive coronary artery disease) [3].

Prognosis:

Premature AMI, particularly in the setting of obstructive CAD and/or female sex, is an aggressive disease with high rates of recurrence and mortality, attributed largely to suboptimal control of modifiable risk factors. Collet et al5 reported that 1 in 3 patients with premature (≤45 years of age) CAD, of whom the majority experienced AMI, had at least 1 recurrent event over a follow-up period of 20 years. Strong independent predictors for recurrent events were persistent smoking, diabetes, hypertension.

Conclusion:

This case illustrates that MI in adolescent population can occur in the absence of: smoking, family history of premature CAD, atherosclerotic risk factors, drug abuse, coronary anomalies, systemic illness, antiphospholipid syndrome and hypercoagulable states. Adolescent (≤18 year) patients presenting with symptoms and ECG changes suggestive of myocardial ischemia or infarction should receive

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appropriate treatment, including the immediate administration of thrombolytic drugs or coronary angioplasty if indicated.

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