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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 10 Number 1

A Survey of the Knowledge, Attitudes and Behaviour of Bangladeshi Youth with respect to Tobacco

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Abstract

The study aims to describe the prevalence of tobacco use among the secondary school students, and assesses the students' attitudes, knowledge and behaviour about tobacco use, their exposure to environmental tobacco smoke (ETS), health impacts of tobacco, smoking cessation and tobacco in school curriculum. It also describes the access and availability of tobacco products by the youth. The study was a cross sectional survey of the students in class six to ten of a secondary school. A two stage cluster sample design was used to produce representative data. The response rate was 93.5%. 318 students took part in the survey. Overall 7.2% of the students had ever smoked cigarettes and 15.1% of them used other forms of tobacco products. 72.3% of the students were exposed to smoke from others in the home and 41.8% were exposed to smoke from others outside their home in the past 7 days. 67.9% students thought that smoking was harmful to their health. Majority (75%) of the current smokers desired to stop smoking now. Some students (20.8%) thought that smoking makes boys look more attractive and have more friends. About three fourths of the students were taught about the dangers of smoking (73.6%) and the effects of tobacco use (73.0%). Over half (53.9%) of them bought cigarettes from shop and they were not refused to buy because of their age. Tobacco is a major preventable cause of premature death and of several diseases. The prevalence of tobacco use among the youth students was high. Young children are exposed to ETS, which is very dangerous for them. Immediate action should be needed to limit the youth exposure to ETS and accessibility. A supportive environment should be created for the young children.

[OMTAJ 2011; 10(1)]

Introduction

Tobacco use is one of the chief preventable causes of death in the world. It causes cancers particularly lung cancer and oral cancer, respiratory disease, diseases of heart and blood vessels, oral mucosal diseases, periodontal diseases and others. Smokers are about 20 times more likely to develop lung cancer than non-smokers. Smoking causes 84 percent of death from lung cancer[1]. In Bangladesh lung cancer is very common. In case of male, lung cancer shares 21% of all cancers. In case of female, there is no data but the rate is high [2]. Tobacco causes cardiovascular diseases and stroke. Men under 65 years of age smoking 25 or more cigarettes a day had a relative risk of developing coronary heart disease of 2.6 times that of non-smokers, and older men had little increased risk [3]. The major etiological factors associated with the development of oral cancer are smoking tobacco, chewing tobacco, chewing betel quid and heavy

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consumption of alcohol [4]. Environmental tobacco smoke causes sever problems to non-smokers and children. Family smoking is a serious risk factor for children [1]. The WHO attributes some 3.4 million deaths a year from tobacco use, a figure expected to rise to about 10 million by the year 2030 [5]. By that time, 70% of these deaths will occur in developing countries. Most people begin using tobacco in their teens, and recent trends indicate rising smoking prevalence rates among children and adolescents and earlier age of initiation. If the patterns continue, tobacco will result in death of 250 million children and adolescents alive today, many of them in the developing countries [6].

Bangladesh is a poor country with high density population. Smoking rates in Bangladesh are much higher in male than female and highest in poorest [7]. The rate decline proportionately as income increases with the lowest rate. Those who can least afford to purchase tobacco are the most likely to consume it [8]. Malnutrition is very common in Bangladesh. In 1995-1996, more than half (59.7%) of Bangladeshi children aged 6 months to 6 years were malnourished [9]. Tobacco is associated with malnutrition. If the poor stopped using tobacco and reallocated their tobacco expenditures to food, 10.5 million fewer people will be malnourished [10].

Youth is the main target of tobacco companies. There is a wide gap regarding the knowledge of harmful effects of smoking on health between never smokers and current smokers. A large number of young people start smoking due to their ignorance of its consequences [4]. Young, teenage smokers were likely to start smoking in response to pressure at school, the positive representations of smoking in the media and bore dome [11]. Smokers believe that smoking helps them to cope with their problems, relieves their tensions and relaxes them. This indicates that when these students think about smoking, these particular beliefs are considered most [12].

The aims and objectives of the study was to document and monitor the prevalence of tobacco use including cigarette smoking, and current use of other smokeless tobacco, cigar or pipe among the school students and to better understand and assess students' attitudes, knowledge and behaviours related to tobacco use, its health impacts including cassation, environmental tobacco smoke and school curriculum.

Materials and Methods

The study population included all students of class six to ten of all secondary school at Shariatpur district in Bangladesh and the sample included 318 students of that district. A two-stage cluster sampling design was used to produce a representative sample of students. The first stage sample frame consists of all Secondary school of Shariatpur district. The list of secondary school was taken from District Education Officer. All regular public and private schools were included and only those with total students less than 100 were excluded. There were 109 secondary schools in Shariatpur district within which only two were public and 107 were private. Within these 109 schools, 12 schools were excluded because in those schools, the number of students was less than 100. The remaining 97 schools were listed and one school was selected from the list by lottery. The second stage sample frame consists of all students of the selected one school. The study used a standardized questionnaire based on Global Youth Tobacco Survey. The questionnaire includes items on the topics- prevalence of tobacco use, age initiation, tobacco cessation, attitude, knowledge and behaviours related to tobacco use and its health impacts, school curriculum, environmental tobacco smokes. The questionnaire was translated into Bangoli language. The survey was planned in London and data was collected from Bangladesh.

The study administration procedures were designed to protect students' privacy by assuring that the student participation was anonymous and voluntary. The self administered questionnaire was distributed to all the students in the class room and the students recorded their responses on the answer sheet. After completing the answer sheets, those took to London for analysis. Data analysis was conducted by SPSS 12.01 software package. Statistical differences were determined by comparing the range of the 95% confidence intervals.

Total number of students was 340, of whom 318 students responded. The response rate was 93.5%.

Prevalence:

Overall 7.2% of the responses had ever smoked cigarettes, even one or two puffs. The rate for boys was 12.0% and for girls was 3.0%. The prevalence of other forms of tobacco products e.g. dip, cigars, pipe and betel quid was 15.1%. Here the rate for boys was 14.0% and for girls was 16.1%. Girls were more likely to use other forms of tobacco products than boys (Table- I).

Table I: Percentage (95% C I) of students who had used tobacco according to sex (n=318).

Category	Ever smoked cigarettes even one or two puffs	Other forms of tobacco users
Boys	12.0 7.3 - 18.3	14.0 8.9 - 20.6
Girls	3.0 0.9 - 6.8	16.1 10.9 - 22.5
Total	7.2 4.6 - 10.7	15.1 11.3 - 19.5

Environmental Tobacco Smoke (ETS):

A number of questions were asked to about exposure to and attitudes about ETS. More than 72% of students had been exposed to smoke from other peoples in their home and more than 41% of the students had been exposed to smoke from other peoples outside their home in the pats 7 days. The students, who had been exposed in their home, many of their parents smoked, and their parents and other family members smoked in their presence. About 97% of students were in favor of banning smoking in the public places such as restaurants, buses, trains, school and playgrounds, and about 96% of the students thought that smoke from

Table-II: Percentage (95% CI) of students reporting exposed to Environmental Tobacco Smoke (n=318).

Category	Exposed to smoke from others in their home in the past 7 days	Exposed to smoke from others outside their home in the past 7 days	Percent who think smoking should be banned from public places	Percent who think smoke from others is harmful to them
Boys	72.7 64.8 - 79.6	45.3 37.2 - 53.7	94.7 89.8 - 97.7	94.0 88.9 - 97.2
Girls	72.0 64.6 - 78.7	38.7 31.3 - 46.5	100	98.2 94.9 - 99.6
Total	72.3 67.1 - 77.1	41.8 36.3 - 47.5	97.5 95.1 - 98.9	96.3 93.4 - 98.1

others was harmful to them (Table- II).

Smoking cessation:

There were some questions about the attitudes towards stopping smoking. Three out of four (75%, 95% CI 42.8% – 94.5%) students, who smoke currently, wanted to stop smoking now and 53.9% (95% CI 25.1% - 80.8%) students had tried to stop during the past year (Table- III). Many students (54.6%) stated that the main reason to stop smoking was that their friends and family members did not like smoking.

Table-III: Percentage (95% CI) of currently smoking boys and girls who desired smoking cessation (n=13).

Category	Percent desired to stop now	Percent desired to stop during the past year
Boys	72.7 39.0-94.0	54.6 23.4-83.3
Girls	100 -	50.0 1.3-98.7
Total	7.5 42.8-94.5	53.9 25.1-80.8

Knowledge & attitudes of students about tobacco use:

Less than two out of ten students (17.9%, 95% CI 13.9% - 22.6%) believed that boys who smoke cigarettes have more friends and just over one out of ten students (11.3%, 95% CI 8.1% - 15.3%) thought that girls who smoke have more friends. About one

fifth (20.8%, 95% CI 16.4% - 25.6%) of the total students thought that smoking makes boys more attractive, whereas over one out of ten (11.3%, 95% CI 6.1% – 15.3%) students thought similarly of girls (Table- IV). Less than two in every ten students

Table-IV: Percentage (95% CI) of responses by boys and girls to GYTS attitude content questions (n=318).

Particulars of the items	Boys	Girls	Total
Thinks boys who smoke have more friends	22.7 16.2-30.2	13.7 8.9-19.8	17.9 13.9-22.6
Thinks girls who smoke have more friends	14.7 9.4-21.4	8.3 4.6-13.6	11.3 8.1-15.3
Thinks smoking makes boys look more attractive	24.0 17.4-31.7	17.9 12.4-24.5	20.8 16.4-25.6
Thinks smoking makes girls look more attractive	16.0 10.5-22.9	7.1 3.8-12.1	11.3 8.1-15.3
Smoke if best friends offered	16.0 10.5-22.9	4.2 1.7-8.4	9.8 6.7-13.6

(18.2%, 95% CI 14.2% - 22.9%) thought that smoking helps people feel more comfortable at celebrations, parties or gatherings. About seven in every ten students (67.9%, 95% CI 62.5% - 73.0%) thought that smoking is definitely harmful to their health. 9.8% (95% CI 6.7% - 13.6%) of students stated that they would smoke if their best friends offered them a cigarettes. About 15.7% (95% CI 11.9% - 20.2%) of students said that some of their closest friends smoke cigarettes, and about 63% family members discussed with their children about the harmful effects of smoking.

School curriculum:

With regard to school curriculum, a majority of the students reported that they were taught in the school during the last year about the danger of smoking and the effects of tobacco use. Over seven in every ten students reported discussing reasons why people their age smoke and almost the same proportion of students stated that they had discussed tobacco and health as part of a lesson (Table- V).

Table-V: Percentage (95% CI) of responses by boys and girls to school curriculum content questions (n=318).

Category	Percent taught dangers of smoking	Percent taught the effects of tobacco use	Percent discussed reasons why people their age smoke	Percent discussed tobacco & health as part of a lesson
Boys	70.0 62.0-77.2	70.0 62.0-77.2	69.3 61.3-76.6	69.3 61.3-76.6
Girls	76.8 69.7-82.9	75.6 68.4-81.9	76.8 69.7-82.9	74.4 67.1-80.8
Total	73.6 68.4-78.4	73.0 67.7-77.8	73.3 68.1-78.1	72.1 66.7-76.9

Access and availability of tobacco products:

Access and availability of tobacco products is very easy in Bangladesh. About 43.5% (95% CI 23.2% - 65.5%) current smoking students stated that they smoked at home. More than six out of ten (63.6%, 95% CI 30.8% - 89.1%) current smoking students purchased cigarettes from a store or a street vendor, and all of them (100%) were not refused cigarette purchase because of their age(Table- VI).

Table-VI: Percentage (95% CI) of responses by boys and girls to GYTS attitude content questions (n=13).

Category	Percent current smokers who smoke at home	Percent current smokers who purchased cigarettes from store	Percent current smokers who were not refused to buy cigarette because of their age
Boys	44.4 21.5-69.2	63.6 30.8-89.1	100
Girls	40.0 5.3-85.3	-	-
Total	43.5 23.2-65.5	53.9 25.1-80.8	100

Discussion

The prevalence of ever smoking in this sample is 7.2%. It is high in comparison with WHO South East Asian Region (SEAR) with a reported average prevalence of 4.3% [13]. But the prevalence reported was significantly lower than that of Nepal, Sri Lanka, New Delhi and Uttar Prodesh of India where the prevalence were 16.3%, 12.5%, 10.0% and 13.6% respectively [14,5,15,16]. The ever smoking prevalence in this sample for girls (3.0%) is significantly lower than that of boys (12.0%). The rate of use of other tobacco products in this sample (15.1%) is higher than that reported for WHO SEAR (13.3%) [13]. In this sample, the rate of use of other tobacco products is higher in girls (16.1%) than boys (15.1%). Other tobacco products, mainly betel quid are available everywhere in Bangladesh, and within many families, it is a traditional item. There is no restriction to buy or to use betel quid. For that reason, the rate could be high.

About three fourths of students are exposed to ETS in their home whilst less than half of the students are exposed to ETS outside their home. The proportion of students exposed to ETS in their home in this sample (72.3%) is almost double than that of SEAR (37.0%) although the percentage of students reported exposed to ETS outside their home in Bangladesh (41.8%) is lower than that of SEAR (49.4%) [13]. This may be because, in Bangladesh smoking in public places and transport are banned. Three fourths of current smokers indicated a wish to stop smoking now. Some students thought that smoking makes boys (20.8%) and girls (13.3%) look more attractive, and smoking helps people (18.2%) feel more comfortable at parties and social gatherings. They also thought that the boys (17.9%) and girls (11.3%) who smoke have more friends. About 68% of students thought that smoking is definitely harmful to their health. The rest of the students were unaware of the harmful effects of smoking on their health. Some students (9.9%) also said that they would smoke if their best friends offered them a cigarette. A large number of young people start smoking due to their ignorance of its consequences. This should be a matter of great concern and needs urgent intervention. About three fourths of the students were thought about the dangers and harmful effects of smoking. The availability and accessibility of tobacco products is a very important factor for the increased level of tobacco use among children and teenagers. We should also need urgent intervention about these.

The prevalence of tobacco use among the youth students in this sample was not high in relation to WHO South East Asian Region. Young children are exposed to ETS, which is very dangerous for them. Access of tobacco products is very easy. Immediate action should be needed to limit the youth exposure to ETS and accessibility. Legislation should be issued to stop selling cigarettes to young children and a supportive environment should be created for the health of young children.

Study Limitation:

The survey was conducted in one secondary school among students aged 11-15 years. In Bangladesh, more than half of adolescents do not go to school. As the survey represents only school going youth, it does not report the true prevalence of tobacco use in the community as a whole. The sample size of 318 was not sufficient for all kinds of sub-group analysis and statistical tests.

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ORIGINAL ARTICLE

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Correlation between inflammatory mediator (TNF-alpha) and inflammatory parameters (ESR, CRP) in Rheumatoid arthritis and their association with disease activities.

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Abstract

Rheumatoid arthritis (RA) is one of the most common causes of morbidity, disability among adult population (third to sixth decades) in our country. Participation of cytokines in the pathogenesis of Rheumatoid arthritis (RA) seems to be unequivocal but their relationship with current serum markers of this disease is not clear. The present study was designed to analyze whether there was any correlation between the levels of Tumour Necrosis Factor-α (TNF-alpha) and the concentration of C-reactive protein (CRP), Erythrocyte Sedimentation rate (ESR) and to evaluate their association with disease activities. Blood samples of 40, diagnosed seropositive Rheumatoid arthritis (RA) and 40 age and sex matched apparently healthy individuals with seronegative Rheumatoid Factor (RF) were taken. Serum TNF-alpha levels were measured by using solid-phase chemiluminescent immunoassay. Quantitative serum CRP and RF were estimated by Turbidometry method. Erythrocyte Sedimentation rate (ESR) was estimated by Westergren method. Qualitative estimation of serum RF was done by RF Latex Agglutination Test. In comparison with control group, RA patients were presented with high mean levels of TNF-alpha (84.9490pg/ml), ESR (60.10mm in 1st hr), CRP (5.3535mg/dl).

ESR levels in the RA group significantly differed from the control group (<0.001). TNF-alpha levels were significantly correlated with RF (<0.05) in case. ESR was significantly correlated with Disease Activity Score28 (DAS28) based on ESR (<0.01) in cases. CRP levels were also significantly correlated with Disease Activity Score28 (DAS28) based on CRP(<0.01).The correlation between TNF-alpha levels with DAS28 based on ESR and CRP were not significant These results suggested that TNF-alpha levels were up-regulated in cases and were significantly correlated with Rheumatoid Factors (<0.05).ESR and CRP levels were also significantly correlated with DAS28 based on ESR (<0.01) and DAS28 based on CRP (<0.01) respectively. Due to the chronic course of this disease large scale population based study should be undertaken and other inflammatory markers should be searched and correlated with the disease in order to develop appropriate diagnosis, monitoring and early management strategies with a view to prevent, minimize and slow the progress of the disease.

[OMTAJ 2011; 10(1)]

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disorder of unknown aetiology and is characterized by chronic, symmetrical, destructive and deforming polyarthritis affecting small and large synovial joints and often ends in deformity, disability and even premature death with associated systemic disturbance[1,2], a variety of extra-articular features and

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the presence of circulating antiglobulin antibodies known as rheumatoid factor[3]. The pathological hallmark of RA is inflammation. The whole process is mediated by cytokine. and prostaglandin[4 5]. These events are initiated by an interaction between Antigen presenting cell(APC) and CD+4 T-cells. APCs display complexes of class II major histocompatibility complex (MHC) molecule and peptide antigens that bind to specific receptors on the T cells[6]. CD4+T cells in response to an unknown antigen consequently recruited monocytes, macrophages,and fibroblasts. Activation of these cells results in secretion of pro-inflammatory cytokines such as tumour necrosis factor (TNF- ▯),), IL-1 and IL-6, IL-8 and granulocyte-macrophage colony stimulating factors (GM-CSF) within the synovial cavity. These cytokines are central to a damaging cascade, ultimately triggering the production of matrix metalloproteinases and osteoclasts, which results in irreversible damage to soft tissues and bones[7]. There is evidence that the disease is triggered by Th1 lymphocyte activation and production of pro-inflammatory cytokines in genetically predisposed individuals with defined HLA class II haplotypes[8]. The occurrence of B-lymphocyte dysregulation is suggested by the association of erosive disease with the presence of rheumatoid factor, which mediates further damage through complement fixation[9]. Both genetic and environmental risk factors play important roles in the development of RA[10].

Rheumatoid arthritis has a worldwide distribution. Both incidence and prevalence of rheumatoid arthritis are two to three times greater in women than in men. Although rheumatoid arthritis may present at any age, patients most commonly are first affected in the third to sixth decades[11]. In our country, the prevalence of rheumatic complaints is 26.3%. Rheumatic disorders are common causes of morbidity, disability and work loss in rural and urban communities of Bangladesh[12]. The long term prognosis is poor: Around 80% of affected patients are disabled after 20 years and life expectancy is reduced by an average of 3 to 18 years[13].

TNF-alpha is a pleiotropic inflammatory cytokine. It is produced mainly by macrophages and monocytes but also by B cells, T cells and fibroblasts. It acts as autocrine, paracrine and also endocrine stimulators[14]. TNF-alpha possesses both growth stimulating properties and growth inhibitory processes, and it appears to have self regulatory properties as well[15]. TNF-alpha is also known as cachactn because it inhibits lipoproein lipase in adipose tissue, thereby reducing the utilization of fatty acid. This results in cachexia[16]. There are strong evidence that TNF-alpha is a key molecule in the control of the inflammatory changes that occurs in the RA synovium .In addition TNF-alpha regulates IL-6 production which has involvement with disease activities in RA[17]. TNF-alpha level can be taken as a good marker of disease progression[18]. Elevated level can be taken as an advanced stage of disease and indication for anti TNF- ▯ therapy[19].

C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are known as acute phase proteins, which reflect a measure of the acute-phase response. Measurement of ESR and CRP can be clinically helpful in three ways: evaluating the extent or severity of inflammation, monitoring disease activity over time and assessing prognosis[20]. Rheumatoid factor is an important ACR criterion for diagnosis and RF belonging to all the major immunoglobulin classes (IgM, IgG and IgA).This circulating antibody acts against multiple antigenic determinants on the Fc fragment of the IgG molecule. IgG RF levels were associated with changes in ESR and grip strength, but IgM RF showed only a weak association with fluctuations in ESR and not with any other clinical parameters. RF can be detected in about 70%-80% of RA patients. It is suggested that serum IgA RF may be a useful marker of disease activity in rheumatoid arthritis[21].

Disease activity score (DAS) is a major scoring system evaluating disease activity of RA and can be defined as a clinical index of RA disease activity that combines information from swollen joints, tender joints, the acute phase response and general health i.e. Visual Analogue Scale (VAS). Disease activity score can be calculated by DAS28 calculator using relevant data i.e. VAS (mm), ESR (mm in 1st hr)/CRP (mg/dl), Tender joint count, swollen joint count[22].

Materials and Methods

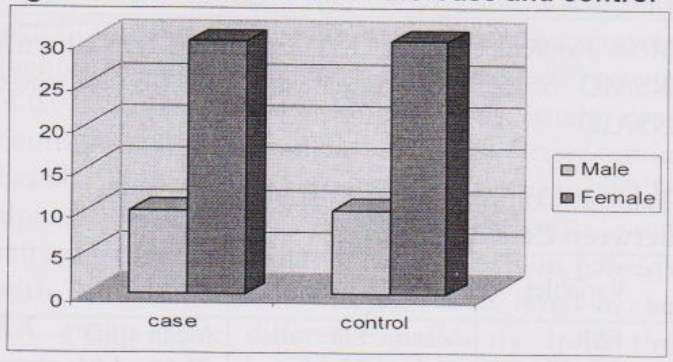
This was a Comparative cross-sectional study and was conducted in Department of Microbiology and Department of Medicine,Sylhet MAG Osmani Medical College & Hospital among Seropositive (RF positive) rheumatoid arthritis as cases and seronegitive (RF negative) age and sex matched apparently healthy subjects as controls to evaluate correlation between TNF-alpha levels with inflammatory parameters CRP, ESR and DAS28 score in sero-positive Rheumatoid arthritis with the aim to evaluate correlation between TNF-alpha levels with inflammatory parameters CRP, ESR and DAS28 score in sero-positive Rheumatoid arthritis.

After fulfilment of the inclusion and exclusion criteria total number of eighty (n=80) 40(n=40), diagnosed cases of seropositive (RF positive) rheumatoid arthritis fulfil the ACR diagnostic criteria of RA[23] as cases and 40 (n=40), seronegitive age and sex matched apparently healthy subjects as controls were selected consecutively. Under all aseptic precaution about 5ml of venous blood was collected. Three (3) ml of collected blood was centrifuged accordingly and serum was taken into appropriately labelled microcentrifuge tubes and kept in -20° C until further analysis. ESR and qualitative RF tests were done at the date of sample collection. Quantitative CRP, RF test and TNF-alpha analysis were done in a single batch at the end of the study. Quantitative Serum TNF-alpha, Quantitative CRP and Quantitative RA Test, Qualitative RA Test, Quantitative ESR were performed by solid phase Chemiluminescence (Immulite) Turbidometry , Latex-agglutination, Westergren method respectively. Disease activity score was calculated by DAS28 calculator using relevant data. Data were processed and analyzed with the help of computer software SPSS (Statistical Package for Social Sciences), version 12.0. The test statistics used to analyze the data were descriptive statistics of respondents, bivariate (cross tabulation) analysis and two independent sample mean test with SD. In descriptive statistics Bar diagrams, tables, charts were considered and in analysis chi square (χ^2) test, Pearson correlation and Liner regression had been used to identify the association between TNF-alpha level and other variables.

Results

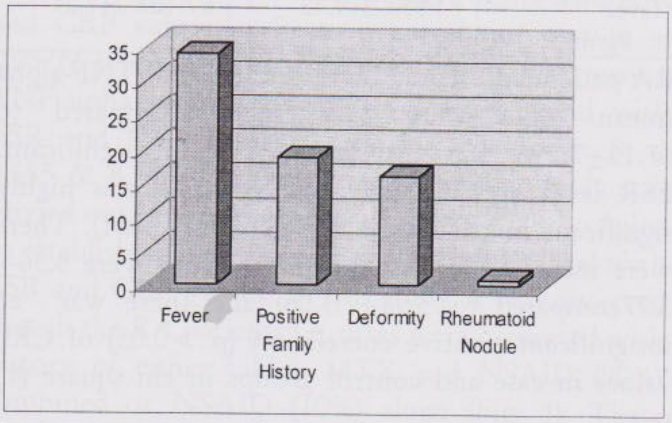
This study was done on 40 patients as cases and 40 apparently healthy age and sex matched individuals were used as controls. RA cases; presenting with Morning stiffness (100%),all of them were seropositive for RF, swollen tender joints with Visual Analogue Scale (VAS) having ranging 4-7 in the 1-10mm scale and duration of illness more than 8 months .

Figure- 1 Sex distribution of the Case and control



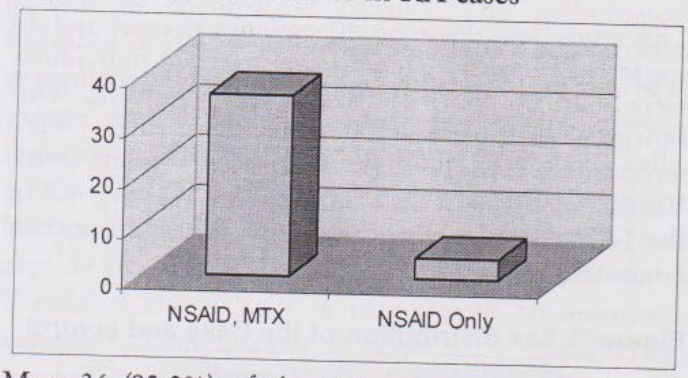
Three fourth 60 (75%) of the subjects were female. The gender ratio was (3:1).

Figure-2 : History & Clinical Features of RA Cases



Among 40 cases 34 (85.0%) presented with fever, 16 (40.0%) presented with deformity on various sites, 19 (47.5%) had positive family history of joint pain or arthritis and only 1 (2.5%) presented with rheumatoid nodules (figure -5.3).

Fig -3Treatment histories in RA cases



Most 36 (90.0%) of the RA cases were treated with NSAID & MTX, whereas, only 4 (10.0%) took NSAID.

Table-I: Comparison of Different Variables between Case & Control

Variables	Case	Control
ESR (mm in 1st hr)	Mean ± SD 60.1± 4.32	Mean ± SD 26.55± 4.01
CRP mg/dl	Mean ± SD 5.36± 3.77	Mean ± SD 3.98± 3.06
TNF-alpha level Pg/ml	Mean ± SD 84.95± 219.43	Mean ± SD 67.16± 217.21

RA patients presented increased levels of TNF-alpha (mean ±SD were 84.94±8.560 compared to 67.15±7.296) but correlation was not significant. ESR level between cases and controls was highly significant in chi square (χ^2) test ($p < 0.001$). There were increased levels CRP (mean ±SD were 5.36± 3.77compared to 3.98± 3.06) and there was an insignificant positive correlation ($p > 0.05$) of CRP values in case and control groups in chi square (χ^2) test.

Table-II: Comparison of ESR levels in case and control groups

ESR (mm in 1st hr)	Case (n%)	Control (n%)
20-40	5(12.5%)	40(100%)
41-60	5(12.5%)	40(100%)
61-80	5(12.5%)	40(100%)
>80	5(12.5%)	40(100%)
Total	40(100%)	40(100%)

Most (95%) of the RA cases had ESR value <80 mm in 1st hr with majority (52.5%) having ESR within 61-80 mm. Difference of ESR level between cases and controls was highly significant in chi square (χ^2) test ($p < 0.001$).

Table-III: Comparison of CRP levels in case and control groups

CRP mg/dl	Case (n%)	Control (n%)
<2	14(35.0%)	29(72.5%)
2-4	05(12.5%)	06(15.0%)
4-6	04(10.0%)	03(7.5%)
6-8	08(20.0%)	02(5.0%)
8-10	05(12.5%)	0(0.0%)
>10	4(10.0%)	0(0.0%)
Total	40(100%)	40(100%)

Majority (52.5%) of the RA cases had CRP value >4 mg/dl. The difference was not significant in chi square (χ^2) test ($p > 0.05$).

Table-IV: Comparison of TNF-alpha **levels in case and control groups**

TNF-alpha pg/dl	Case (n%)	Control (n%)
<10	08(20.0%)	13(32.5%)
10-50	24(60.0%)	23(57.5%)
50-100	03(07.5%)	02(05.0%)
>100	05(12.5%)	02(05.0%)
Total	40(100%)	40(100%)

Majority (60.0%) of the RA cases had TNF-alpha level between 10-50 pg/ml. The difference was not significant in chi square (χ^2) test ($p > 0.05$). Positive trend correlation (regression coefficient B = 0.685) of TNF-alpha with both ESR and CRP values in Cases were found in linear regression but were not significant ($p > 0.05$) in Pearson correlation test ($r = 0.057$, $r = 0.231$).

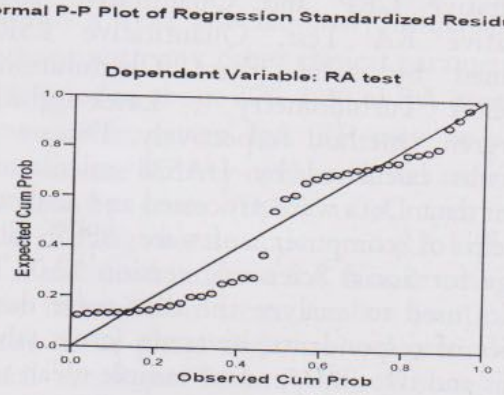


Fig.4 Linear Regression of TNF-alpha values with quantitative values of RF in case

The study revealed very significant positive correlation ($p < 0.01$) of TNF-alpha with

quantitative value of RF in Pearson correlation test(r = 0.403). The linear regression showed the positive trend (regression coefficient B = 1.79)

Discussion

Rheumatoid arthritis (RA) is a chronic, progressive, immune mediated inflammatory disease of middle age characterized by inflammation resulting in structural joint damage and functional disability[24]. TNF-alpha is a pivotal mediator and driver of inflammation in RA. Inflammation is closely related to the production of C-reactive protein CRP) and other inflammatory parameters[25]. In clinical settings, RF can be detected about 70%-80% of RA patients and the presence of RF associate with the severity of RA [26]. In comparison with the control group(Table:1), RA patients presented increased levels of TNF-alpha (mean ±SD were 84.94±8.560 compared to 67.15±7.296) but correlation was not significant. ESR level between cases and controls was highly significant in chi square (χ^2) test ($p < 0.001$). The linear regression showed the positive trend with regression coefficient B = 5.46. There was an insignificant positive correlation ($p > 0.05$) of CRP values in case and control groups in chi square (χ^2) test. The linear regression showed the positive trend (regression coefficient B = 1.79). In RA cases TNF-alpha levels were significantly correlated ($p < 0.01$) with Rheumatoid Factors (RF) in Pearson correlation test(r = 0.403) and linear regression also showed the positive trend(regression coefficient B = 1.79) (Fig.4)

In this study there were 30 female and 10 male cases with a ratio of 3:1(Fig:1). This can be compared with the sex ratio of 3:1 reported by Doherty et al[11]. The present study included a series of 40 patients of RA cases; presenting with Morning stiffness (100%), Fever (85%), deformity (40%), Rheumatic nodules (2.5%) (Fig:3). All of them were seropositive for RF, swollen tender joints (Fig: 5.8), with Visual Analogue Scale (VAS) having ranging 4-7 (Fig: 5.6) in the 1-10mm scale and duration of illness more than 8 months. These clinical and laboratory findings were in conformity with the American College of Rheumatology (ACR) diagnostic criteria for RA[23]. The results showed that the levels of CRP, TNF-alpha were increased in cases but did not differ from control group significantly. But the ESR level is significantly increased than that of control group. Over all, these changes were representative of the spectrum of effects that were triggered in response to the autoimmune injury that characterized RA.

In the present study it was showed that in comparison with the control group, RA cases presented with high mean levels of CRP and TNF-alpha levels though they were not statistically significant. But ESR levels in the RA group showed highly significant difference in chi square (χ^2) test ($p < 0.001$). The observation of this study was consistent with Frode et al,[28]. that was carried out in Brazil. They showed correlation between TNF-alpha, Interleukin-2 soluble receptor and inflammatory parameters CRP and ESR in patients with RA and observed that only ESR levels in the RA group were differed significantly from the control group. Similar observations were recorded in a recent Iranian study by Rostmain et al, [28]. The study revealed an insignificant positive correlation ($p > 0.05$) of quantitative value of TNF-alpha with ESR and CRP values in Pearson correlation test (r = 0.057& r = 0.231) in cases. But in linear regression TNF-alpha levels showed the positive trend with ESR and CRP values (regression coefficient B = 0.685 & B = 7.19) (Fig: 4, 5). A similar study was carried out in Austria by Mangge et al,[29] , who failed to establish any correlation of TNF-alpha level with ESR and CRP values. In this study it was observed that all the RA patients i.e. cases were presented with history of either taking MTX and NSAID (90%) combined or NSAID (10%) alone (Fig: 3). These therapies might have down regulated the level of TNF-alpha. Robak T et al,[30]. observed the influence of the treatment on the serum concentrations of TNF-alpha They reported lowest values of TNF-alpha in the group of patients treated with methotrexate and gold salts and. low values in patients treated with sulphasalazine and NSAID as single drug. This might be the reason for which DAS28 were not correlated significantly with TNF-alpha levels in this study. A similar study by Wascher et al.,[31]. failed to establish any correlation between DAS28 and TNF- level. The present study

revealed very significant positive correlation ($p < 0.01$) of RF with TNF-alpha levels in Pearson correlation test($r = 0.403$). The linear regression also showed the positive trend (regression coefficient B = 1.79) (Figure-6) in RA cases. This kind of association was very much relevant with RA pathogenesis and supported by the research findings of Matheson et al.,[32] . who carried out a study in Sweden. They had found significant correlation between TNF-alpha level and RF of RA patients.

Rheumatoid arthritis (RA) is a common health problem among adult population of third to sixth decades in both rural and urban communities of our country, causing significant morbidity, disability and work loss. The long term prognosis is poor with 80% disability after 20 years and reduction of life expectancy by an average of 3 to 18 Early and appropriate management could help to maintain their good health and play role in the development of our country. The study showed increased levels of, ESR, CRP and TNF-alpha in seropositive RA cases compared to healthy controls, but significant difference was found only for ESR values. In conclusion, for some variables which were evaluated in this study the differences with control were not statistically significant, they followed the same trends as predicted. These findings may increase our confidence to rely on this old, less costly and easily performable test for the diagnosis and assessment of disease prognosis. Positive correlation with lack of significant statistical difference for TNF-alpha might be due the use of anti-inflammatory and disease modifying drugs received by the patients prior to enrolment in the study. Selection of untreated cases could generate interesting findings.

Recommendation

1. The findings of the present study require to be validated with a large scale population based study.
2. Levels of these inflammatory markers should be compared in both treated and untreated cases
3. Other inflammatory markers should be searched for association and correlation with disease activity.

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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 10 Number 1

Child rearing practices among female tea garden workers in selected tea garden in Sylhet.

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Abstract

Tea garden workers are different from that of Bengali culture and heritage. This cross sectional study was conducted among 236 female workers having at least one under five child with a view to know their child rearing practices. Non random sampling technique was followed. The survey was carried out from 1 October, 2010 to 1 January, 2011. Mothers of the children were interviewed through pretested semi-structured questionnaires while they were available at the dispensary of tea garden. The result of this study reveals that out of 236 new borns 113 (47.88%) were given colostrum without giving any prelacteal feeds. Only 23.30% were put on breast as soon as born. Prelacteal feeding were given to 123 (52.09%) neonates. Of the prelacteal feeds 34.74% were given honey and 12.28% were given sugar water. 100 percent mothers offered breast milk but exclusive breast feeding was virtually absent. Significant number 175 (74.15) child continued breast feeding for more than 2 years. Early initiation of weaning was observed in the study. Regarding child immunization 90.67% children were fully immunized as stated by mother. So based on these study findings it can be concluded that creating awareness and imparting child health education to female workers are important factors to improve child rearing practices among the female garden workers.

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Introduction

The care of children deserves high priority to ensure that they grow up into fit and healthy adults close attention to child is therefore an important investment in the next generation[1]. Traditionally two groups in every society have been considered worthy of receiving particular attention, women during the period of their pregnancies and children particularly during their infancy[2]. The present study aimed at finding out the child rearing practices which includes colostrum feeding, exclusive breast feeding, giving prelacteal feeds to babies as well as weaning and immunization status of under 5 children in selected tea gardens namely Borzan and Kalagul tea estate in Sylhet.

Material and Methods

A descriptive type of cross sectional study was conducted among 236 female tea garden workers having at least one child of under five years. Convenience type of non random sampling technique was applied. The survey was carried out from 1 October, 2010 to 1 January, 2011. A total 236 under five children were included in the study. The mothers of the children were interviewed through pretested semi structured questionnaires while they were available at the dispensary of tea garden. Simple statistical method were applied here for data analysis

Results

Table-1: Age distribution of respondents.

Age (years)	Frequency	Percentage %
15-20	03	1.27
20-25	53	22.45
25-30	114	48.30
30-35	51	21.61
35-40	15	6.35
Total	236	100%

Table-II: Time of initiation of breast feeding.

Time of initiation	No. of infants	Percentage %
Soon after birth	55	23.30
Within 6 hours	123	52.11
6 hours - 24 hours	50	21.19
After 24 hours	8	3.39
Total	236	100%

Table-III: Distribution of types of prelacteal feeding.

Types	No. of infants	Percentage %
Honey	82	34.74
Sugar water	29	12.28
Misri Water	10	4.23%
Cows Milk	2	0.84%
Total	113	100%

Table-IV: Vaccination status of under five children.

Status	No. of children	Percentage %
Fully Immunized	214	9.67
Non Immunized	22	9.32
Total	236	100%

The study revealed that out of 236 respondents majority were within the age group of 25-30yrs followed by 22.45% were in age group of 20-25 yrs and 21.61% were in age group of 30-35yrs. Remaining 6.35% and 1.27% belong to age group of 35-40yrs & 15-20yrs respectively (Table-I). Out of 236 total mothers studied 55 (23.30%) had initiated breast feeding soon after birth, within 6 hours 123 (52.11%) within 6-24 hours 50 (21.19%) and on 2nd day 8 (3.39%) respectively (Table-II). Out of 236 newborns 113 (47.88%) were given colostrum without giving any prelacteal feeds. Prelacteal feeding were given to 123 (52.09%) neonates. Different types of prelacteal feeding offered to neonates. They were honey 82 (34.74%), sugar water 29 (12.28%), Misri water 10 (4.23%) and cows milk 2 (0.84%) (Table III). The study revealed that as many as 218 (92.37%) mother offered colostrum to their babies while 18 (7-62%) did not. In this study 236 (100%) newborns were breast fed and exclusively breast feeding was virtually absent. The study revealed that weaning was started too early. Out of 236 children 18 (7.62%) started weaning within 0-1 month, 32 (31.55%) within 1-2 month, 54 (22.88%) within 2-3 months, 65 (27.54%) within 3-4 months, 27 (11.44%) within 4-5 months, 28 (11.86%) within 5-6 months and 12 (5.08%) within 6-7 months. Various types of weaning food were given to the babies. In this study it was found that smashed kichuri was given to 143 (60.59%) babies, suzi 93 (39.04%), rice 38 (16.10%), cows milk 21 (8.89%), rice powder 20 (8.47%), potato 2 (0.84%), sagu 2 (0.84%). The study revealed that duration of breast feeding was prolonged. A significant number of babies 175 (74.15%) continued breast feeding more than 2 years.

Regarding vaccination this study showed that 219 (92.79%) had BCG scar mark on left upper arm while 17 (7.20%) devoid of scar mark. From recall statement of mother it was found that 214 (90.67%) children were fully immunized and 22 (9.32%) were totally non-immunized. Findings revealed on recall was the limitation of this study.

Discussion

The childhood period is a vital period as they are vulnerable to disease, death and disability owing to their age, sex, place of living, socio-economic class and a host of other variables[3]. The present study revealed that initiation of breast feeding within 1 hour was 55 (23.30%) and within 6 hours was 123 (52.11%) which was much less than that of findings stated by Leter et al. It was 78% within 1st hour and 91% within first six hours[4]. This study revealed that 218 (92.37%) babies were given colostrum after birth. This study findings had similarity with the study done by Sadullah M et al. His study found that 91.67% babies were given colostrum[5]. There was similarity between these two findings. It was also found in present study only 18 (7.62%) did not offer colostrum to their babies. Choudhury et al found that one third of the studied mothers in rural of Sonargoan of Dhaka district did not give colostrum to the neonates[6]. After child birth workers of the tea garden traditionally offer colostrum to their newborns.

In this study out of 236 newborns prelacteal feeding was given to 123 (52.09%) neonates. Shamim et al in

his one study found that 100% of studied mothers gave some form of prelacteal feeding[7]. Regarding prelacteal feeding findings of Shamim et al was nearly two times higher than our present findings. Das found that only 5% rural infants got supplementary food at 6 months of age[8]. His finding had some similarity with our present study which was 5.08%.

In this study it was identified that as many as 175 (74.15%) children continued breast feeding for more than 2 yrs. Present study showed that from recall statement of mother 214 (92.79%) children were fully immunized and rest 22 (9.32%) were non immunized. According to EPI coverage evaluation survey 2010 (79%) children under 1yr were fully immunized[9]. In our study immunization coverage was higher than the national coverage. As because these findings were made from recall statement it would be considered as limitation of our study.

In conclusion, all tea gardens workers are illiterate getting no light of education. No doubt they are our national assets. Based on study findings it can be concluded that creating awareness and imparting child health education among female tea garden workers are important factors to improve the child rearing practices among the female garden workers.

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ORIGINAL ARTICLE

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A comparative study on renoprotective effect of losartan and ramipril in type 2 diabetic patients with grade 1 hypertension and early nephropathy

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Abstract

The objective of the study was to estimate the renoprotective effect and tolerability of losartan and ramipril It was a prospective, open label, parallel group and randomized done in the Department of Pharmacology and Therapeutics, Sylhet M.A.G.Osmani Medical College, Sylhet, from July 2008 to December 2009. In this comparative clinical trial, 41 type 2 diabetic patients with newly diagnosed grade 1 hypertension and early nephropathy, from out patient department of Sylhet Diabetic Hospital, completed the 2 months treatment with ramipril (n=20) and losartan (n=21) in two divided groups. Urinary protein, urinary creatinine, urinary protein-to-creatinine ratio (PCR) and serum creatinine levels were estimated before and 2 months after initiation of treatment. For the purpose of calculating glomerular filtration rate (GFR); age, sex, height and weight of the study subjects were recorded and body mass index (BMI) were also calculated. Blood pressure and serum glucose level were measured routinely. Age range of study subjects were 35 to 70 years.

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Significant reductions of mean urinary protein-to-creatinine ratio were observed in both the studied groups from pre treatment level to the end point of the study; p= 0.004 in ramipril group, p=0.002 in losartan group. The difference of mean reductions in protein-to-creatinine ratio between the studied groups was not significant (p = 0.724). Difference of changes in mean blood pressures (p = 0.415) & GFR levels (p = 0.106) were not significant. In this study, 2 patients (10%) in ramipril group discontinued the drug due to adverse effects (severe cough) but no such event occurred in losartan group. It may be concluded that losartan is equally renoprotective as ramipril in type 2 diabetes with grade 1 hypertension and early nephropathy.

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Introduction

Diabetes mellitus is the most common of the metabolic disorders. Hypertension is approximately twice as frequent in diabetic as in those without the disease[1]. Hypertension in turn increases the susceptibility to develop diabetic nephropathy associated with poor hyperglycemic control[2]. The cumulative risk of nephropathy in type 2 diabetes is 25% in European alike about 50% in Afro Caribbean, Asian-Indian and Japanese [3]. Without specific interventions, 20-40% of type 2 diabetic patients with microalbuminuria progress to overt nephropathy, but by 20 years after onset of overt nephropathy, only about 20% will have progress to end stage renal disease[4]. British Hypertension Society guidelines for hypertension management 2004 (BHS-IV), advocates a target blood pressure in diabetes of less than 130/80 mmHg and drug treatment is indicated in patients with sustained systolic blood pressures 140-159 mm Hg or diastolic blood pressures 90-99 mmHg[5] that is Grade 1 hypertension[6]. Type 2 diabetic nephropathy is defined by an early morning urinary albumin-to-creatinine ratio of > 300mg/gram[7] or spot urinary

protein-to-creatinine ratio of > 500mg/gram[8]. Criteria of early nephropathy[9] are proteinuria < 100mg/dl, serum creatinine < 1.6 mg/dl, GFR > 70 ml/min/1.73m^2 GFR < 60ml/minute/1.73m^2 for > 3 months, with or without kidney damage is also a criterion of chronic kidney disease[10].

Renoprotection means reduction in the ratio of albumin-to-creatinine (ACR) in an early morning urine sample[7] or reduction in the spot urinary protein-to-creatinine ratio (PCR) from baseline[8]. Lowering proteinuria always retards renal disease progression[11]. Reduction of proteinuria is followed by less GFR decline[12]. Angiotensin II is a key player in the development of renal failure, either directly by promoting tissue fibrosis or indirectly through its action on glomerular hemodynamic and proteinuria[11,13] Therefore, inhibition of the renin-angiotensin system, through either angiotensin converting enzyme (ACE) inhibitor ramipril or angiotensin II receptor blocker(ARB) losartan, may have a positive impact on proteinuria renal failure progression[14], possibly by reversing the increased intraglomerular pressure[15]. Inhibition of renin angiotensin system causes a reduction in urinary protein excretion that is in part independent of the reduction in blood pressure, but depends on the activity of the renin angiotensin system. [11, 16]

The effects of ACEI and ARB on renal outcomes (end stage kidney disease, doubling of creatinine, prevention of progression of micro to macroalbuminuria, remission of micro to normoalbuminuria) are similarly beneficial[17]. But it is uncertain whether ARBs are equally effective anti proteinuric agents as ACE inhibitors. Although the survival benefits of ACEI are known for patients with diabetic kidney disease, the relative effects on survival with ARB are unknown due to the lack of adequate direct comparison studies[17].

Materials and Methods

This was a prospective, open label, parallel group and randomized study, carried out during the period of July 2008 to December 2009. Newly diagnosed grade 1 (mild) (BP < 160/100 mm Hg)
hypertensive type 2 diabetic patients of age 35-70 years attending the out patients department of Sylhet Diabetic hospital, Sylhet, without receiving any antihypertensive drug treatment with proteinuria <100mg/dl or <1.44gm/day), Glomerular filtration rate above 70 ml/min/1.73m^2 were taken as study population[9]. Exclusion criteria[9] were patients having any condition (other than cardiovascular disease) that could restrict long term survival, known allergy to study drugs, fever, urinary tract infection, diseases that cause proteinuria (cardiac disease, thyroid disease), serum creatinine level ≥ 1.6mg/dl , glycosylated heamoglobin value ≥ 12% and serum potassium level ≥ 5.1 mmol/L. Outcome was measured by monitoring reduction in protein-to-creatinine ratio (PCR) in spot urine sample. Changes in calculated value of glomerular filtration rate (GFR), and mean blood pressure were also measured. For adverse drug reaction, serum potassium and serum creatinine levels were monitored.

Study procedure: Detail history, clinical examination, physical and anthropometric measurement of the study participants were taken in a prescribed data collection form. The participants were divided into two groups by all odd reg. numbers in group 1 and all even reg. numbers in group 2. Group1 received tablet ramipril 2.5 mg single dose daily[18] and group 2 received tablet losartan 50 mg single dose daily[19] for 2 months. To avoid confounding, renoprotective amlodipine, diltiazem[4] etc were not used in combination either with ramipril or losartan. Baseline characteristics as age, sex, body weight and height were observed and recorded.

Variables like (i) systolic and diastolic blood pressure were measured and mean blood pressure was calculated (ii) urinary protein, urinary creatinine were measured and urinary protein-to-creatinine ratio was calculated (iii) Serum creatinine was measured for GFR calculation. Blood pressures of the samples were monitored fortnightly.

Patients were advised to attend Sylhet Diabetic Hospital just after 2 months. At the end of 2 months, on the schedule day along with clinical examination, patient's body weight was recorded, mean blood pressure was calculated. Blood and spot urine samples were collected from the patients, for calculation of GFR and protein-to-creatinine ratio.

Serum potassium was also estimated for any adverse drug reaction.

Laboratory methods: From each study subject 3 ml venous blood sample was collected by disposable plastic syringe and was transferred immediately into a dry and clean centrifuge test tube without any anticoagulant. Serum was separated by centrifugation at the rate of 3000 rpm for 15 minutes. Estimations were carried out as early as possible. Whenever there was delay, sample was stored in a refrigerator at -20°C. From each study subject, spot mid stream urine sample was collected in a dry, clean and plain plastic container. Urinary protein and urinary creatinine were estimated immediately and protein-to-creatinine ratio was calculated.[20]. Blood sugar (2 hours after breakfast) was estimated by glucose-oxidase (GOD-PAP) method, serum creatinine by modified Jaffes method, urinary protein by dye binding method, urinary creatinine by alkaline picrate precipitation method, serum potassium by ion selective method and HgA_{1c} by filter method. Glomerular filtration rate was calculated by Cockcroft-Gault formula [6],

Primary efficacy end point[8]: The primary efficacy measure is the mean reduction in the spot urinary protein-to-creatinine ratio from baseline to the end of the (2 months) study.

Secondary end points[9]: GFR, Blood pressure, the rates of clinical events: end stage renal disease, myocardial infarction, stroke, CCF, the rate of death from all cause, the rate of adverse events.

All statistical analysis was done by SPSS software package, 13.5 for windows. Values were presented as mean ± SD. 95% confidence limit was taken as level of significance. Paired 't' test was done to compare between means within the groups and un-paired 't' test was done to see any significant difference between the study parameters of group 1 and group 2.

Ethical issues: The protocol was approved by the Ethics Review Committee of Sylhet M.A.G. Osmani Medical College, Sylhet.

Results

Fortyone patients were taken into account as study sample. The study subjects were matched in respect to their sex, age, body weight, height and body-mass index and the values are shown in the table I.

Table I:

Sex, age, height, weight, BMI stratification of study subjects treated by tablet ramipril or tablet losartan

Baseline variable	Ramipril	Losartan
Male	9 (45.0%)	9 (42.9%)
Female	11 (55.0%)	12 (57.1%)
Age (in year)	47.80 ± 7.67	47.95 ± 9.02
Height (in meter)	1.58 ± 0.06	1.56 ± 0.08
Weight (in Kg)	66.20 ± 8.70	63.71 ± 8.82
BMI (Kg/m^2)	26.55 ± 3.56	26.14 ± 3.64

Table II

Effects of ramipril for 2 months on mean BP, PCR and GFR in type 2 diabetic patients with grade 1 hypertension and early nephropathy (Mean ±SD)

Ramipril	Before administration; m-0	After 2 months
Mean BP	107.45 ± 3.59	101.85 ± 7.04**
PCR#	765.8 ± 331.1	467 ± 285.3**
GFR	86.7 ± 18.07	80.15 ± 19.01**

#PCR = protein-to-creatinine ratio.

**significant difference before and 2 months after administration of ramipril at $p < 0.01$ (Student's paired t-test)

In the losartan-treated group before administration of losartan and at the end of 2 months the mean blood pressure was 107.95 ± 3.90 vs. 100.71 ± 6.88 mmHg ($p < 0.001$), urinary protein level was 31.43 ± 16.26 vs. 22.14 ± 15.94 mg/dl.($p = 0.028$), Urinary creatinine was 47.52 ± 20.93 vs. 52.43 ± 24.15 mg/dl.($p = 0.419$), urinary protein-to-creatinine ratio was 706.33 ± 323.73 vs. 448.95 ± 243.68 mg/gm.(p

= 0.002) and GFR was 92.38 ± 15.63 vs. 90.67 ± 21.29 ml/min/1.73m^2 (p=0.498).

Table III

Effects of losartan for 2 months on mean BP, PCR and GFR in type 2 diabetic patients with grade 1 hypertension and early nephropathy (Mean ± SD)

Losartan	Before administration m=0	After 2 months
Mean BP	107.95 ± 3.9	100.71 ± 6.88**
PCR#	706.3 ± 323.7	449 ± 243.7**
GFR	92.38 ± 15.63	90.67 ± 21.29NS

#PCR=protein-to-creatinine ratio
**significant difference before and 2 months after administration of losartan at p<0.01, NS=no significant difference observed at p>0.05 compared to pre-treatment level (Student's paired t-test).

Mean changes in mean BP, PCR and GFR after 2 months of administration of ramipril or losartan are presented in table IVRamipril and losartan reduced mean blood pressure but the difference was not significant.
Ramipril and losartan reduced mean protein-to-creatinine ratio but the difference was not significant. Ramipril and losartan decreased mean GFR but the difference was not significant. The results showed no significant difference between ramipril and losartan in mean change in protein-to-creatinine ratio, administered for 2 months in type 2 diabetic patients with grade1 hypertension and early nephropathy.

Table IV

Comparison of effects of ramipril and losartan for 2 months on mean BP, PCR and GFR in type 2 diabetic patients with grade 1 hypertension and early nephropathy (mean changes compared to pre-treatment level). (Mean ± SD)

parameter	Ramipril	Losartan	t value	p value
Mean BP	-5.6 ± 5.36	-7.24 ± 5.43	0.97	0.337
PCR	-298.75 ± 407.41	-257.38 ± 328.12	-0.36	0.724
GFR	-6.55 ± 6.83	-1.71 ± 11.38	-1.66	0.106

Student's unpaired t- test
p>0.05 indicates that no significant difference is observed.

Adverse drug reactions observed in either ramipril or losartan treated group are presented in table V. In ramipril treated group, 1(5%) patient complained of malaise, 3 (15%) patients developed cough and 2 (10%) of them were bound to discontinue taking ramipril but no such adverse drug reactions were observed in losartan treated group. Evidence of renal failure (serum creatinine level >1.8mg/dl), hyperkalemia (serum potassium level > 5.5 mmol/L), symptomatic hypotension or angioedema were observed in neither ramipril nor losartan treated group.

Table V

Adverse drug reactions	Group	
	ramipril n=20	losartan n=21
Symptomatic hypotension	nil	nil
Renal failure	nil	nil
Hyperkalemia	nil	nil
Angioedema	nil	nil
Cough	3 (15%)	nil
Malaise	1 (5%)	nil

Discussion

The renoprotective effect of ramipril is well established[9] in type 2 diabetes with hypertension and nephropathy. But it has some serious adverse effects like dry cough, hypotension, angioedema etc. compelling the patients to discontinue the drug[21]. Alternately, losartan appears to exert less or devoid of these above mentioned adverse effects[22]; moreover, ARB's renoprotective effect was found not inferior[9] to ACEI in DETAIL study with Telmisartan and Enalapril, 1996. If losartan and ramipril appear equally effective; the former would be better treatment option.

In the present study, ramipril and losartan significantly reduce proteinuria, protein-to-creatinine ratio and both systolic and diastolic blood pressure at low doses in type 2 diabetic patients with grade 1 hypertension and early nephropathy.

MARVAL study done by Viberti and Wheeldon, (2002) found valsartan (in place of losartan) as an antihypertensive agent reduced both systolic and diastolic blood pressure in microalbuminuric type 2 diabetic patients[23]. A review article by Ahmed, (2003) expressed that ACEI perindopril lowers both systolic and diastolic blood pressure in renal disease[24]. In the present study, there had significant reduction of mean blood pressure in both the groups but the difference was not significant. This observation was in consistent with the study done by Lacourciere et al., (2000) where enalapril (in place of ramipril) and losartan were studied and there observed no significant difference in mean reductions of blood pressure[19]. It was also observed in DETAIL study (Barnett et al., 2004) that both telmisartan and enalapril reduced blood pressure and their difference of mean reductions was non significant[9].

The present study was confined only to early neprophathic[9] diabetic patients as was that of Barnett et al., 2004. At the end of study it was found that both ramipril and losartan significantly reduced the urinary protein. But the difference of mean reductions between them was not significant. This observation was in consistent with the study done by Lacourciere et al., (2000) where enalapril (in place of ramipril) and losartan were studied and no significant difference in mean reductions of urinary albumin was found[19]. Taal and Brenner, (2000) observed that ACEI and AT1RA (angiotensin type 1 receptor antagonist) have equivalent effects on proteinuria in renal disease[13].

Both in ramipril and losartan groups, non significant increment of urinary creatinine were observed. An 8 weeks study done by Campbell et al., (2003) on hypertensive chronic nephropathy patients, compared the renoprotective effect of benazepril and valsartan. The study found that the difference of changes in mean urinary creatinine was not significant among the groups[12].

From the measurements of urinary protein and urinary creatinine, outcome variable PCR of the study was calculated. Both In ramipril and losartan group group, mean reduction of protein-to-creatinine ratio was highly significant But the difference of mean reductions was not significant.

A recent study by Parving et al., (2008) on type 2 diabetes with hypertension and nephropathy, found that combined effect of aliskiren (oral renin inhibitor) and losartan compared with placebo and losartan, reduced the mean urinary albumin-to-creatinine ratio[7]. Another study, done by Esnault et al., (2004) found that the reduction in urinary protein-to-creatinine ratio did not significantly differ between ramipril and valsartan treated groups[25].

Ideally, GFR should not be decreased with any ACEI or ARB. But in current study, it was observed that calculated GFR was decreased in both ramipril and losartan treated groups. But the difference was not significant. In a five-year study, done by Barnett et al., (2004) on type 2 diabetes with hypertension and nephropathy; the renoprotective effect of telmisartan and enalapril were compared by mean change in glomerular filtration rate (determined by measuring the plasma clearance of iohexol). The difference of mean changes was not significant[9].

The present study included the low proteinuric (<100mg/dl) patients in type 2 diabetes with hypertension, with low level of serum creatinine (<1.6 mg/dl) and GFR >70ml/min/1.73m^2 that is, the study had included only the early nephropathic patients and was observed remarkable antiproteinuric effects of ramipril and losartan in low doses. In a recent study, done by Hoque et al., (2009) found no statistically significant changes in urinary protein excretion even at high doses of enalapril and losartan in type 2 diabetic patients[26]. But the investigators cited the examples that heavy proteinuria (>2gm/day or >133mg/dl) and the patients with high serum creatinine (>2.5mg/dl), enalapril or losartan were not sufficient enough to reduce proteinuria in type 2 diabetes with hypertension. Both in present study (at low doses) and Hoque et al., (2009) study (at high doses), it was observed that ramipril or enalapril apparently appeared to have more antiproteinuric than losartan but the difference was not significant as reflected in protein-to-creatinine ratio in present study but was significant in other study[26].

During the study period, it was observed that adverse drug reactions like intolerable cough, malaise were more in ramipril group than losartan group. No such event was occurred in losartan group. In Lacourciere et al., (2000) study it was also observed that enalapril was associated with a significantly higher incidence of cough[19] (p= 0.006).There were no history of hypotension, stroke, CCF, myocardial infarction, angoiedema, hyperkalemia , acute renal failure or death during the study period in either group.

In conclusion, Losartan is equally renoprotective as ramipril in type 2 diabetes with grade 1 hypertension and early nephropathy. Losartan showed no serious adverse effects resulting discontinuation of the drug likes ramipril. So, in clinical practice, losartan may prove a useful alternative drug for the patients who can not tolerate ramipril due to its adverse effects. This study was conducted on a small number of patients; it was a single center trial and follow up was limited to 2 months only. As, the trial was fairly of short duration (2 months), analysis of long term efficacy was not possible. Tight glycaemic control was not possible for out patient samples. Because, direct comparison was carried out between two treatment groups of patients, the findings would have been more significant if a placebo group had been used. Virtually, a randomized, placebo-controlled, double-blind, study was ethically not possible.

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ORIGINAL ARTICLE

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Efficacy of citalopram in irritable bowel syndrome – a prospective double blind randomized placebo control study

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Abstract

Irritable bowel syndrome (IBS) is a common clinical problem encountered by primary health care physicians and gastroenterologists. Epidemiologic studies indicate a high prevalence of IBS in the general population worldwide. The economic impact of IBS is enormous. The pathophysiology of IBS is not clearly understood. It is a chronic disease and is difficult to treat. But effective management may lessen the symptoms of IBS and lead to remission for many years. Antidepressants have been used in the treatment of IBS for a long time. Tricyclic antidepressants (TCA) and Selective Serotonin Reuptake Inhibitors (SSRIs) are used commonly. Among SSRIs- sartraline, citalopram and paroxetine are most commonly used drugs. Although SSRIs are being widely used in Bangladesh for treating IBS patients for a long time, their efficacy has not been studied in well designed clinical trial. This prospective, double blind, randomized clinical trial has been conducted on IBS patients, using citalopram and placebo in separate group in parallel design to see the benefit of the drug over placebo therapy. Patients of 15 to 60 years old and both sexes were included from the out patient department (OPD) of gastroenterology, Banghabandhu Sheikh Mujib Medical University (BSMMU). Diagnosis of IBS was made on the basis of Rome II criteria and who did not have features of red flags. All patients underwent certain screening investigations and in few patients colonoscopy were done to exclude organic diseases. Improvement was assessed by changes in symptoms like abdominal pain, stool frequency and consistency and flatulence as baseline and weekly for 6 weeks follow up. A validated IBS-QOL instrument consisted of 34 questions used to assess improvement of quality of life before and after treatment. A total of 70 patients were enrolled in this study. Nine patients dropped out. Sixty one patients completed the trial. Among them 40 patients were diarrhoea predominant and 21 patients were constipation predominant. In this study at the end of 6 weeks therapy, it is observed that improvement in various symptoms in patients taking citalopram was statistically significant. Improvement in various symptoms in patients taking placebo was also statistically significant. However, differences of improvement between the two groups in relieving various symptoms were not statistically significant. Mean QOL score before treatment was 103 in citalopram group and 106 in placebo group. After 6 weeks of treatment mean QOL score was 82 in citalopram group and 95 in placebo group indicating. Improvement in both groups was statistically significant. The difference between the two groups was also significant. No worsening of symptoms or and no side effects of the therapeutic agents was observed in any patient during the trial.

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Introduction

Functional gastrointestinal disorders are extremely common. These disorders, including IBS and non-

ulcer dyspepsia (NUD) are the most common disorders encountered by the gastroenterologists and constitute a considerable economic burden to the health care system[1]. IBS is the best-recognized functional gastrointestinal disorder[2]. It is a chronic continuous or remittent gastrointestinal illness characterized by frequent unexplained symptoms that include abdominal pain, bloating and bowel disturbance, which may be either diarrhea or constipation or an erratic bowel habit that has features of both.[3] The prevalence of IBS has not been firmly established, but it has been estimated that IBS affects 14- 24% of women and 5-15% of men in a western country[4]. The worldwide prevalence is 10-20 percent.[5] IBS is more common in female than male. On an average female to male ratio is 2.3:1[6,7,8]. IBS was 20.6% in male and 27.7% in female in a rural community in Bangladesh[10]. Exact pathophysiology of IBS remains poorly understood[11]. There is no single pathophysiological marker of IBS. It is however, generally accepted that it is either abnormal intestinal motility and/or enhanced visceral sensitivity[6]. Abdominal pain and disordered defecation i.e. either constipation or diarrhea or both are the main symptoms of IBS, but these are also common features in organic gastrointestinal disease[12].Traditionally IBS is diagnosed only after exclusion of organic disease with the aid of hematological tests, stool microscopy, thyroid hormone test, contrast X-ray of colon or flexible sigmoidoscopy, where indicated[13].There is no standard treatment for IBS. Alleviating symptoms is one of the primary challenging goals of caring for IBS patients[14]. Various pharmacological agents are available for treating IBS. Commonly used drugs are bulking agents, antidiarrhoeal agents, antispasmodics and antidepressant drugs[15]. Despite their wide spread use it is very difficult to demonstrate their efficacy in controlled clinical trial, because there is no objective or biochemical marker for improvement of IBS and there is high placebo response (up to 70%)[16]. Antidepressants have been used in IBS patients for long time, in Bangladesh. Tricyclic antidepressants (TCA) and selective serotonin reuptake inhibitor (SSRIs) were commonly used. Among SSRIs - sartraline, citalopram and paroxetine are most commonly used. Although SSRIs are being widely used in Bangladesh for treating IBS patients for a long time, their efficacy has not been studied in well designed clinical trial. So, this prospective double blind randomized clinical trial has been conducted in IBS patients, using Citalopram and placebo in separate group of patients to see the short-term efficacy of Citalopram in relation to change of symptoms score in all groups of patients and to see the change of quality of life (QOL) score before and after treatment in comparison with placebo.

Materials and Methods

This prospective double blind randomized placebo controlled study was conducted among the patients attending to gastroenterology OPD of (BSMMU) during the period from March 2006 to March 2007. Patients aged between 15 to 60 years, fulfilling the Rome II criteria for IBS diagnosis, having no red flags sign and having secondary education level so that they could fill-up questionnaire perfectly were included in the study. Pregnant and lactating mother and patients having concomitant sever illness were excluded from the study. Detailed history and meticulous physical findings were done. Complete blood count, blood glucose, serum TSH, stool R/M/E was done in all patients and in few patients colonoscopy was done to exclude any organic disease. All patients advised to exclude milk and milk products during the study period. Any patients having treatment for IBS were excluded from the study sample. For the purposes of this study diarrhoea was defined as patients self described passage of wet, soft stool more than 3 motions per day. Constipation was described as the passage of hard stool evacuated after straining and less than 3 motions per week. Patients were randomly allocated to receive either Tab. Citapram (Citalopram) or placebo for six weeks selected according to a random number table. A total of 70 patients were included in this study. Thirty five patients were treated with Tab. Citapram 20mg (Citalopram) and 35 were treated with placebo. Components of placebo were lactulose, wheat ear, colloidal silicon dioxide, talc and magnesium stearate. Placebo tablets were identical in appearance and colour. All patients were instructed to take tablet in once daily dose at night. Changes of symptoms and quality of life of patient was assessed by using a previously used specially designed symptoms scoring system[17] and validated IBS-QOL instrument[18]. Symptoms scoring system of IBS included four major symptoms abdominal pain, stool frequency, consistency and flatulence.

Symptoms score was applied before starting the treatment as baseline and weekly for 6 weeks. This scoring was done by doctor on the basis of weekly interview. QOL instrument were translated into Bengali and were given to each patients before and after treatment. Patient himself scored on IBS-QOL instrument. All data were recorded in a printed data sheet. Unpaired 't' test was used to assess the difference between the groups in case of symptom analysis and paired 't' test in the same group before and after treatment to see the improvement of quality of life.

Results

Among 70 patients following randomization, 35 patients (male 32, female 3) were assigned to receive Citalopram, 35 patients (male 29, female 6) to receive placebo preparation. There were no statistically significant difference between the test and control group with respect to age and sex. Age ranges of the patients were 15 to 60 years. Mean age of treatment group and placebo group were 27.3 ± 5.28 years and 30.49 ± 8.68 years respectively **(Table-1)**

Table-1
Baseline characteristic of the patients with IBS

Parameters	Citalopram Group (N = 31)	Placebo Group (N = 30)
Age	27.32 ± 5.28 years	30.49 ± 8.68 years
Sex Male Female	 28 3	 24 6
Diarrhoea Predominant	20	20
Constipation Predominant	11	10

There were no significant differences in severity of symptoms between placebo and treatment group. Total 9 patients were dropped out from this study, of which 4 were from Citalopram group and 5 were from the placebo group; one patient in citalopram group discontinued the drug due to excessive drowsiness and one patient due to excessive fatigue, other 2 patients due to unknown cause. Two patients in placebo group discontinued the drug due to non response, other 2 due to unknown cause. Total 61 patients completed the trial, forty patients were diarrhoea predominant and 21 patients were constipation predominant. Among them 31 (20 diarrhoea predominant and 11 constipation predominant) patients received citalopram, and 30 (20 diarrhoea predominant and 10coustipation predominant) patients received placebo treatment.

Among 31 patients in citalopram group, 23 (74%) patients suffered from a pain score between 5 and 10 points at baseline. At the end of this study only 9 (29%) patients had same level of pain, sixteen patients (51%) had marked improvement in pain score (less than 4) **(Table-II)**. In the placebo group 24 (80%) patient had a pain score between 5-10 points at the baseline. At the end of the study 12 (40%) patients had same level of pain. Fifteen (50%) patients had improvement of pain score (less than 4) **(Table-III)**. Improvement in pain score after treatment in both citalopram and placebo group were statistically significant (p value <0.05 and < 0.02 respectively) [table-x and xi] but the difference of improvement between citalopram and placebo groups was not statistically significant ($p < 0.371$)

Table-II
Abdominal pain : Citalopram group (n=31)

Symptom score	Before treatm.	After 1 wk	P value <0.01	After 2 wk	P value <0.02	After 3 wk	P value <0.02	After 4 wk	P value <0.02	After 5 wk	P value <0.02	After 6 wk	P value < 0.05
None (0)	1	2		4		7		3		5		6	
Occasional (1)	7	10		13		12		20		18		16	
Frequent (2)	7	15		11		11		6		6		7	
Permanent (3)	16	4		2		1		2		2		2	

Table-III

Abdominal pain: Placebo group (n=30)

Symptom score	Before treatm.	After 1 wk	P value <0.05	After 2 wk	P value <0.02	After 3 wk	P value <0.05	After 4 wk	P value <0.05	After 5 wk	P value <0.05	After 6 wk	P value < 0.02
None (0)	1	3		1		2		2		3		3	
Occasional (1)	5	10		11		13		14		15		15	
Frequent (2)	11	11		14		11		10		11		9	
Permanent (3)	13	6		4		4		4		1		3	

Of the patients receiving citalopram - 9 patients (29%) had stool frequency more than 3 times/day in more that 50% of time at baseline. After 6 weeks only 2 patients (6%) had the same frequency of stool motion **(Table-IV)**. In the placebo group 14 patients (46%) had stool frequency more than 3 times/day in more than 50% of time at baseline. After 6 weeks 11 patients (36%) had the same frequency of stool motion **(Table-V)**. Improvement in patients in respect to bowel frequency in both citalopram and placebo groups were statistically significant ($p<0.01$ and <0.01 respectively) **(Table-IV and V)** in respect to baseline. The difference of improvement between citalopram and placebo groups is not statistically significant ($p<0.632$)

Table-IV

Altered stool frequency > 3 times/day : Citalopram group (n=31)

Symptom score	Before treatm	After 1 wk	P value <0.05	After 2 wk	P value <0.02	After 3 wk	P value <0.02	After 4 wk	P value <0.02	After 5 wk	P value <0.02	After 6 wk	lu e ◁0 0
None (0)	14	18		15		16		17		15		16	
Occasional (1)	8	6		9		9		9		11		13	
Frequent (2)	3	3		6		6		5		4		1	
Permanent (3)	6	4		1		0		0		1		1	

Table-V

Altered stool frequency > 3 times/day: Placebo group (n=30)

Symptom score	Before treatm.	After 1 wk	P value <0.01	After 2 wk	P value <0.01	After 3 wk	P value <0.01	After 4 wk	P value <0.01	After 5 wk	P value <0.01	After 6 wk	P value < 0.01
None (0)	7	9		8		10		9		11		11	
Occasional (1)	9	7		7		4		5		5		8	
Frequent (2)	7	8		10		14		13		13		10	
Permanent (3)	7	6		5		2		3		1		1	

Among the patients receiving citalopram 10 patients (32%) had soft stool more than 50% of time at the baseline. After 6 weeks only 2 (6%) had this same level of consistency **(Table-VI)**. Among the placebo group 15 patients (50%) has soft stool in more than 50% of time at the baseline. After 6 weeks 5 patients (16%) had the same level of consistency **(Table-VII)**. Improvement in both group in respect to soft stool were statistically significant ($p<0.01$ and <0.01 respectively) **(Table-IV to VII,)** in respect to baseline. The difference of improvement between citalopram and placebo groups is not statistically significant ($p<0.712$)

Table-VI

Soft stool: Citalopram group (n=31)

Symptom score	Before treatm.	After 1 wk	P value <0.1	After 2 wk	P value <0.05	After 3 wk	P value <0.01	After 4 wk	P value <0.01	After 5 wk	P value <0.02	After 6 wk	P value < 0.01
None (0)	10	9		10		7		10		12		9	
Occasional (1)	6	6		4		10		8		9		10	
Frequent (2)	8	8		12		12		13		10		10	
Permanent (3)	10	8		5		2		0		0		2	

Table-VII

Soft stool: Placebo group (n=30)

Symptom score	Before treatm.	After 1 wk	P value <0.1	After 2 wk	P value <0.02	After 3 wk	P value <0.02	After 4 wk	P value <0.0	After 5 wk	P value <0.02	After 6 wk	P value < 0.01
None (0)	5	7		7		7		7		9		6	
Occasional (1)	2	4		2		3		6		4		7	
Frequent (2)	8	4		12		9		10		12		12	
Permanent (3)	15	15		9		11		7		5		5	

Of the patients receiving citalopram- 12 patients (38%) had stool frequency less than 1 time/day in more than 25% of time at baseline. After 6 weeks 8 patients (25%) had the same level of frequency of stool motion **(Table-VIII)**. In the placebo group 6 patients (19%) had stool frequency less than 1 time/days, during 25%-50% of time at baseline. After 6 weeks 1 patient (3%) had the same level of frequency of stool motion **(Table-IX)**. Improvement in patients in respect to bowel frequency was less than 1 time/day in both group, which is statistically significant ($p < 0.01$ and $P < 0.05$ respectively) **(Table-VIII and IX)** in respect to baseline. The difference of improvement between citalopram and placebo groups is not statistically significant ($p < 0.514$)

Table-VIII

Altered stool frequency < 1 time/day: Citalopram group (n=30)

Symptom score	Before treatm.	After 1 wk	P value <0.1	After 2 wk	P value <0.05	After 3 wk	P value <0.1	After 4 wk	P value <0.1	After 5 wk	P value <0.05	After 6 wk	P value < 0.02
None (0)	19	18		20		19		21		20		24	
Occasional (1)	7	8		7		9		7		4		5	
Frequent (2)	5	5		3		2		3		2		2	
Permanent (3)	0	0		1		1		0		0		1	

Table-IX

Altered stool frequency < 1 time/day: Placebo group (n=30)

Symptom score	Before treatm.	After 1 wk	P value <0.1	After 2 wk	P value <0.05	After 3 wk	P value <0.02	After 4 wk	P value <0.05	After 5 wk	P value <0.01	After 6 wk	P value < 0.05
None (0)	22	22		24		22		20		20		22	
Occasional (1)	2	5		2		5		8		6		6	
Frequent (2)	6	2		2		2		1		2		1	
Permanent (3)	0	1		2		1		1		2		1	

Among the patients receiving citalopram- 9 patients (29%) had hard stool in more than 25% of time at baseline. After 6 weeks 4 patients (12%) had the same level of consistency of stool. In the placebo group 7 patients (22%) had hard stool in more than 25% of time at baseline. After 6 weeks 3 patients (9%) had same level of consistency of stool **(Table-X)**. Improvement in patients in respect to in both citalopram and placebo group were statistically significant (p value < 0.05 and < 0.01 respectively)

(Table-X and XII) in respect to baseline. The difference of improvement between citalopram and placebo groups is not statistically significant ($p < 0.639$)

Table-X

Hard stool: Citalopram group (n=31)

Symptom score	Before treatm.	After 1 wk	P value <0.02	After 2 wk	P value <0.01	After 3 wk	P value <0.01	After 4 wk	P value <0.05	After 5 wk	P value <0.05	After 6 wk	P value < 0.05
None (0)	15	15		14		13		15		21		21	
Occasional (1)	7	8		9		10		10		5		6	
Frequent (2)	4	5		5		7		3		4		4	
Permanent (3)	5	2		3		1		3		2		0	

Table- XI

Hard stool: Placebo group (n=30)

Symptom score	Before treatm.	After 1 wk	P value <0.1	After 2 wk	P value <0.01	After 3 wk	P value <0.1	After 4 wk	P value <0.01	After 5 wk	P value <0.02	After 6 wk	P value < 0.01
None (0)	20	20		19		18		22		20		22	
Occasional (1)	3	3		4		5		2		3		5	
Frequent (2)	4	4		5		4		5		3		2	
Permanent (3)	3	3		2		3		1		4		1	

Among the patients receiving citalopram 18 patients (58%) had flatulence more than 25% of time at baseline. After 6 weeks 11 patients (35%) had the same level of flatulence (Table-XII). In the placebo group 25 patients (80%) had flatulence more than 25% of time at baseline. After 6 weeks 21 (67%) had the same level of flatulence (Table-XIII). Improvement in patients in respect to flatulence in both citalopram and placebo group were statistically significant ($p < 0.05$ and < 0.01 respectively) (Table XII and XIII) in respect to baseline. The difference of improvement between citalopram and placebo groups is not statistically significant ($p < 0.232$)

Table-XII

Flatulence: Citalopram group (N = 31)

Symptom score	Before treatm.	After 1 wk	P value <0.02	After 2 wk	P value <0.02	After 3 wk	P value <0.02	After 4 wk	P value <0.02	After 5 wk	P value <0.02	After 6 wk	P value < 0.05
None (0)	0	3		3		1		3		2		2	
Occasional (1)	5	10		8		10		13		13		18	
Frequent (2)	6	10		13		14		10		11		8	
Permanent (3)	8	8		7		6		5		5		3	

Table-XIII

Flatulence: Placebo group (N = 30)

Symptom score	Before treatm.	After 1 wk	P value <0.01	After 2 wk	P value <0.02	After 3 wk	P value <0.02	After 4 wk	P value <0.02	After 5 wk	P value <0.01	After 6 wk	P value < 0.01
None (0)	1	2		3		2		3		2		1	
Occasional (1)	4	3		5		5		5		9		8	
Frequent (2)	7	12		15		17		16		12		12	
Permanent (3)	18	13		7		6		6		7		9	

A validated IBS-QOL has been used which consists of 34 questions. Each had potential score of 1 to 5 points. So minimum score is 34 and maximum score is 170. Patient himself/herself scored on QOL instrument before and after treatment. In Citalopram group score before treatment was 103.64 and in placebo group mean score was 106.36. After treatment, mean score of treatment group was 82.80

and in placebo group was 95.58 (**Table-XIV**). The improvement in QOL score in both citalopram and placebo group before and after treatment was statistically significant (P value <0.05 and <0.05 respectively). Difference in improvement between treatment and control group at the end of treatment was also statistically significant (P value <0.05) (**Table-XV**).

Table-XIV

IBS-QOL mean score before and after treatment

	Before treatment	After treatment	P value
Citalopram group (n=31)	103.64	82.80	(P <0.05)
Placebo group (n=30)	106.36	95.58	(P <0.05)

Table-XV

IBS-QOL Score between Citalopram and Placebo group after 6 week of treatment.

	Treatment Group	Placebo group	P value
QOL Score	82.80	95.58	< 0.05

Discussion

The potential effectiveness of antidepressants in managing IBS symptoms was first examined 20 years ago. Two early studies[19, 20] of imipramine reported that this agent was efficacious in alleviating IBS-associated abdominal pain, nausea, sleeplessness, and depression. A recent meta-analysis examined data obtained from 12 randomized, placebo-controlled trials of antidepressants in IBS[21]. Study medications included tricyclic antidepressants (amitriptyline, clomipramine and imipramine), a heterocyclic (doxepin), desipramine, and an antiserotonin agent, mianserin. The summary odds ratio for improvement in GI symptoms with antidepressant therapy was 4.2 (95% confidence interval [CI] =2.3 to 7.9). The standardized mean improvement in pain was equal to 0.9 standard deviation units (95% confidence interval [CI] =0.6 to 1.2), which is considered to be a large treatment effect. In reviewing their 5-year clinical experience with antidepressants in outpatients with IBS, (N=138). Clouse et al[22] reported improvement in 89% and complete remission of bowel symptoms in 61% of patients during antidepressant therapy with tricyclic antidepressants or anxiolytics. Median doses to achieve remission were lower than those used to obtain an antidepressant effect. The presence/absence of psychological symptoms was not predictive of treatment remission. However, a pain-predominant IBS symptoms pattern was more commonly associated with symptom remission.

Several recent case reports have suggested that serotonergic antidepressants (fluvoxeamine[23], paroxetine[24], mirtazapine[25]) are efficacious in alleviating IBS symptoms. Several other studies have demonstrated efficacy of tricyclic antidepressants in the treatment of irritable bowel syndrome[2, 2], but the use of selective serotonin reuptake inhibitors (SSRIs), a pharmacologically more selective class of antidepressants, has only been studied in a few trials which yielded inconclusive results. Creed et al [2] compared cost-effectiveness of psychotherapy, the SSRI paroxetine 20 mg daily and usual care in a large sample of severe IBS patients. After one-year follow-up, the severity and frequency of abdominal pain had improved similarly in all groups. However, psychotherapy and paroxetine were superior to usual care in improving the physical component of health related quality of life, and psychotherapy was associated with a significant reduction in health care costs compared to usual care. Kuiken et al[2] performed a double blind, randomized, placebo-controlled study in 40 non-depressed IBS patients with 20 mg of the SSRI fluoxetine for 6 weeks. Rectal sensitivity and rectal compliance, which were the primary endpoints in this study, were not significantly altered by fluoxetine compared to placebo. Furthermore, abdominal pain, other gastrointestinal symptoms or global symptom relief did not differ between both groups after 6 weeks treatment. Tabas et al[2] compared treatment with 10 or 20 mg of paroxetine or placebo for 12 weeks in 81 IBS patients that did not respond to fiber. Paroxetine

significantly improved overall well-being, which was the primary endpoint without a relationship to changes depression or anxiety levels. Paroxetine did not affect abdominal pain and bloating, but significantly improved straining, urgency and feelings of incomplete evacuation of rectum. In a very recent controlled study from Iran, fluoxetine was found to be superior to placebo in improving symptoms of pain, bloating and constipation in constipation-predominant irritable bowel syndrome[2] .

Study done by Prakash S. Masand et al[3] , showed that citalopram can cause ≥ 50% improvement of abdominal pain in 80% patients and ≥50% reduction in the frequency of symptoms. Approximately one half of the patients met criteria for remission (≥ 70% improvement) of abdominal pain. Another study done by Tack J. et al.[3] showed that 6 weeks treatment with citalopram (3 weeks 20 mg, 3 weeks 40 mg) was superior to placebo in alleviating IBS symptoms. Citalopram had a beneficial effect on abdominal pain bloating impact of symptoms on daily life and overall well-being. There was only modest effect on stool pattern. The therapeutic effect is independent of effect on anxiety, depression and colonic sensorimotor function.

In the present study, it was found that both citalopram and placebo are effective in relieving various symptoms of IBS but there was no significant difference between two. During 6 weeks of follow up of patients it was seen that there was fluctuation of improvement of various symptoms. It is likely to be due to natural fluctuation course of IBS symptoms. IBS-QOL instrument was used as a parameter of improvement of this trial. It showed that both citalopram and placebo significantly improve the QOL. The improvement of patient taking citalopram is also significantly differs from the placebo group. The underlying mechanisms of these effects are unknown but may attribute in part to the activity of citalopram at the 5-HT_3 receptor. Some investigators have suggested that the beneficial effect of serotonergic and adrenergic antidepressants in IBS may be partially due to the anti-nociceptive (analgesic) effect of these agents independent of their antidepressant effect[32]. This hypothesis requires further study to determine the mechanism of action of antidepressant in general and citalopram in specific in alleviating IBS symptoms. Tolerance of the drug was excellent, and no difference in adverse events was noted between citalopram and placebo. The onset of the effect of citalopram on symptoms severity occurred within 3 weeks, which is faster than the usual occurrence of an antidepressant effect. Daily diaries confirmed a symptomatic effect as early as within the first week for severity of abdominal pain, flatulence. Compared to recent multi-center therapeutic trials in IBS, the placebo effect in the present study is modest.

Studies with SSRIs in IBS have shown conflicting results; only two studies demonstrated a significant effect of SSRI on cardinal IBS symptoms including abdominal pain compared to placebo[2] . There may be several reasons for these divergent findings. First different patient samples may have been recruited with respect to gender, previous treatment, psychiatric co-morbidity, visceral hypersensitivity, and other variables. Second, trial design, methodology and endpoints differ significantly between the studies mentioned. Finally, different SSRIs have been used at different doses and there is evidence that they differ slightly in pharmacological profile[32]. Paroxetine, for instances, has some anticholinergic properties, while citalopram is believed to be the most selective SSRI[32]. The strength of this study include the use of Rome II criteria to diagnose IBS and physical findings plus and screening investigations including colonoscopy in few patients were utilized to confirm the diagnosis.

Limitations of this study were, flexible sigmoidoscopic or colonoscopic evaluation was not done in all patients and patients were selected from a tertiary health care center only. Based on the present study, the SSRI citalopram is a potential valuable addition to other therapeutic options for IBS. Citalopram provided rapid symptomatic benefit, was well tolerated and was not associated with side-effects of tricyclic antidepressant such as drowsiness or constipation. Larger scale studies are needed for further evaluation of the efficacy of citalopram or

other SSRIs for the IBS patients seen in the primary and secondary health care centers.

In conclusion, from this study it can be concluded that citalopram was effective in reducing various symptoms in IBS patients but the effect was not significantly different from that of placebo. However, it is more effective than placebo in improving QOL. Based on the present study, the SSRI citalopram is a potentially valuable addition to other therapeutic options for IBS. As these preliminary results appear to be promising, larger placebo-controlled trials with adequate power are warranted for further evaluation of the potential efficacy of citalopram and other SSRIs before their recommendation as therapeutic agents for the treatment of IBS patients in Bangladesh.

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ORIGINAL ARTICLE

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A comparative study of surgical site wound infection in Dhaka medical College Hospital and Holy Family Red Crescent Medical College Hospital and detection of methicillin resistance *Staphylococcus aureus*

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Abstract

A comparative study of surgical site wound infection in Dhaka Medical College Hospital and Holy Family Red Crescent Medical College Hospital was carried out from July 2009 to December 2009. The major pathogens of wound infection in both hospitals were *E. coli* and *S. aureus*. The prevalence of *Pseudomonas* in DMCH was 20% and in HFRCMCH was 16%. More than 75% strains of *S. aureus* were methicillin resistance. The prevalence of *Methicillin resistance Staphylococcus aureus* (MRSA) in anterior nares of attendances and hospital staffs of both hospitals were very high. Sensitivity and specificity of latex agglutination test of *S. aureus* was 100% and methicillin resistant *S. aureus* isolates from both patients and carrier showed same coagulase type VI.

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Introduction

Surgical site wound is usually synonyms as Post operative wound and vice versa. The CDC's National Nosocomial Infection Surveillance (NNIS) system has developed and standardized the criteria for defining surgical site infection. By these criteria surgical site infection (SSI) are classified as being incisional or organ/ space. Incisional SSI are further divided into those involving only skin and subcutaneous tissues (superficial incisional SSI) and those involving deeper soft tissues of incision (deep incisional SSI). Organ/space SSIs involve any part of the organ or space other than incised body wall layers that was opened or manipulated during an operation .

A wide range of bacteria are responsible for surgical site wound infection. Wariso and Nwachukwu (2003)[2] from Nigeria investigated a total of 2458 wound swab samples. In descending order of frequency, the organisms include *Staphylococcus aureus* (31.60%) *Escherichia coli* (25.97%), *Pseudomonas aeruginosa* (21.21%) and *Klebsiella* spp. (10.82%), *Proteus* spp. (8.23%), non haemolytic *Streptococcus* (1.29%). Berceanu and co-workers (2003) [3] in Romania studied 119 bacterial strains isolated from post operative wounds. Regarding their frequency, the following strains were isolated: *Escherichia coli* (57%), *Staphylococcus aureus* (31%) *Pseudomonas aeruginosa* (8%) and *Proteus* spp (4%).

Methicillin-resistant *Staphylococcus aureus* are significant pathogens that now cause both nosocomial and community-acquired infections. Resistance to methicillin in *staphylococci* is characterized by presence of *mecA* genes. Staphylococci resistance to oxacillin /methicillin occurs when an isolate carries an altered penicillin-binding protein, PBP2a; which is encoded by the *mecA* gene. The alteration of the penicillin-binding protein does not allow the drug to bind well to the bacterial cell, causing resistance to *beta*-lactum producing antimicrobial agents [4]. The anterior nares, axillae, perineal, perianal and inguinal regions are common site of MRSA carriage. Since these strains tend to be multiple antibiotic resistances, they

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pose a major difficulty in treating systemic infections[5].MRSA infection on surgical wards is becoming increasingly common, especially in critically ill patients who have spent prolonged periods on the intensive care unit .

The aim of the study is to investigate the nature of surgical site wound infection and to investigate the presence of one of the major resistance pathogen known as MRSA.

Meterials and methods

A total of 40 samples were collected from the different wound sites of patients admitted in surgical ward of Dhaka medical college hospital (Public hospital) and Holy Family Red Crescent Medical College Hospital (Private hospital) from July 2009 to December 2009. Duplicate wound swabs were collected; one for preparation of smear for microscopy and other for seeding of culture. Sterile cotton tipped swab was used for collecting the sample by using zig-zag motion to swab wound surface and rotating the swab during collection. Special attention was given to avoid contact surrounding skin. Twenty samples each from right and left sides of anterior nares of hospital staffs and attendances of both hospitals were collected by rubbing up to one and half cm of nostrils and making five rotations in each nostril by the sterile cotton wool swabs moistened with sterile normal saline (0.89% NaCL solution). All specimens were inoculated into Blood agar, McConkey Agar (MCA) and Mannitol Salt Agar (MSA) media and incubated at 37 C overnight. Bacterial isolates were identified by colony morphology, staining and appropriate biochemical tests. Oxacillin disk diffusion test was done for detection of methicillin resistance *Staphylococcus aureus* (MRSA).

MRSA latex agglutination test

Latex particles against sensitized with a monoclonal antibody against penicillin binding protein 2a (PBP2a) will specifically react with methicillin resistance *Staphylococci* to cause agglutination visible to the unaided eye . The commercially available MRSA Latex agglutination kit was used to detect the monoclonal antibody against the penicillin binding protein.

PBP2a extraction procedure

Extraction reagent 1 (200μL) was added to a centrifuge tube. Sufficient freshly grown bacterial was taken and suspended in the tube approximately 1.5x10 cells/ tube. The tube was capped, placed into boiling bath and heated for 3 minutes. The Tube was removed and allowed to cool at room temperature about 30 C. Extraction reagent 2 (50 μL) was added to the tube and mixed it well. The mixture was centrifuged at 3000rpm for 5 minutes to separate the cell from supernatant. The supernatant was used as test specimen.

Latex agglutination procedure

For each specimen, two circles were labeled on the test card (one as the test and other as the control). 50 μL of specimen was placed on the test and control circles. Then one drop (25 μL) of sensitized latex was added to the test circle and one drop (25 μL) of control latex was added to the control and mix thoroughly. The test card was rotated by hand for three minutes and placed in bench and resulting agglutination pattern was read by naked eye. The interpretation of results was: Strong agglutination against a clear background (3+). Agglutination against a slightly turbid background (2+).Slight agglutination against a turbid background(1+).Homogenous white suspension with no visible agglutination (-). Coagulase typing of MRSA Coagulase typing can classify Staphylococcus spp. by its antigenic property into eight different types (Coagulase type I-VIII) and was done by using "Coagulase typing kit".

One colony of *S.aureus* was inoculated in Brain heart Infusion broth (37g dehydrated brain heart infusion broth media per liter distilled water) to produce coagulase and incubated at 37 C overnight. the culture fluid was centrifuged 3000 rpm for 30 minutes and supernatant was used as the test specimen of "Coagulase antigen solution". Nine test tubes were prepared. An amount of 50 μL of coagulase antigen solution was added into each of the tubes. Into the first tube, 50 μL of anti-type immune serum was added. Similarly 50 μL of anti-type II-VIII immune sera were put into the second to eight tubes. In the final ninth tube 50 μL of diluted rabbit sera (negative control) was added. The test tubes were stirred with mixer and then incubated at 37 C for one hour. An amount of 100 μL of diluted normal

rabbit plasma was added into all the tubes. The tubes were again stirred well with mixer at 37 C. After one hour, judgment of coagulation was done and in undetermined case, judgment was done 2, 4, 24, or 48 hours after addition of the rabbit plasma. Test tubes were declined and clotting was observed in each test tube including the negative control (the 9th tube containing normal rabbit serum).

Results

The 40 samples ware collected from different types of surgical site wounds in Dhaka medical college hospital (Public hospital) and Holy Family Red Crescent Medical College Hospital (Private hospital). *E. coli* (48%) was the predominant organisms in HFRCMCH (Private hospital) and *S. aureus* (31.3%) was the major pathogens for surgical site wound infection in DMCH (Public hospital). The prevalence of *Pseudomonas* in DMCH was 20% and in HFRCMCH was 16%. The presence of *Proteus, Klebsiella, Streptococcus pyogens* were almost similar in both places (Figure I).

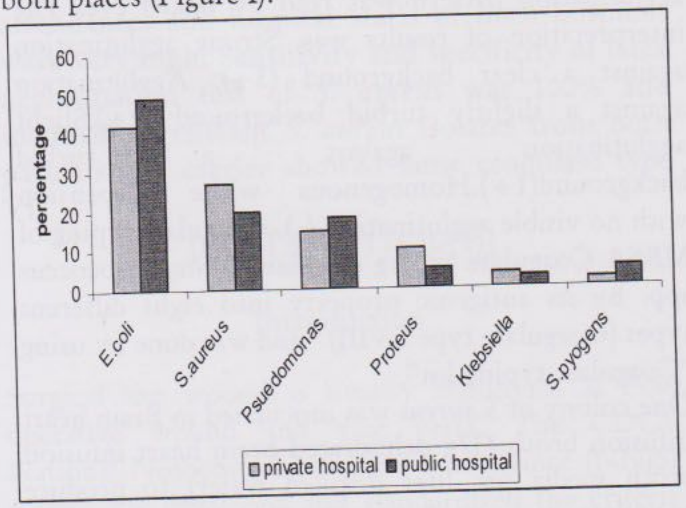

Figure I Prevalence of pathogens in wound infection of Public (DMCH) and private (HFRCMCH) hospital.

The methicillin resistance *Staphylococcus aureus* was determined by oxacillin disc diffusion test. The average presence of MRSA in wound infection of public and private hospitals were almost similar. It was observed that the prevalence of Methicillin resistance *Staphylococcus aureus* was 76% and Methicillin sensitivity *Staphylococcus aureus* was 24%. (Figure 2)

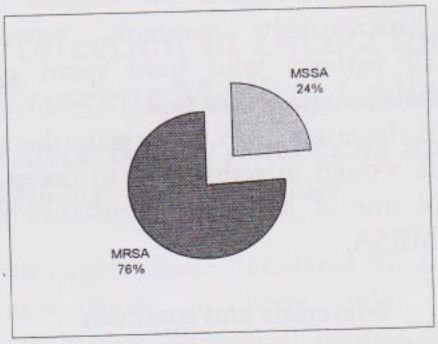

Figure 2: Percentage of distribution of MRSA and MSSA in *S. aureus* isolated from wounds of patients.

Organisms were isolated from anterior nares of hospital staffs and attendances in DMCH and HFRCMCH throughout the study period. In case of private hospital (HFRCMCH), anterior nares of attendances (50%) contained more *S. aureus* then hospital staffs (35%) and similarly anterior nares of attendances (70%) in public hospital contained more *S. aureus* than Hospital staffs (45%). The prevalence of *Methicillin resistance Staphylococcus aureus* (MRSA) in anterior nares of attendances and hospital staffs of both hospitals were very high. (Table 1)

Table 1 Prevalence of organisms in anterior nares of hospital staffs and attendances.

Types of organisms	HFRCMCH (Private hospital)		DMCH(Public hospital)	
	Hospital staffs	Attendances	Hospital staffs	Attendances
S. aureus	7 (35)	10 (50)	9 (45)	14 (70)
MRSA	*5 (71)*	*7 (70)*	*6 (67)*	*12 (86)*
MSSA	*2 (29)*	*3 (30)*	*3 (33)*	*2 (14)*
Pseudomonas	4 (20)	3 (15)	3 (15)	3 (15)
Proteus	2 (10)	4 (20)	2 (10)	2 (10)
No organisms	7 (35)	3 (15)	6 (30)	1 (5)
Total	20 (100)	20 (100)	20 (100)	20 (100)

Two immunological tests were done for all Methicllin resistance *Sthaphylococcus aureus* (MRSA); Methicillin resistance gene (*mecA*) in *S. aureus* was confirmed by detecting the presence of penicillin

binding protein 2a(PBP2a) in MRSA latex agglutination test (LAT) and relationship of carrier and patient was determined by coagulase typing.

LAT test is highly sensitive for detection of MRSA. All isolates from patients and carriers were found 100% sensitive to Latex agglutination test (Table 2)

Table 2 MRSA Latex agglutination test.

Category	MRSA screen latex agglutination test
True positive(TP)	100%
False positive(FP)	0
False negative(FN)	0
Sensitivity	100%
Specificity	100%

MRSA strains from wound infections of patients and MRSA strains from nasal samples of carriers were the same Coagulase type VI (Table 3).

Table 3 Coagulase typing of MRSA isolates.

MRSA isolates	Coagulase type of isolates
From patients	Type -VI
From carriers	Type -VI

Discussion

Surgical site wound infections with increase in prevalence of MRSA has become a major concern for hospital management. This study shows an alarmingly high incidence of MRSA infection in both hospitals of Bangladesh, which is much higher than the reports of the researchers in different other countries . Such a high rate of MRSA in the study may be due to several factors; non judicious use of antibiotics, lack of MRSA control measure, failure of proper detection of MRSA for which carriers remains undetected, overcrowding, poor hygiene etc. Considering the strains of bacteria, *E .coli* was the most frequently isolated organism from wound infection. Almost similar rate was reported by Saini et al (2004) from India. Higher prevalence of *E. coli* in our study might be due to its frequent presence in hospital environment from where study cases were selected and in most post operative wounds *E. coli* is usually the predominant organism [2].

A lower rate of *Pseudomonas* has been reported by Giacometti *et al* (2000) [3] from Italy (23%) and Mahmood (2000) [4] from Pakistan (13%). But Shasuzzaman and co-workers (2003) [5] from Bangladesh has reported higher rate of Pseudomonas 37.2%. In this study the rate of Pseudomonas in wound infection is 10.5%. Other organisms in order of frequency of isolation included *Proteus* (8.1%), *Klebsiella* (4.2%) and *CoNS* (2.7%). Almost similar result has been reported by Shittu and co workers (2000) .The rate of infection by *Strep. pyogens* in this study has been observed to be quite low; similar result was reported by Jinnah and co workers (1998) from Bangladesh (3.1%). This static and low arte of infection by *Streptococcus pyogenes* in different studies may be due to the fact that penicillin has always been used successfully for combating infection by *Strep.pyogens.*

Asymptomatic nasal carriage acts as reservoir for the spread of this organism within hospital. So, detection of carrier is important for control of MRSA infection. Most of the organisms were *S. aureus* in both private and public hospital and resistant organisms (MRSA) were highly prevalent (67-80%). This finding is consistent with the finding of Ahiq (1989) from Pakistan where isolation rate was *S.aureus* 65.3%. Regular screening of hospital staffs and elimination of carriage stage may reduce the rate of MRSA infection in a hospital.

MRSA screen Latex agglutination test (LAT) detected all MRSA isolates in this study. The sensitivity and specificity of MRSA screen latex agglutination test was 100% in the present study. This result is in agreement with Cavassani and co-workers (1999) from Switzerland, who reported sensitivity of 100% and specificity 99.1%. Typing of MRSA strains were done in this study by coagulase typing and this system has been used widely in epidemiological investigation of staphylococcal infection. Coagulase typing showed that all MRSA isolates from patients and carriers were Coagulase type VI. This finding differs from other reports on coagulase typing. This typing system is also widely used Japan, where predominant coagulase type were type II and type IV. This difference in predominant coagulase types might be due to geographical variation.Carriage of MRSA in healthcare settings has been associated with some hospital outbreaks and considered as a potential risk for MRSA infection among hospitalized patients. Reliable detection and elimination of MRSA carriage in attendances and

binding protein 2a(PBP2a) in MRSA latex agglutination test (LAT) and relationship of carrier and patient was determined by coagulase typing.

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hospital staffs are therefore necessary for effective infection control intervention in a hospital [2] .

Finally, it is important to implement an effective infection control program by practicing hand washing, isolation precaution, antibiotic policy in surgical units of both public and private hospitals for control of transmission of MRSA and other resistance pathogens.

Acknowledgement

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Needs and Demand for Health Care Services Among the Rural Female Population in Selected Areas

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Abstract

This study was carried out to know about the needs and demand for health of rural population in a selected area of Sylhet and Sunamjanj Districts. This cross-sectional study was done among 665 women having at least one child below 5 years of age from the period of September 2007 to October 2007, October 2008 to November 2008 and August 2009 to October 2009 in some villages of Sylhet and Sunamgonj Districts. The data was collected by using pre-tested semi-structured questionnaires. The study revealed that the majority (48.12%) of the respondents were within the age group of 26- 35 years. Majority (42.10%) of them were illiterate. Considering the occupational status majority (92.33%) were housewife. Highest (43.31%) families have got the monthly income below Tk. 5000. Regarding health needs and demand most of the respondents (42.41%) demand for adequate supply of necessary drugs in the hospital followed by (40.15%) respondents for regular visit of health workers in a community and (38.05%) for availability of doctors in a hospital.

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Introduction

The idea of health needs is an elusive concept, related lowly to our understanding and lack thereof. Where as, demand is an attempt by an individual in need, to seek services form the health system. So the measure for needs and demands then, relates directly to the measurement of health. There are gradations of needs and demands and most apparently it is a subjective, rather than an objective concept. Hence needs and demands should be prioritized. Deficiencies in health that call for preventive, curative, control or eradication measures. The need for medical care, safe water supply, adequate nutrition, immunization, family planning are all community health needs [1]. Health needs as seen by the people are not exactly the same as seen by experts. Having an understanding of the needs of individuals is not the same as understanding the needs of populations [2].

Health needs assessment is very important to ensure resource efficiency and avoid wastage, increase the possibilities for reducing health inequities, assist the establishment of priorities in limited resource environments and to provide an appropriate evidence base for health planning. Health needs and demand is influenced by several factors such as socio-economic status, demographic characteristics, nutritional status, environmental situation- eg. water, refuse, sanitation, health services, perception of illness & health expectations and life style. Socio-economic factors such as family income, occupational status, working conditions, educational level, life style, poverty, culture and ethnicity related to health status, health demand, use of type of service and access to care. The 1992 Health of the Nation initiative was a government attempt to assess national health needs and determine priorities for improving health [7].

There is a clear need for practice based data on needs and demands for care of patients Data on health services use inevitably depends on the supply of

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services [5, 6]. Several methodological problems based current approaches present for health needs. A popular and expedient approach is to ask professionals to act as proxy informers of patient's need.[3]. Not all peoples who are ill or experiencing distress or disability use services and the extent of this need may not be known by providers [4]. The resources available for health care are limited. Many people have inequitable access to adequate health care, and many governments are unable to provide such care universally.

When we conducted our survey in the respective villages, we intended to know about the extent of primary health care services provided by the Govt. of Bangladesh eg. whether adequate health education is provided to the people, whether adequate medicines are available in the rural health centers, whether health facilities are modern and adequate to detect and control the commonly occurring diseases.

More than 80% of our total population is residing in rural area, which is very poor and mostly deprived from modern health facilities than urban population [10].One of the study shows that rural people are getting 50% less modern health facilities than urban population [11]. The aim and objective of present study was to collect information about the health needs and demand among the rural population of female.

Materials and Methods

A descriptive type of cross-sectional study was conducted among 665 women had at least one child below the age of 5 years. The study place was villages of Takipur, Boroigaon, Nowka- kandi, Baishkhola, Dokkhin Bagbari under Chattak Upazilla of Sunamgonj District. Mokampunji, Ujaninagar under Jointa Upazilla of Sylhet District in 2007. Viallage of Mewa of Dobagh union under Bianibazar upazilla of Sylhet District in 2008. Villages of Sylhetiapara, Suterkandi, Debgram, Dattagram under Bianibazar Upazilla. Pakri, Nizpara, Shikarkha, Mukambari, under Jaintapur Upazilla of Sylhet District and Baznamohal under Chattak Upazilla of Sunamganj District in 2009.The study period was September 2007 to October 2007, October 2008 to November 2008 and August 2009 to October 2009. Sampling method was non-random (convenience) type and data were collected by face to face interview by 4th year MBBS students (Session 2003-2004, 2004-2005 and 2005-2006) of MAG Osmani Medical College, Sylhet with the help of pre-tested semi-structured questionnaire during the study period. Simple statistical methods are applied for data analysis.

Results

The study revealed that among 665 respondents majority 48.12% were within the age group of 26- 35 years followed by 40.90% were in the age group of 16-25 years. Majority of them were illiterate 42.10% followed by up to primary level of education 22.71%.Regarding occupational status of the respondents majority 92.33% were housewife and 3.61% were laborers. Considering monthly income of a family 43.31% had income of taka less then 5000 and 38.80% had income between taka 5000-10000. Regarding age of under 5 children majority 33.89% within the age group of 2-3 years followed by 29.44% were up to one year of age. About health needs, study revealed that majority (42.41%) of the respondents needs and demand were adequate supply of necessary drugs in the hospital followed by (40.15%) respondents demand for regular visit of health workers in a community and (38.05%) for availability of Doctors in hospital . About sanitation, 23.76% respondents demand for proper sanitation (tube well and sanitary latrines), 18.80% respondents demand for establishments of health sub centre near their locality., 17.59% for health service at reasonable cost, 7.82% respondents demand for establishment of community clinic near home. They also demand for free health service and medication 3,30% and free supply of mosquito nets and spray 3.01%.

Table I. Age distribution of the respondents

Age in years	2007	2008	2009	Total no	Percentage %
< 15	0	0	0	0	0
16-25	62	64	146	272	40.90

26-35	82	70	168	320	48.12
36-45	07	20	43	70	10.53
> 45	0	0	03	03	0.45
Total	151	154	360	665	100

Table 11. Educational status of the respondents.

Educational status	2007	2008	2009	Total no	Percentage %
Illiterate	66	68	146	280	42.10
Read & write	17	13	47	77	11.58
Up to primary	31	30	90	151	22.71
Up to secondary	23	26	56	105	15.79
SSC	10	15	17	42	6.32
HSC	04	02	04	10	1.50
Total	151	154	360	665	100

Table III. Monthly income of the respondents

Monthly income (in Taka)	2007	2008	2009	Total no	Percentage %
< 5000	79	64	145	288	43.31
5000-10000	61	64	133	258	38.80
> 10000	11	26	82	119	17.89
Total	151	154	360	665	100

Table – IV. Respondents opinion about health needs and demand

Respondents opinion	2007 n= 151	2008 n= 154	2009 n= 360	Total no. N=665	Percentage %
Adequate supply of necessary drugs	141	88	53	282	42.41
Regular visit of health worker	144	39	84	267	40.15
Availability of doctors in hospital	141	52	60	253	38.05
Proper sanitation (safe water& sanitary latrine)	47	23	88	158	23.76
Needs health sub center near their locality	125	-	-	125	18.80
Needs health service at reasonable cost	117	-	-	117	17.59
Hospital near home& community clinic	-	-	52	52	7.82
Free supply of mosquito net& spray	-	-	20	20	3.01
Free health service and medication	-	22	-	22	3.30

* multiple response

Discussion

Economic status bears an important relationship with needs and demand.. The study revealed that majority of the respondents were illiterate 42.10% .Adult literacy rate in Bangladesh (Pop.15+) in both sexes 56.3% (source SVRS 2008,BBS)[20] which is almost similar with the finding of present study 57.90%. Education is a crucial element in economic and social development. Without economic growth, development can neither be broad based nor sustained. Study revealed that majority 92.33% respondents were housewife and 43.31% had monthly income of a family less than Tk 5000. Here, economic status of a family was below average. Economic status of a community determine its purchasing power, standard of living, quality of life and family size as well as the adequacy of health services, all of which directly influence the pattern of disease and health status. The community with a high per capita GNP is likely to have a better health status than one with a low GNP [12]. Currently, the allocation for health development is around 1% of

GNP in Bangladesh, while minimum allocation to the health sector should be at least 5% of GNP according to WHO.[12].

Health planning is necessary for the economic utilization of material, man-power and financial resources. The purpose of health planning is to meet the health needs and demands of the people. About health needs, study revealed that majority (42.41%) of the respondent's needs and demand were adequate supply of necessary drugs in the hospital. National drug expenditure as a proportion of total health expenditure in developing countries varies from 7% to (66%)[12]. Rational use of drugs is, therefore, important and essential to acquire proper medicine and dispense them in public health care systems. The number of drugs from the national essential drugs list was 49% and the value of of drugs procured in the public sector was 85% in India [12]. The poorly organized drug distribution network in rural areas resulted in non-availability of essential medicines in a primary level of hospital.

Several rural health posts remain vacant, public health care therefore, fails to get delivered. In this study (38.05%) respondents demanded for availability of Doctors in hospital and (40.15%) respondents demand for regular visit of health workers in a community. In Bangladesh, population per physician 2785, population per bed 1860, population per nurse 5782 (source DGHS 2010)[13]. Numbers of medical assistant under DGHS 4699, sanitary inspectors 491, health inspectors 1400, assistant health inspectors 4200 and health assistants 21000.(source DGHS, 2005)[14]. On the other hand in Sylhet Division vacant sanctioned post of doctors 55%, medical assistant 32%,health inspector 20%, assistant health inspector 18%, health assistant 18% (source Health Bulletin June, 2010 by DGHS)[15]. Demand from patients for a service can depend on the characteristics of the patient and also be induced by availability of doctors, nurses, and other health professionals. Demand can also be induced by supply : geographical variation [17,18]. Supply will depend on the interests of health professionals, the priorities of the government and the amount of money is available. Need, demand and supply overlap, and the relation is important to consider when assessing health needs [19]. Due to lack of modern facilities in rural community, most of the doctors and health professionals lost their interest to serve in Upazilla and Union level. This is one of the reasons why the post is vacant in rural health centre in Bangladesh.

About sanitation, 23.76% respondents demand for proper sanitation (tube well and sanitary latrines), Sanitation covers the whole field of controlling the environment with a view to prevent disease and promote health. According to report of health bulletin 98.23% people uses safe drinking water (tap and tube well) and 62.23% people using sanitary latrines. (source, SVRS, 2008, BBS)[20]. Using of safe water supply is improved but utilization of sanitary latrine is not satisfactory in the rural community. It may be due to lack of awareness among the rural population about sanitation.

Study reveals that 18.80% respondents demand for health sub centre near their locality, and 7.82% respondents demand for establishment of community clinic near home. In a Country at present the total numbers of union sub-centre is 1362, union health and family welfare centre 87, at the union level .Total number of community clinic 9,722 will be started at ward level.(source DGHS 2010). Proper delivery of primary health care in Bangladesh Govt. has been decided to establishment of 18,000 community clinics, one for every 6,000 rural populations.(source- DGHS 2010) Community clinics will play the central role in delivering the primary health care through effective community participation. The community clinics have upward referral linkage at the union and upazilla level[15].

In this study 17.59% respondents demand for health service at reasonable cost. Health care is now one of the largest sectors in most developed countries [8].The cost of health care are rising. Medical advances and demographic changes will continue the upward pressure on costs [9]. Availability tends to be inversely related to the need of the population served [16].

This study has shown the feasibility of a survey to collect information about needs and demand in rural populations on the basis of perceptions of their problem. If health needs are to be identified then an effective intervention should be available to meet these needs and improve health.

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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 10 Number 1

Modified Gasserian Ganglion block – A study in surgery for Deviated nasal septum

Sajjad Ahmed[1], Sabyasachi Roy[2], AKM Hafiz[3]

Introduction

Local anaesthetic techniques were popularized early in the history of surgery with advent of injectable nerve blocking agents. In the early days of general anaesthesia, local anaesthesia was preferred in all cases that it was applicable due to the significant risks associated with general anaesthesia. Many procedures performed today under general anaesthesia, such as tonsillectomy, rhinoplasty, and even bronchoscopy, were performed under local anaesthesia to avoid the perils of general anaesthetics. With the introduction pulse oximetry, safer inhaled anaesthetics, and combined intravenous and inhaled general anaesthesia has become much safer, resulting in many surgeons being unfamiliar with regional nerve blocks to perform surgery[1].

There are many advantages of regional anaesthesia. First, the patient is conscious during surgery. Therefore, the patient can maintain his own airway, contain his own gastric secretion, and warn surgeon of impending complications, for example vertigo in *stapes* surgery. Next, unlike general anaesthesia, patients are awake and usually have a smooth postoperative course. This allows for less nursing care after procedures, and shorter recovery times facilitating outpatients surgery. Another advantage is the elimination of painful afferent stimuli for the operative site plus the blockade of efferent nerves to endocrine glands eliminates or greatly reduces the metabolic endocrine changes seen after surgical operations. Finally, local anaesthesia is much less expensive[2].

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Disadvantages of local anaesthesia are significant as well. First, the patient may prefer to be asleep. Also, operating on an awake patient may take more patience and skill from the entire surgical team. Next, some blocks require up to 30 minutes or more to be fully effective. Another disadvantage is that analgesia may not always be totally effective, and general anaesthesia may be required secondarily. Next, generalized toxicity may occur if local anaesthetic drugs are given intravenously by mistake or an overdose is given. Also, widespread sympathetic blockade can result in hypotension. Finally, there is a small but definite incidence of proloned nerve damage[3] .

Gasserian Ganglion:

Anatomy

The gasserian Ganglion (trigeminal ganglion, semilunar ganglion) sits in Meckels cave, an invagination of the dura matter of the posterior cranial fossa.

Materials and Methods

In this study we selected 40 patients. Then we divide the patients into two groups. Group A contain 20 patients & group B contains 20 patients. Group A underwent operation under general anaesthesia & Group B underwent operation by modified gasserian ganglion block. At the end of operation wemeared blood loss from suker bottle & from soaked gauze. In addition we measure pain using visual analog scale (VAS). (Table-I). And we found blood loss significantly less in Group B patient then Group A. In the same analgesic requirement in the Group B (Table-II &III) was significantly less.

An anterolateral approch is most commonly used. After taking written consent wewent for theprocedure. Counseling was an important task.

10 minutes befor starting the procedure to reduce anxiety & tension we did give 25mg Pethidine IV & 75mg pethidine with 12.5mg prochlorperazine mesylate IM. An 8 to 10cm 22-gauge needle is inseted approximately 3 cm lateral to the angle of the mouth at the level of the second molar tooth; it is advanced posteromedially & angled superiorly such that the needle is alighned with the pupil in the anterior plane with the midzygomatic arch in the lateral plane. Without entering the mouth the needle should pass between the mandibular ramus & the maxilla, & lateral to the pterygoid process. We did not try to enter the cranium through foramen ovale[5]. As we have no facilities for CT scan, Ultrasound, or SIAM in our operation rooms we did practise in a modified way. Following anatomy we tried to go to the sie blindly & after negative aspiration of CSF & blood, 2ml of Lignocaine with Adrenaline at the ratio of 1:200,000 is injected. Then confirmed by asking patients about numbness. During surgery the surgeons applied local anaesthesia with adrenaline for better resection & less bleeding. Though sucker machine remain active every patient was advised to swallow if any liquid down to oropharynx.

Table-I

Blood loss intraoperative period

Group	Blood loss (ml)	P value
Group A	120±76	<0.025
Group B	53±40	

Table-II

First analgesic demand in postoperative period

Group	Time in minute	P value
Group A	25±55	<0.015
Group B	51±20	

Table-III

Total analgesic demand in 24hrs postoperative period (maintained by Diclofenac Sodium [Inj. Voltalin])

Group	Dosage in mg	P value
Group A	150±25	<0.02
Group B	100±20	

Conclusion

Regional anaesthesia can be used alone or in combination with general anaesthesia as a safe and effective way to relieve pain in operations of the submucosal resection of deviated nasal septum. Otolaryngologist should be equipped in its use. The acquisition of this skill is easy for the Otolaryngologist because of his intimate knowledge of the anatomy of the area. In this study we showed three table & significantly we could achieve our targeted goal in our country's Government level hospital where SMR surgery can be done for deviated nasal septum. As our method was simple, so even surgeon becomes familiar to this block. That causes large number of operations of SMR are being performed in the Sylhet MAG Osmani Medical College Hospital. As complications of general anaesthesia need not brought come in mind, reduction of significant blood loss, the patients could take orally immediately after operation, so it can be done as day case basis.

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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 10 Number 1

A comparative study on the effectiveness of anti-hypertensive drugs in combination with NSAIDs.

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Abstract

Osteoarthritis and essential hypertension are two common co-morbid diseases prevailing over our adult population frequently requiring combined medication. NSAIDs appear to blunt the antihypertensive action of some antihypertensive drugs if they are taken concurrently. Two mostly used NSAIDs-diclofenac and ibuprofen were studied to see their probable BP elevating effect on two commonly used antihypertensives-amlodipine and perindopril.

A prospective clinical trial was conducted on 81 hypertensive patients with or without osteoarthritis for three months. Baseline BP was recorded at the beginning of study (phase 0). Twenty eight hypertensive patients without osteoarthritis were treated with either amlodipine (n=14) or perindopril (n=14). Fifty three hypertensive-osteoarthritic patients were treated with antihypertensive agents plus NSAIDs. Among them 13 patients were treated with amlodipine+diclofenac, 13 patients with amlodipine+ibuprofen, 13 patients with perindopril+diclofenac and 14 patients with perindopril+ibuprofen during first month (phase 1). During second month (phase 2) all NSAIDs of first phase were replaced by paracetamol as a rescue agent. During third month period (phase 3) NSAIDs of first phase were reinstituted replacing paracetamol. Blood pressure was measured in supine position with standard mercury sphygmomanometer at the inception and at the end of each phase in the morning.

Significant decrease of BP was observed throughout the study period in both amlodipine- and perindopril treated groups (hypertensive non-osteoarthritic patients). In all combined regimens (NSAIDs+antihypertensives), there was increase of BP after phase 1 which was decreased after phase 2 and again increased after phase 3.The BP elevating effect of NSAIDs was more observed in case of perindopril used in combination with diclofenac or ibuprofen ($p < 0.0001$), than with amlodipine. There was no significant weight changes observed throughout the study period signifying that fluid retention was not responsible for BP elevating effect of any NSAID used in the study.

It may be concluded that diclofenac and ibuprofen attenuate the effects of antihypertensive drugs while paracetamol appears to have no interaction. Interaction of NSAIDs was more pronounced with perindopril than with amlodipine administered in combination with either diclofenac or ibuprofen.

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Introduction

Osteoarthritis is one of the most common diseases diagnosed in patients ≥50 years of age; the others being CAD, dyslipidemia, hypertension, type 2 diabetes and osteoarthritis[1].

In Bangladesh, prevalence of hypertension with systolic blood pressure ≥140 mmHg was 10.5% and with diastolic blood pressure ≥ 90 mmHg was 9.0%[2]. Studies from India and Bangladesh have shown upward trend in the prevalence of hypertension[3].

Osteoarthritis is responsible for a huge burden of pain and disability in elderly people. It is characterized by degeneration of articular cartilage and simultaneous proliferation of new bone, cartilage, and connective tissue[4]. Rheumatic disorders are common causes of morbidity, disability, and work loss in rural and urban communities of Bangladesh[5]. Females are at higher risk of developing osteoarthritis than elderly male[1]. It is uncommon in adults under age 40 and highly prevalent in those over age 60[6]. The prevalence of osteoarthritis is higher in the urban affluent community than in the rural and urban slum[5].

Though the treatment of HTN is very effective and well tolerated, sometimes, the achievement is not satisfactory due to noncompliance, inappropriate prescription, untoward life style, co-medication with pro-hypertensive agents, pharmacokinetic and/or pharmacodynamic drug interactions[7].

Blood pressure lowering effect of antihypertensive drugs appears to be affected to variable degrees by NSAIDs. Diuretics, angiotensin-converting enzyme inhibitors (ACEIs), beta-blockers, and angiotensin II receptor blockers (ARBs) are most susceptible. Calcium channel blockers and centrally acting antihypertensives are less affected[8,9,10]. The BP elevating effect of NSAIDs varies with the specific NSAID used and the individual antihypertensive agent, if they are taken concurrently[11]. More than 5 days of treatment with either drug is normally required for the interaction to manifest[12].

Some antihypertensive drugs are more susceptible and others are more resistant to the interaction with NSAIDs. Calcium channel blockers are less affected, becoming drugs of choice for the subset of hypertensive population needing concomitant analgesic/anti-inflammatory treatment[7].

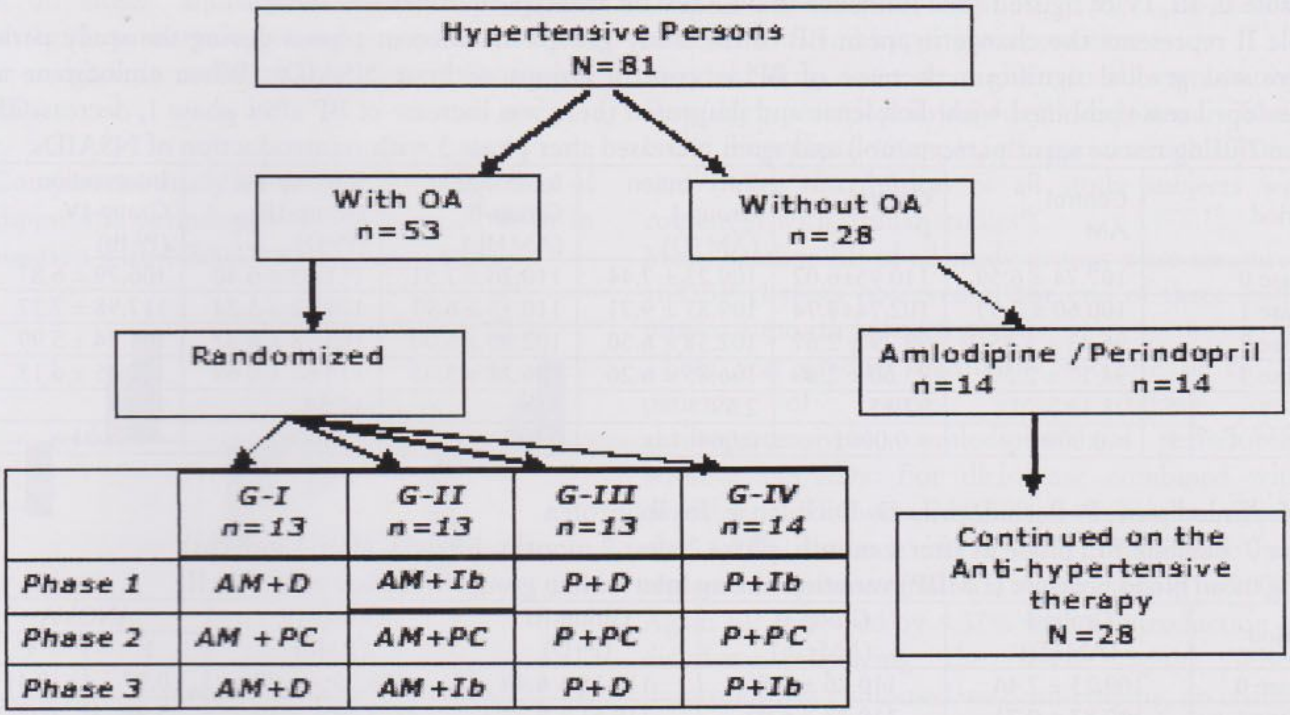
Among NSAIDs—diclofenac and ibuprofen are widely used due to their low incidence of gastrointestinal ADRs and short half lives. On the other hand, calcium channel blockers and ACE inhibitors are two commonly used antihypertensive drugs. The study was done to see the interaction of antihypertensive drugs amlodipine and perindopril with NSAIDs diclofenac and ibuprofen in hypertensive patients with or without osteoarthritis.

Materials and Methods

A prospective parallel group trial was conducted in the Department of Pharmacology and Department of Medicine, Sylhet MAG Osmani Medical College & Hospital during the period from 1st July, 2009 to 30th June 2010. The aim of the study was to see the interaction between anti-hypertensive drugs (amlodipine & perindropril) and NSAIDs (ibuprofen & diclofenac) used in combination in the treatment of hypertension with osteoarthritis. For this purpose 81 diagnosed hypertensive patients of both sexes of 40 to 80 years of age were included. Hypertensive patients with other co-morbidities like diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD), renal failure (RF) were excluded from this study. After approval from the hospital ethical committee written informed consent was obtained from the patients.Then data were collected in a pre-designed questionnaire. The study participants were divided into two groups, control and intervention. Hypertensive patients without OA (n=28), treated with anti-hypertensive drugs, amlodipine (n=14) and perindopril (n=14) were considered as controls. Hypertensive patients with concomitant osteoarthritis (n=53) was treated as intervention group.

Intervention group was randomly subdivided into four groups: Group-I (n=13) was treated with amlodipine + diclofenac, Group-II (n=13) was treated with amlodipine + ibuprofen, Group-III (n=13) was treated with perindopril + diclofenac, Group-IV (n=14) was treated with perindopril + ibuprofen.

Blood pressure of all study subjects was measured in supine position in morning using standard mercury sphygmomanometer, at the inception (phase 0; baseline) with only antihypertensives, and at the end of the first month (phase 1) combined with NSAIDs, of the second month (phase 2) NSAIDs replaced by paracetamol, and of the third study month (phase 3)



AM- Amlodipine, P- Perindopril, Ib- Ibuprofen, D- Diclofenac, PC- Paracitamol

with reintroduction of NSAIDs instead of paracetamol. Control subjects were treated with only antihypertensives in all phases. Mean blood pressure was calculated.

Results

Table 1 shows the baseline characteristics. Lying mean BP of controls (AM & P) and intervention groups (AM+D, AM+Ib, P+D & P+Ib) were 107.74, 110.95, 109.23, 110.26, 111.15 & 106.79 mmHg respectively.

Study Group Parameter	Control AM	Control P	Intervention Group-1 (AM+D)	Intervention Group-2 (AM+Ib)	Intervention Group-3 (P+D)	Intervention Group-4 (P+Ib)
Randomized (n)	14	14	13	13	13	14
Male/Female (n)	5 / 9	9 / 5	10 / 3	7 / 6	9 / 4	12 / 2
Age (Years: Mean ± SD)	52.79 ± 9.51	52.71 ± 9.60	57.90 ± 11.50	51.69±6.18	54.92 ± 12.19	59.00±7.87
Weight (kg: Mean ± SD)	61.71 ± 6.04	67.57 ± 5.56	66.50 ± 7.00	64.08 ± 5.54	68.00 ± 4.67	69.36 ± 4.13
Lying Mean BP (mm Hg : Mean ± SD)	107.74 ± 6.59	110.95 ± 6.02	109.23 ± 7.44	110.26 ± 7.51	111.15 ± 6.40	106.79 ± 6.87

In table II, III, IV & figure I - the influence of NSAIDs on antihypertensives was shown.
Table II represents the change in mean BP of the study groups in different phases during the study period. There was gradual significant decrease of BP in control groups without NSAIDs. When amlodipine and perindopril was combined with diclofenac and ibuprofen there was increase of BP after phase 1, decrease after phase 2(using rescue agent paracetamol) and again increased after phase 3 with reintroduction of NSAIDs.

Period		Control AM	Control P	Intervention Group-I (AM+D)	Intervention Group-II (AM+Ib)	Intervention Group-III (P+D)	Intervention Group-IV (P+Ib)
Phase 0		107.74 ± 6.59	110.95±6.02	109.23 ± 7.44	110.26 ± 7.51	111.15 ± 6.40	106.79 ± 6.87
Phase 1		100.60 ± 2.97	102.74±4.74	109.87 ± 9.71	110.33 ± 6.97	119.51 ± 5.24	117.98 ± 7.37
Phase 2		96.43 ± 3.45	99.29 ± 2.67	102.38 ± 6.50	102.90 ± 6.00	105.38 ± 6.32	105.24 ± 5.99
Phase 3		94.17 ± 2.59	95.60 ± 2.89	106.85 ± 6.26	106.28 ± 5.05	115.62 ± 6.69	115.45 ± 6.15
ANOVA	F	28.12	32.45	2.59	3.98	12.54	12.67
	P	< 0.0001	< 0.0001	0.064	0.013	< 0.0001	< 0.0001

(AM- Amlodipine, P- Perindopril, D- Diclofenac, Ib- Ibuprofen
Phase 0- baseline BP, phase 1- after 1 month, phase 2-after 2 months, phase 3- after 3 months)
Lying mean blood pressure (LMBP) variation among intervention groups was shown in table III.

Period	Group-I (AM+D)	Group-II (AM+Ib)	Group-III (P+D)	Group-IV (P+Ib)	ANOVA	
					F	P
Phase 0	109.23 ± 7.44	110.26 ± 7.51	111.15 ± 6.40	106.79 ± 6.87	0.97	0.41
Phase 1	109.87 ± 9.71	110.33 ± 6.97	119.51 ± 5.24	117.98 ± 7.37	5.94	0.002
Phase 2	102.38 ± 6.50	102.90 ± 6.00	105.38 ± 6.32	105.24 ± 5.99	0.83	0.48
Phase 3	106.85 ± 6.26	106.28 ± 5.05	115.62 ± 6.69	115.45 ± 6.15	9.65	<0.001

(AM- Amlodipine, P- Perindopril, D- Diclofenac, Ib- Ibuprofen
Phase 0- baseline BP, phase 1- after 1 month, phase 2- after 2 months, phase 3- after 3 months)
There was no significant variation in phase 0 and after phase 2.
Significant variation was observed after phase 1 and phase 3 among intervention groups signifying the influence of NSAIDs on anti-hypertensive drugs.
Comparison of BP changes between groups (unpaired t test) after the end of phase 3 was presented in table IV. Amlodipine containing regimen shows more significant reduction than perindopril containing regimen. BP elevating Influence of NSAIDs (D/Ib) was more marked with perindopril than with amlodipine.

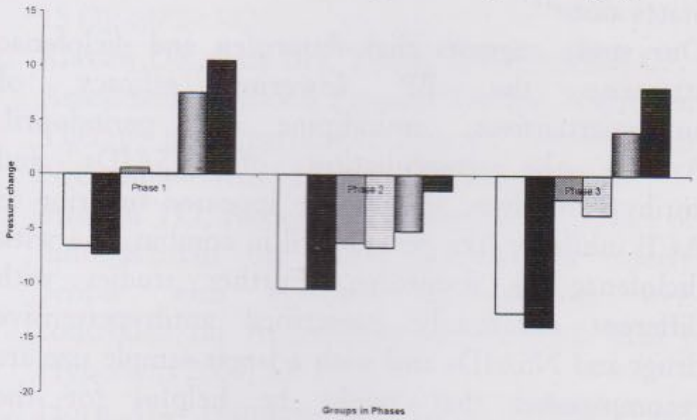
Mean BP of different Groups			t value	P value
Group value	Groups	Mean BP(±SD)		
G-I (AM+D) 106.85 ± 6.26	G-II (AM+Ib)	106.28 ± 5.05	0.25	0.80
	G-III (P+D)	115.62 ± 6.69	3.45	0.002
	G-IV (P+Ib)	115.45 ± 6.15	3.60	0.001
G-II (AM+Ib)	G-III (P+D)	115.62±6.69	4.01	0.0005
	G-IV (P+Ib)	115.45 ± 6.15	4.21	0.0003
G-III (P+D) 115.62±6.69	G-IV (P+Ib)	115.45 ± 6.15	0.06	0.95
Unpaired t test done. P<0.05 considered as significant.				

(AM- Amlodipine, P- Perindopril, D- Diclofenac, Ib- Ibuprofen)

Figure I shows comparative study on the BP lowering effect of amlodipine and perindopril administered alone or in combination with NSAIDs (diclofenac or ibuprofen).
Perindopril showed almost equally effective antihypertensive action as amlodipine studied for 3 months in non-osteoarthritic patients. When hypertensive-osteoarthritic patients were treated with either diclofenac or ibuprofen, BP lowering effect of amlodipine was not so marked as in non-arthritic patients. Perindopril showed increased BP in osteoarthrotic patients recorded in phase 1 and phase 3. Paracetamol did not antagonize BP lowering

effect of either amlodipine or perindopril in osteoarthritic patients suggesting that paracetamol is a safer analgesic in osteoarthritic patients than other NSAIDs.

Fig: Comparative study on the BP lowering effect of amlodipine and perindopril administered alone or in combination with NSAIDs (percentage changes).



AM- Amlodipine, P-Perindopril, PC-Paracetamol, D-Diclofenac, Ib-Ibuprofen
(-) means decrease of blood pressure in percent.

There were no significant weight changes in any study group (control/intervention) during any phase of study.

Discussion

Non-steroidal anti-inflammatory drugs (NSAIDs) appear to attenuate the efficacy of some antihypertensive drugs. In normotensive osteoarthritis patients, there may be an increase of BP on prolonged use of NSAIDs.

Osteoarthritis and primary hypertension are common in old age, may co-exist and demand long term treatment for symptomatic well being and to avoid morbid consequences. We studied two commonly prescribed NSAIDs (diclofenac and ibuprofen) administred in combination of two antihypertensive drugs (amlodipine and perindopril). Amlodipine is a calcium channel blocker and perindopril is an ACE inhibitor.

The aim of the study was to evaluate the influence of ibuprofen and diclofenac on BP lowering effect of amlodipine and perindopril, and also to assess the safer combination option for co-existent osteoarthritis and hypertensive patients.

Standard drug doses were given to all - amlodipine 5mg/day[7], perindopril 4mg/day[13], diclofenac – 50mg b.d[14], ibuprofen -400mg t.i.d[7], paracetamol 1000mg t.i.d[15]. Age distribution of all study subjects was consistent with similar studies[16].

Mean baseline BP of all study groups were measured and BP changes observed at the end of three study phases, 1 month for each phase.

There was gradual significant decrease of BP in patients of control groups taking only antihypertensives - amlodipine and perindopril, without NSAIDs. For diclofenac combined with amlodipine, BP increased 0.59% from baseline. There was 6.82% decrease in BP when diclofenac was replaced by paracetamol as a rescue agent ($P=0.002$). Again BP increased by 4.37% with reintroduction of diclofenac replacing the rescue agent. When ibuprofen was combined with amlodipine, no change was observed from baseline after 1 month. Decrease in BP by 6.73% was seen in washout period ($P=0.001$), again increased by 3.28% with reintroduction of ibuprofen. For perindopril combined with diclofenac 7.52% increased BP was seen from baseline after 1 month. Decrease in BP by 11.82% was seen in washout period ($P=0.0003$) and again 9.72% increased BP noted with reintroduction of diclofenac. When perindopril was combined with ibuprofen, 10.48% increased BP was seen from baseline, after 1 month. Decrease in BP by 10.80% was seen replacing ibuprofen by paracetamol, again increased by 9.70% after resuming the previous NSAID.

The pro-hypertensive effects of NSAIDs presumably attributed to several mechanisms. Their analgesic and anti-inflammatory effects are mostly derived from cyclooxygenase (COX) inhibition. COX inhibition leads to decreased PGI_2 production in the vascular endothelium, with no change in TxA_2 synthesis in the platelets, predisposing to vasoconstriction, thrombosis and endothelial lesions. Moreover, all NSAIDs impede physiological prostaglandin synthesis in the kidneys resulting in fluid retention and local vasoconstriction[7].

According to Fogari et al (2002)[16] and Pevlicevic et al (2008)[7], similar BP changes were observed during

different phases (antihypertensives were lisinopril/hydrochlorthiazide combination, amlodipine, valsartan and lisinopril; NSAIDs were ibuprofen, acetaminophen, piroxicam and indomethacin). In our study, there was BP elevation with introduction of NSAIDs, reduction of BP when NSAIDs were replaced by paracetamol (predominant analgesic action), and again BP elevation after reintroduction of NSAIDs, in contrast with significant BP lowering throughout the study periods in control groups without NSAIDs. This observation suggests interaction of NSAIDs with antihypertensives, blunting their BP lowering effects. At the end of the study after 3 months (end of phase 3), there was marked increase of BP in case of perindopril combined with diclofenac or ibuprofen compared with amlodipine combined with diclofenac or ibuprofen. This finding was similar with Pavlicevic et al (2008)[7], who observed that ibuprofen and piroxicam interacted more with ACE inhibitor (lisinopril combined with hydrochlorothiazide), than with amlodipine.

In hypertensive patients with osteoarthritis treated with paracetamol BP lowering effect of amlodipine and perindopril remains unaltered. This reflects that paracetamol has no interaction on antihypertensive drugs.

To assess the probable mechanism of NSAIDs on BP elevating influence, we measured weight changes of study subjects in different phases.

There were no significant weight changes in any phase implicating that, probably the NSAIDs do not influence BP elevation by fluid and salt retention. This finding was also consistent with Pavlicevic et al (2008)[7]. In one study by Klassen et al (1995)[8], there was significant weight gain when NSAID naproxen combined with calcium channel blocker nicardipine. Despite the significant increase in body weight, the antihypertensive action of the Ca^{++} channel blocker nicardipine was not significantly affected by co-treatment with naproxen. Probably the observed BP elevation was largely due to vasoconstriction might be related to inhibition of vasodilatory prostaglandin synthesis by COX- inhibition of NSAIDs and less so to volume expansion.

There were some studies where no significant influence of NSAIDs seen on BP[17]. It was estimated that a 5 to 6 mmHg increase in diastolic BP maintained over a few years may be associated with a 67% increase in total stroke incidence and a 15% increase in events associated with coronary heart disease[11]. It has been estimated that the avoidance of minor change in systolic BP in patients with osteoarthritis, subjected to treatment with NSAIDs would avoid over 30000 deaths due to MI in United States alone[12].

Our study suggests that ibuprofen and diclofenac attenuate the BP lowering efficacy of antihypertensives, amlodipine and perindopril. Among the combination of NSAIDs and antihypertensives, amlodipine appeared superior to ACE inhibitor like perindopril in combination with diclofenac or ibuprofen. Further studies with different commonly prescribed antihypertensive drugs and NSAIDs and with a larger sample size are recommended that might be helpful for the physicians to select better combinations of NSAIDs with antihypertensive drugs.

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different phases (antihypertensives were lisinopril/hydrochlorthiazide combination, amlodipine, valsartan and lisinopril; NSAIDs were ibuprofen, acetaminophen, piroxicam and indomethacin). In our study, there was BP elevation with introduction of NSAIDs, reduction of BP when NSAIDs were replaced by paracetamol (predominant analgesic action), and again BP elevation after reintroduction of NSAIDs, in contrast with significant BP lowering throughout the study periods in control groups without NSAIDs. This observation suggests interaction of NSAIDs with antihypertensives, blunting their BP lowering effects. At the end of the study after 3 months (end of phase 3), there was marked increase of BP in case of perindopril combined with diclofenac or ibuprofen compared with amlodipine combined with diclofenac or ibuprofen. This finding was similar with Pavlicevic et al (2008)[7], who observed that ibuprofen and piroxicam interacted more with ACE inhibitor (lisinopril combined with hydrochlorothiazide), than with amlodipine.

In hypertensive patients with osteoarthritis treated with paracetamol BP lowering effect of amlodipine and perindopril remains unaltered. This reflects that paracetamol has no interaction on antihypertensive drugs.

To assess the probable mechanism of NSAIDs on BP elevating influence, we measured weight changes of study subjects in different phases.

There were no significant weight changes in any phase implicating that, probably the NSAIDs do not influence BP elevation by fluid and salt retention. This finding was also consistent with Pavlicevic et al (2008)[7]. In one study by Klassen et al (1995)[8], there was significant weight gain when NSAID naproxen combined with calcium channel blocker nicardipine. Despite the significant increase in body weight, the antihypertensive action of the Ca^{++} channel blocker nicardipine was not significantly affected by co-treatment with naproxen. Probably the observed BP elevation was largely due to vasoconstriction might be related to inhibition of vasodilatory prostaglandin synthesis by COX- inhibition of NSAIDs and less so to volume expansion.

There were some studies where no significant influence of NSAIDs seen on BP[17]. It was estimated that a 5 to 6 mmHg increase in diastolic BP maintained over a few years may be associated with a 67% increase in total stroke incidence and a 15% increase in events associated with coronary heart disease[11]. It has been estimated that the avoidance of minor change in systolic BP in patients with osteoarthritis, subjected to treatment with NSAIDs would avoid over 30000 deaths due to MI in United States alone[12].

Our study suggests that ibuprofen and diclofenac attenuate the BP lowering efficacy of antihypertensives, amlodipine and perindopril. Among the combination of NSAIDs and antihypertensives, amlodipine appeared superior to ACE inhibitor like perindopril in combination with diclofenac or ibuprofen. Further studies with different commonly prescribed antihypertensive drugs and NSAIDs and with a larger sample size are recommended that might be helpful for the physicians to select better combinations of NSAIDs with antihypertensive drugs.

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ORIGINAL ARTICLE

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Role of folic acid, Selenium and vitamin E in arsenic metabolism

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Abstract

Arsenic a naturally occurring metalloid is a known toxin and carcinogen. It exists in both organic and inorganic form, trivalent arsenite (iAs^{III}) in drinking water is more toxic than pentavalent (iAs^{V}) found in food. Ingested arsenic is methylated to monomethylarsonic acid (MMA) and dimethyl arsinic acid (DMA) in liver. Nutrients folic acid, selenium, vitamin E, B_6, B_{12} and Zink facilitate the first and second stage methylation and excretion of inorganic arsenic.

[OMTAJ 2011; 10(1)]

Introduction

Arsenic is widely distributed throughout the whole nature as a result of weathering dissolution, fire, volcanic activity, anthropogenic input, industrialisation and mining. Majority of human beings are chronically exposed to arsenic through food and drinking water. Drinking water contamination by arsenic is a major health problem in an underdeveloped country like Bangladesh. Recent measurements of water level arsenic, show that in many parts of Ganges and Brahmaputra basin more than 60% of shallow and deep tube wells contain arsenic above WHO guideline of 0.01mg/L[2,1].

Arsenic is a known carcinogen and epidemiological studies suggest that persons with impaired arsenic metabolism are at increased risk of certain cancers[11], including skin and bladder carcinoma. It has been classified by WHO as group-I carcinogen[12]. Arsenic has also been related to cardiovascular[13], respiratory[15], gastrointestinal[14] and endocrine[16] disorders.

Ingested arsenic must undergo detoxification, in order that it is removed from the body, a process brought about by liver. Arsenic metabolism involves methylation to mono methyl arsonic acid (MMA III) and dimethyl arsinic acid (DMA III) [25]. Wide variations in the clinical manifestations of arsenic toxicity in a given population and several observational and biochemical studies[20] have led to a prevalent supposition that nutritional status may account for substantial portion of this variability. Studies suggest that some nutrients folic acid[8], selenium[9], vitamin E[7], B_6, B_{12}, Zinc[10] facilitate the first and second stage methylation and excretion of inorganic arsenic[6].

Materials and Methods

Animals: Healthy young adult male rats of Long Evans Norwegian Strains, weighing 160-180g and 3-4 months old were taken for the purpose of study. They were kept in stainless steel cages in animal house. Sawdust was used as bedding and changed every alternate day. A 12 hours light/12 hour's dark cycle was maintained. They were fed standard pellet diets and allowed to drink *adlibitum*. A total of thirty rats were used in this study. They were divided into five groups, each group having six rates (n=6).

Control group received only standard diet and *adlibitum*. One of the groups received only arsenic in drinking water (1mg/L) while other groups received folic acid, (200μg/day), selenium (0.4μg/day) and vitamin E (1mg/day) along with arsenic (1mg/L) in drinking water *adlibitum*, for a period of fourteen days.

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Measurement of stool arsenic: Stool samples were collected on day 0 and day 14. They were dried weighed and stool arsenic estimation was done by silver diethyl dithio carbamate method (SDDC).

Liver arsenic estimation: The animals were sacrificed on day 14 under light chloroform anaesthesia. Liver was taken out. 500mg of liver tissue was taken and arsenic was estimated by silver diethyl dithio carbamate method (SDDC).

Results

Mean stool arsenic in control group on day 0 and day 14 was 3.55±0.34 and 3.30±0.32mg/g dry weight of stool (Table)

Table showing stool and liver arsenic concentration following administration of arsenic, vitamin E, folic acid and selenium

Groups	Stool arsenic mg/g dry weigh4t		Liver arsenic mg/gm
	Day 0	Day 14	Day14
Control	3.55±0.34	3.30±0.32	2.84±0.22
Only arsenic (1mg/L)	3.88±0.48	2.79±0.54	3.57±0.46
Arsenic (1mg/L)+ Vitamin E (1mg/day)	3.80±0.73	2.84±0.57	2.44±0.51
Arsenic (1mf/L)+ Folic acid (200µg/day)	3.55±0.37	2.67±0.29	2.20±0.33
Arsenic (1mg/L)+ Selenium (0.4µg/day)	3.86±0.65	4.58±1.29	2.34±0.34

Compared to control group stool arsenic level decreased to 2.79±0.5mg/g dry weight of stool, in rats that received only arsenic, a decrease by 26.14%. Stool arsenic level also decreased in rats that received vitamin E (2.84±0.57) and folic acid (2.67±2.29) a decrease by 24.61%. Stool arsenic level increased in rats that received selenium (4.58±1.29) an increase by 1.96% compared to control. Liver arsenic level was 2.84±0.22mg/g of liver tissue in control group, it increased to 3.57±0.46mg/g of liver tissue in rat that received only arsenic, an increase by 27.50%. A decrease in liver arsenic levels was observed in groups that received vitamin E, folic acid and selenium. Liver arsenic level was 2.44±0.51, 2.20±0.33 and 2.34±0.34mg/g of liver tissue respectively.

Discussion

Rats that received only arsenic in drinking water *adlibitum* throughout the study period decease in stool arsenic and significant increase in liver arsenic was observed. Rats that received arsenic along with selenium there was significant increase in stool arsenic level and decrease in liver arsenic level suggestive of increased arsenic metabolism and its hepatobiliary excretion[17]. Arsenite and selenite enhance biliary excretion of their metabolite by formation of diglutatione compund[4,5]. Human trials conducted by giving organic selenium in the form of selenized yeast to arsenic exposed individuals caused significant decrease in arsenic content (hair, nails) of body[1,2]. Significant decrease in stool and liver arsenic levels was observed in rats that received folic acid. Decrease in liver arsenic levels in folic acid group is suggestive of hepatic methylation of arsenic. Studies both on animal and human trials have confirmed involvement of folic acid in hepatic methylation of arsenic[18,19].

Nutrition plays a vital role in health and disease and certain vitamins such as folic acid[8], vitamin E[7], vitamin B_1 and B_6[10] and trace elements Zinc[10] and selenium[9] play a vital role in arsenic detoxification in liver. Nutritional status facilitates the first and second stage methylation and excretion of inorganic arsenic[6]. Arsenic metabolism involves methylation to monomethyl arsonic acid (MMA III) and dimethyl arsinic acid (DMA III) through a folate dependent pathway[18]. Although folate is relatively ubiquitous in our food, folate deficiency is not uncommon, largely because naturally occurring folates are highly susceptibale to oxidative degradation that occurs during cooking[21]. A high incidence of folate deficiency and hyperhomocystenemia have been reported in several areas of rural Bangladesh[20]. Homocysteine is a potent inhibitor of most transmethylation reactions including those of arsenic and can only be achieved with folic acid supplementation[20].

Future further studies aimed in determining whether folic acid and selenium supplementation decrease arsenic related morbidity and mortality is needed.

There are concerns about toxicity of chronic intake of selenium therefore well controlled human trials

are necessary to determine dose, efficacy and safety of selenium.

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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 10 Number 1

Clinical Characteristics of chronic calcific pancreatitis

Habibur Rahman[1], Dewan Saifuddin Ahmed[2], Zahid Hassan[3], N.S. Chowdhury[4] Liakat Ali[5], Mahmud Hasan[6].

Abstract

A prospective study of 28 cases of chronic calcific pancreatitis (CCP) was carried out and is shown that in Bangladesh this malady afflicts younger people than in Europe and USA. Males are predominantly affected. Diabetes mellitus was found in eight patient (29%). Majority of the patient (82%) come from rural areas. Protein malnutrition was found uncommonly. There was no history of alcoholism. Severity of the diabetes does not follow a straight line relationship with the degree of ductal damage suggesting that development of diabetes may not be simply secondary non-specific pancreatic damage in chronic calcific pancreatitis.

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Introduction

Chronic Calcific Pancreatitis (CCP) is a chronic inflammatory disease of the pancreas characterized by irreversible change of the parenchyma which may be either focal, segmental or diffuse[1]. Chronic calcific pancreatitis (CCP), not related to alcohol intake and found mostly in children and young adults of many tropical developing countries, is termed as tropical calcific pancreatitis (TCP)[2]. The clinical course is characterized by recurrent or persistent abdominal pain[3]. A substantial proportion of TCP patients present with a type of diabetes termed as fibro calculus pancreatic diabetes (FCPD)[4] by the WHO study group on diabetes mellitus, which grouped it as a subtype of malnutrition related diabetes mellitus (MRDM). Etiopathogenesis of both TCP and FCPD and the interrelationship between morphological pancreatic and endocrine pancreatic dysfunction in the etiopathogenesis of diabetes in FCPD cases are still unclear. It is generally thought that FCPD is Secondary to TCP where endocrine insufficiently is produced by non-specific damage of the pancreatic tissue[3] and this notion has recently been supported by the ADA Expert committee on diagnosis and classification of diabetes mellitus by terming FCPD as a secondary form of diabetes[4]. Studies of these patients in Bangladesh suggest that the relationship between TCP and FCPD may not be straightforward one.

Chronic calcific pancreatitis is found not uncommonly in gastroenterological practice. The etiology, clinical features and natural history has not yet been defined in Bangladesh. So this study was done to find out the etiology, clinical feature, natural history and to elucidate whether diabetes in CCP is secondary to non-specific damage in chronic calcific pancreatitis.

Materials and Methods

A total number of 28 patients under 30 years of age with clinical evidence of chronic pancreatitis were consecutively selected in the department of gastroenterology BSMMU and out patient department of BIRDEM over a period of two years. The diagnosis of CCP was made by combination of clinical, biochemical and Radiological features. All patients presented with upper abdominal pain were first screened for pancreatic calcification by plain x-ray and ultra sonogram of the abdomen. Glycemic status in all study subjects were assessed by oral glucose tolerance test and diabetes was diagnosed by WHO criteria.

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Results

Twenty eight patients with chronic calcific pancreatitis were studied. There was male, female ratio 18:10. The mean age of the patient was 23±5.68. Mean duration of symptoms was 8±5.72. Majority of the patients (82%) come from rural area. BMI of the study subject was 18±2.98. All the patients presented with abdominal pain. Family history of CCP was found in one cases. Four patients had family history of diabetes mellitus. Most of the patients (78%) come from lower middle class of socioeconomic status. Eight patient of CCP developed diabetes mellitus. Lipid profile shows no significant abnormality in study subject. ERCP was done in 21 cases. Two patients (7%) presented with pancreatic pseudocyst. One patient (4%) shows moderate ductal changes and remaining 20 patients (72%) shows marked ductal changes.

Table-I Clinical and socio demographic characteristics of the study subjects.

	(N=28)
Age in year M±SD	23±5.68
Male : Female	18:10
Rural : Urban	23:5
Annual income in thousand taka per anum (Median range)	40 (8-360)
Family history of diabetes mellitus	04
Family history of CCP	01
Abdominal pain	28
Mean duration of symptoms in years	8±5.72
BMI (M±SD)	18±2.98

Table-II Clinical Features (N=28)

Symptoms	No. patients	%
Upper Abdominal Pain	28	100
Severity of pain		
Mild	05	18
Moderate	07	25
Severe	16	57
Radiation of back	09	32
Vomiting	12	43
Weight loss	07	25
Jaundice	02	07
Abdominal tenderness	08	29
Abdominal mass (paseudo cyst.)	02	07

Table - III Frequency distribution of the study subjects by age

Age	CCP (N-28)
0-9	(0%)
10-20	10 - (36%)
21-30	18 - (64%)

Table - IV Glycemic status, C-peptide value of the study subjects.

Group	Serum Glucose (mmd/L)	
	Omin	120 min
CCP (Non diabetic) No = 20	4.47±1.13	7.27±204
CCP (Diabetic) N = 8	6.28±2.25	15.21±2.84

Table - V ERCP findings in study subjects.

Group	Mild Changes	Moderate Changes	Marked Changes
CCP (Non diabetic) No - 20	0	1 (7.6%)	12 (92.3%)
CCP (Diabetic) N = 8	0	0	8 (100%)

Discussion

The clinical course of chronic calcific pancreatitis is characterized by recurrent episodes of upper abdominal pain of variable intensity for many years. In our series, chronic recurrent abdominal pain was the predominant clinical features and was present in 100% of patients. But in others series a few patients (5%) were relatively pain free . Pancreatic calcification is diagnostic for chronic calcific pancreatitis and the presence of this sign was used as a diagnostic criterion in our study. Pancreatic calcification was also found in 25-50% of patients in other series . Age distribution of the CCP patient in the present study was similar to that of other studies .

There was male preponderance in CCP subjects (M:F=18:10) in this study may be due to the fact that male patients are exposed more to various toxic substances than females. Alternatively, males in our society are in advantageous position, so they may travel more to cities for health care compared to females. Male preponderance was also observed in other study[1] . Most of the patients (82%) in this

study came predominantly from rural areas. Similar rural preponderance was also observes in other study[11].

Chronic pancreatitis results in irreversible destruction of pancreatic tissue and with progressive loss of parenchyma, exocrine and or endocrine insufficiency may occur. However there is a tremendous reserve in pancreatic secretion and pancreatic insufficiency may remain sub-clinical for a long time. Therefore steatorrhoea, malabsorption and diabetes mellitus are relatively late findings[12]. Steatorrhoea and malabsorption were not found in any of our cases. Diabetes mellitus found in (28%) patients in the present series which is lower than the 74% reported by amman et al[13]. This may be due to the selection of the patient. Most of the patients in the present series selected from gastroenterologist where the patient is usually presented with abdominal pain. Whereas patient presented at BIRDEM out door predominantly with diabetes mellitus.

Marked ductal changes in (71%) of patients in both diabetic and non-diabetic group suggest that there is no straight- line relationship between the degree of pancreatic exocrine damage and development of diabetic state in CCP patient.

In conclusion, chronic calcific pancreatitis in Bangladesh occurs mainly in men in the younger age group. The predominant clinical feature is recurrent upper abdominal pain in the epigastrium. Significant proportion of patient developed diabetes mellitus during the course of the diseases. Chronic diarrhoea and steatorrhora is rare symptoms in CCP. Diabetes in CCP may not be simply due to non-specific pancreatic damage which contradicts the views of the ADA expert committee and others regarding its secondary nature.

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[OMTAJ 2011; 10(1)]

Introduction

Chronic Calcific Pancreatitis (CCP) is a chronic inflammatory disease of the pancreas characterized by irreversible change of the parenchyma which may be either focal, segmental or diffuse[1]. Chronic calcific pancreatitis (CCP), not related to alcohol intake and found mostly in children and young adults of many tropical developing countries, is termed as tropical calcific pancreatitis (TCP)[2]. The clinical course is characterized by recurrent or persistent abdominal pain[3]. A substantial proportion of TCP patients present with a type of diabetes termed as fibro calculus pancreatic diabetes (FCPD)[4] by the WHO study group on diabetes mellitus, which grouped it as a subtype of malnutrition related diabetes mellitus (MRDM). Etiopathogenesis of both TCP and FCPD and the interrelationship between morphological pancreatic and endocrine pancreatic dysfunction in the etiopathogenesis of diabetes in FCPD cases are still unclear. It is generally thought that FCPD is Secondary to TCP where endocrine insufficiently is produced by non-specific damage of the pancreatic tissue[3] and this notion has recently been supported by the ADA Expert committee on diagnosis and classification of diabetes mellitus by terming FCPD as a secondary form of diabetes[4]. Studies of these patients in Bangladesh suggest that the relationship between TCP and FCPD may not be straightforward one.

Chronic calcific pancreatitis is found not uncommonly in gastroenterological practice. The etiology, clinical features and natural history has not yet been defined in Bangladesh. So this study was done to find out the etiology, clinical feature, natural history and to elucidate whether diabetes in CCP is secondary to non-specific damage in chronic calcific pancreatitis.

Materials and Methods

A total number of 28 patients under 30 years of age with clinical evidence of chronic pancreatitis were consecutively selected in the department of gastroenterology BSMMU and out patient department of BIRDEM over a period of two years. The diagnosis of CCP was made by combination of clinical, biochemical and Radiological features. All patients presented with upper abdominal pain were first screened for pancreatic calcification by plain x-ray and ultra sonogram of the abdomen. Glycemic status in all study subjects were assessed by oral glucose tolerance test and diabetes was diagnosed by WHO criteria.

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Results

Twenty eight patients with chronic calcific pancreatitis were studied. There was male, female ratio 18:10. The mean age of the patient was 23±5.68. Mean duration of symptoms was 8±5.72. Majority of the patients (82%) come from rural area. BMI of the study subject was 18±2.98. All the patients presented with abdominal pain. Family history of CCP was found in one cases. Four patients had family history of diabetes mellitus. Most of the patients (78%) come from lower middle class of socioeconomic status. Eight patient of CCP developed diabetes mellitus. Lipid profile shows no significant abnormality in study subject. ERCP was done in 21 cases. Two patients (7%) presented with pancreatic pseudocyst. One patient (4%) shows moderate ductal changes and remaining 20 patients (72%) shows marked ductal changes.

Table-I Clinical and socio demographic characteristics of the study subjects.

	(N=28)
Age in year M±SD	23±5.68
Male : Female	18:10
Rural : Urban	23:5
Annual income in thousand taka per anum (Median range)	40 (8-360)
Family history of diabetes mellitus	04
Family history of CCP	01
Abdominal pain	28
Mean duration of symptoms in years	8±5.72
BMI (M±SD)	18±2.98

Table-II Clinical Features (N=28)

Symptoms	No. patients	%
Upper Abdominal Pain	28	100
Severity of pain		
Mild	05	18
Moderate	07	25
Severe	16	57
Radiation of back	09	32
Vomiting	12	43
Weight loss	07	25
Jaundice	02	07
Abdominal tenderness	08	29
Abdominal mass (paseudo cyst.)	02	07

Table - III Frequency distribution of the study subjects by age

Age	CCP (N-28)
0-9	(0%)
10-20	10 - (36%)
21-30	18 - (64%)

Table - IV Glycemic status, C-peptide value of the study subjects.

Group	Serum Glucose (mmd/L)	
	Omin	120 min
CCP (Non diabetic) No = 20	4.47±1.13	7.27±204
CCP (Diabetic) N = 8	6.28±2.25	15.21±2.84

Table - V ERCP findings in study subjects.

Group	Mild Changes	Moderate Changes	Marked Changes
CCP (Non diabetic) No - 20	0	1 (7.6%)	12 (92.3%)
CCP (Diabetic) N = 8	0	0	8 (100%)

Discussion

The clinical course of chronic calcific pancreatitis is characterized by recurrent episodes of upper abdominal pain of variable intensity for many years. In our series, chronic recurrent abdominal pain was the predominant clinical features and was present in 100% of patients. But in others series a few patients (5%) were relatively pain free . Pancreatic calcification is diagnostic for chronic calcific pancreatitis and the presence of this sign was used as a diagnostic criterion in our study. Pancreatic calcification was also found in 25-50% of patients in other series . Age distribution of the CCP patient in the present study was similar to that of other studies .

There was male preponderance in CCP subjects (M:F=18:10) in this study may be due to the fact that male patients are exposed more to various toxic substances than females. Alternatively, males in our society are in advantageous position, so they may travel more to cities for health care compared to females. Male preponderance was also observed in other study[1] . Most of the patients (82%) in this

study came predominantly from rural areas. Similar rural preponderance was also observes in other study[11].

Chronic pancreatitis results in irreversible destruction of pancreatic tissue and with progressive loss of parenchyma, exocrine and or endocrine insufficiency may occur. However there is a tremendous reserve in pancreatic secretion and pancreatic insufficiency may remain sub-clinical for a long time. Therefore steatorrhoea, malabsorption and diabetes mellitus are relatively late findings[12]. Steatorrhoea and malabsorption were not found in any of our cases. Diabetes mellitus found in (28%) patients in the present series which is lower than the 74% reported by amman et al[13]. This may be due to the selection of the patient. Most of the patients in the present series selected from gastroenterologist where the patient is usually presented with abdominal pain. Whereas patient presented at BIRDEM out door predominantly with diabetes mellitus.

Marked ductal changes in (71%) of patients in both diabetic and non-diabetic group suggest that there is no straight- line relationship between the degree of pancreatic exocrine damage and development of diabetic state in CCP patient.

In conclusion, chronic calcific pancreatitis in Bangladesh occurs mainly in men in the younger age group. The predominant clinical feature is recurrent upper abdominal pain in the epigastrium. Significant proportion of patient developed diabetes mellitus during the course of the diseases. Chronic diarrhoea and steatorrhora is rare symptoms in CCP. Diabetes in CCP may not be simply due to non-specific pancreatic damage which contradicts the views of the ADA expert committee and others regarding its secondary nature.

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Neonatal surgery in a tertiary care hospital – 7 years experience

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Shafiqul Islam[5], Anisur Rahman[6].

Abstract

The study on neonatal surgery was carried out on 262 patients admitted in the department of pediatric surgery of Rangpur Medical College Hospital during the period of January, 2003 to December, 2009. The patients were diagnosed on the basis of history, physical findings and investigations. Highest number of patients were within the age of 5 days 152(58.02%) and there was male preponderance. Most of the patients were treated surgically after evaluation and resuscitation when necessary. Outcome was good in majority of the cases.

Introduction

With better understanding of neonatal physiology and improvements in diagnostic facilities and neonatal intensive care units (NICU), the outcome of neonatal surgery has improved in developed countries. In developing countries, however, neonatal surgery is problematic, particularly in the emergency settings, but there are few reports from these countries. Over one third of the global 10.8 million deaths of children under age 5 in the year 2000 occurred in neonatal period[1]. Neonatal mortality is still higher. In order to achieve the Millennium Development Goal (MDG-4) target of a two-thirds reduction in under five mortality from 1990 to 2015[2], major reduction is required in neonatal mortality[3]. Congenital anomalies have become the 4th cause of neonatal death and most of these are curable surgically[4].

Surgery and anaesthesia of neonates evokes responses that are unique. Overriding questions in the family concerned are: whether the infant will survive the stress of surgery and anaesthesia and whether the one with the prevailing, particularly congenital anomaly will revert to normal. Only infant mortality rate measures the quality of life and health care in a country and success of neonatal surgery is an audit of health delivery by any institution[5]. The challenges of offering neonatal surgical service in a peripheral Medical College Hospital are similar to other parts of the developing world. Limited human and material resources, poor infrastructure and problems of poverty have had a negative impact on its implementation.

Bangladesh is a densely populated country having high maternal and child mortality. Rangpur Medical College Hospital is a only divisional level tertiary care public hospital of the country having pediatric and neonatal surgical care facilities in this region but development of infrastructure has not kept pace to match the status and expectations. Before 2000, neonatal surgery in Rangpur was in a narrow range of procedures by general surgeons. Since then there has been an increase in the range and volume of neonatal surgical procedures occasioned by the presence of paediatric surgeons. As expected challenges have emerged threatening the establishment of this service. This study was done to assess the outcome of neonatal surgery at Rangpur division with a view to provide solutions for improved care in the years to come. The specific objectives were to determine the pattern of neonatal

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surgical problems, their management and outcome and to find out the ways to reduce neonatal mortality.

Materials and methods

Two sixty two neonates were admitted in the department of Pediatric Surgery of Rangpur Medical College Hospital from January, 2003 to December, 2009 over a period of 7 years. Male female ratio was 2.74 :1. The follow up period was 1 month to 7 years. These patients were evaluated with regard to age, sex, clinical features, physical findings, investigations, diagnosis, treatment, some demographic variables and final outcome.

Results

Among the admitted 13287 child in the department of Paediatric Surgery of Rangpur Medical College Hospital during the study period, 262(1.97%) were neonates and 235(89.69%) of them were emergency admission. Most of the neonates 152(58.02%) were presented within their 1st 5 days of life with various types of surgical problems. Male female ratio was 2.74:1. Most neonates were delivered normally, vaginally 241(91.98%), at home 175(66.79%) at full term 243(92.75%) with their birth weight within 2-2.5 kg 188(71.76%). Most of the mother have no antenatal check up during their whole pregnancy period. Age of the mother was below 20 years in 165(62.98%) with general ill health 146(55.73%) having multiple child 162(61.84%).

Socioeconomic status was low in 172(65.65%). Most of them, 137(52.29%) came from rural areas of different districts of Rangpur division and other surrounding districts. Father 127(48.47%) and mother 175(66.79)% were illiterate. Majority of the patients were referred to the hospital by qualified doctors. Family history was not informative in this study. Year wise admission, different age groups, sex, socioeconomic status, mode and place of delivery, antenatal check up, parity, maternal age and health, disease profile, treatment, outcome, postoperative complications and hospital stays are shown in table and figure 1-11.

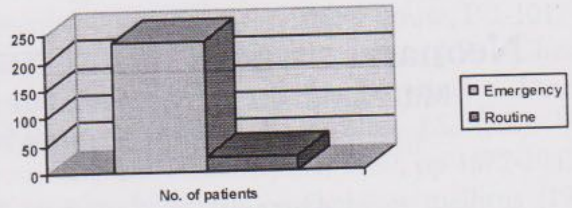

Figure 1 : Type of admission

Table 1 : Year wise pediatric and neonatal admission

Sl. No.	Year	Pediatric patient	No. of neonate
1	2003	1469	28
2	2004	1816	33
3	2005	1917	37
4	2006	1776	36
5	2007	2258	45
6	2008	2134	44
7	2009	1917	39
Total		**13,287**	**262**

Table 2 : Age of the patients

Age	No. of patients	Percentage
0-5 days	152	58.02
>5 days-10 days	37	14.12
>10 days-20 days	41	15.65
>20 days-28 days	32	12.21
Total	262	100

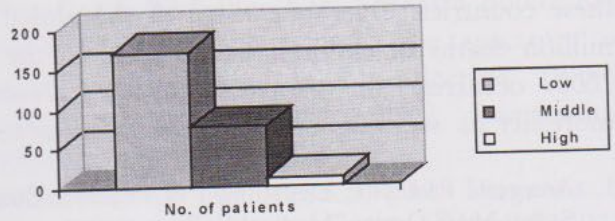

Figure 2 : Socioeconomic status

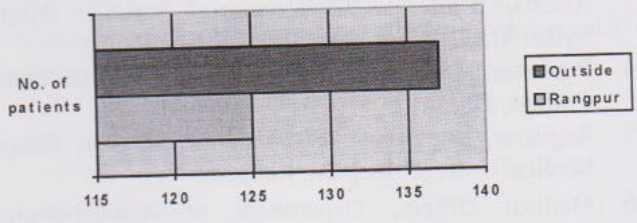

Figure 3 : Inhabitance

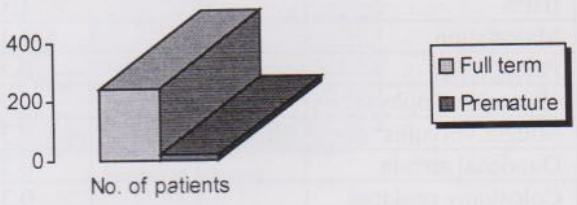

Figure 4 : Maturity of neonates

Table 3 : Birth weights

Weights	No. of patients	Percentage
>2.5 kg	49	18.70
>2-2.5 kg	188	71.76
1.5-2 kg	21	8.02
<1.5 kg	4	1.53

Table 4 : Parity

Parity	No. of patients	Percentage
1st	100	38.17
2nd	58	22.14
3rd	62	23.66
4th	27	10.31
>4th	15	5.73

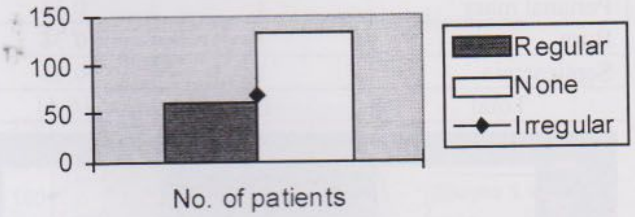

Figure 5 : Antenatal check up of mothers

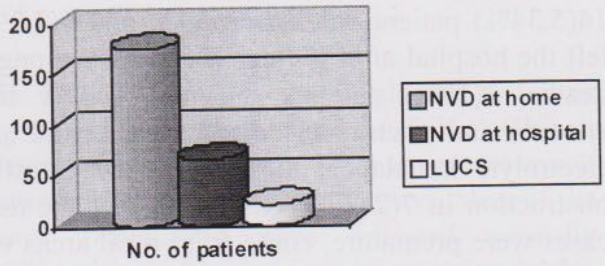

Figure 6 : Place and mode of delivary

Investigations findings were normal CBC in most cases. Plain radiography was done in all cases of intestinal obstruction showing multiple gas fluid levels in majority of the cases. Invertogram was done in most patients with anorectal malformation showing gas shadows proximal to PC line in 65(78.31%). X-ray lumbosacral spine was done in cases of spina bifida and shows vertebral defects in most cases. Contrast x-rays were done specially in all cases of Hirschsprung's disease and shows distal narrowing, coning and proximal dilatation in 16(47.06%) and residual contrast in 24 hours late film in 10(29.41%). Ultrasonogram was done in most of the urological problems. Rectal biopsy was done in 30(88.24%) cases of suspected Hirschsprung's disease showing absence of ganglion cell in 28(93.33%) of cases.

The most common neonatal surgical problem was anorectal malformations, 83(31.68%), among them 71(83.53%) have high and 12(14.46%) low variety ARM. This is followed next by Hirschsprung disease that was represented by 34(12.98%).

Among the 262 patients 184(70.23%) were treated surgically, and 78(29.67%) conservatively. There was uneventful recovery in 174(94.57%) and 12(6.52%) patients developed postoperative complications. Among the postoperative complications, there was wound infection in 5(2.72%) and wound dehiscence in 4(2.17%) and septicemia in 3(1.63%). Wound infection was treated by regular dressing and secondary suture needed in wound dehiscence cases. Mortality was 20(7.63%) of which surgically treated patient was 12(5.98%) and conservatively treated patient 8(10.26%). Due to poverty and illiteracy

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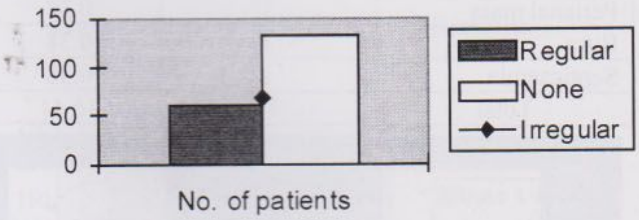
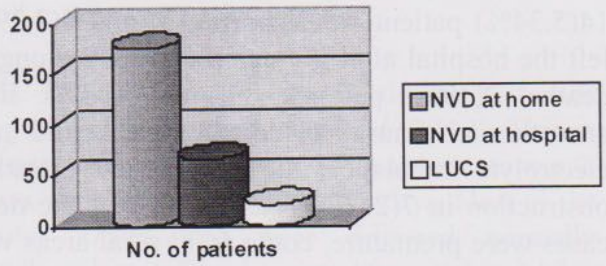


Figure 5 : Antenatal check up of mothers



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14(5.34%) patient were absconded and 6(2.29%) left the hospital after giving risk bond. Among 20 deaths, 2(10%) patients did not recover from anaesthesia. Cause of death was fluid and electrolyte imbalance due to neonatal intestinal obstruction in 7(2.67%) cases. Most of the death cases were premature, come from rural areas with gross fluid electrolyte imbalance, low socioeconomic status and presented late with their problems. Hospital stay was within 1 week in 240(91.60%).

All patient were advised during discharge to come for follow up. Most of them come for follow up andtheir condition showed improvement, there was good appetite, weight gaining and normal bowel and bladder habit.

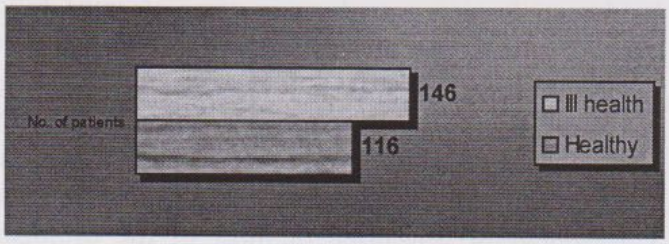

Figure 7 : Maternal health

Table 5 : Maternal age

Age	No. of patients	Percentage
15-20 yrs	165	62.98
>20-25 yrs	66	25.19
>25-30 yrs	21	8.02
> 30 yrs	10	3.82

Table 6 : Common surgical problems in neonates

Diseases	No. of patients	Percentages
GIT disorders	185	70.61
Urogenital disorders	18	6.87
Neurosurgical diseases	16	6.11
Miscellaneous diseases	43	16.41

Table 7 : Gastrointestinal problems

Diseases	No. of patients	Percentages
ARM	83	31.68
HPD	34	12.98
Intestinal obstruction	28	10.69
Omphalocele	9	3.44
Gastroschisis	6	2.29
Acute abdomen	6	2.29
Intestinal atresia	4	1.53
Meconium ileus	2	0.76
IHPS	3	1.15
Malrotation	3	1.15
Patent VID	2	0.76
Cloacal extrophy	2	0.76
Midgut volvulus	1	0.38
Duodenal atresia	1	0.38
Colostomy prolapse	1	0.38
Total	185	70.61

Table 8 : Urogenital problems

Diseases	No. of patients	Percentages
Retention of urine	7	2.67
Posterior urethral valve	5	1.91
Hypospadias	3	1.15
Inguinal hernia	2	0.76
Ovarian cyst	1	0.38
Total	18	6.87

Table 9 : Neurosurgical problems

Diseases	No. of patients	Percentages
Meningocele	11	4.20
Cephal haematoma	3	1.15
Encephalocele	1	0.38
Head injury	1	0.38
Total	16	6.11

Table 10 : Miscellaneous diseases

Diseases	No. of patients	Percentages
Abscess	11	4.20
Umbilical diseases	10	3.82
Cellulitis	8	3.05
Birth trauma	7	2.67
Sacrococcygeal teratoma	2	0.76
Bilateral cleft lip	1	0.38
Cystic hygroma	1	0.38
Perianal mass	1	0.38
Burn	1	0.38
Septicaemia	1	0.38
Total	43	16.41

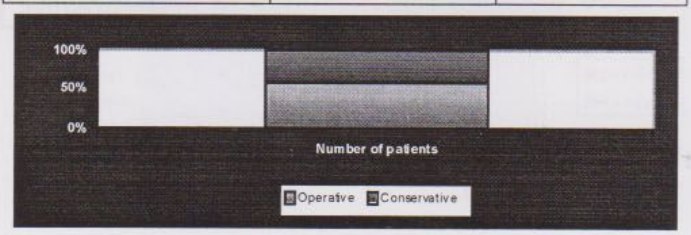

Figure 8 : Method of treatment

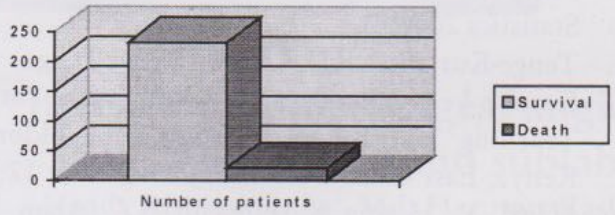

Figure 9 : Outcome

Table 11 : Mortality

Diseases	No. of patients	Percentage
Intestinal obstruction	7	2.67
High ARM	3	1.15
Intestinal atresia	2	0.76
Gastroschisis	2	0.76
Acute abdomen	1	0.38
PUV	1	0.38
Complicated meconiu ileus	1	0.38
HPD	1	0.38
Birth trauma	1	0.38
Encephalocele	1	0.38
Total	20	7.63

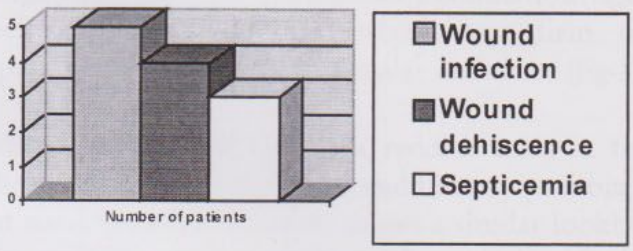

Figure 10 : Post-operative Complications

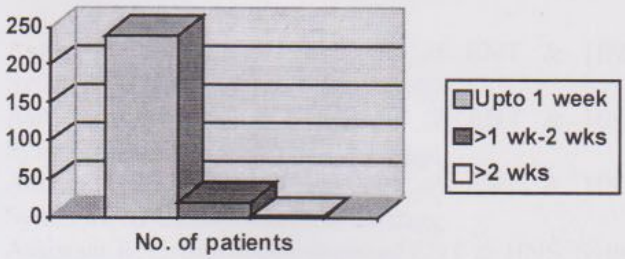

Figure 11 : Hospital stay

Discussion

Of the 262 neonates, 192 were male and 70 female giving a male to female ratio of 2.74:1. This is consistent with other studies[5]. The age ranges was 0-28 days with the median age of 7.8 days. Most of the neonates 175(66.79%) were delivered normally vaginally at home. Weight ranged from 1.3 to 3.5 kg. These findings are almost similar with the study of Hanif et al[6] and Tenge Kuremu et al[5].

Socioeconomic status was low in 172(65.65%). Most of them, 137(52.29%) came from rural areas of different districts of Rangpur division and other surrounding districts. Father 124(47.33%) and mother-176(67.18%) were illiterate. Most patients, 157(59.92%) were referred to the hospital by qualified doctors. These variables though determine the outcome are not within the interventional reach of the surgeon and are also consistent with other studies[6].

The most common neonatal surgical problem was anorectal malformations, 83(31.68%). This is followed next by Hirschsprung disease. This finding is also consistent with the study of Hanif et al who showed ARM as the commonest neonatal surgical problems followed by HPD[6]. Neonatal intestinal obstruction was the commonest surgical emergencies. This finding is similar with the study of Neuenschwande et al[7].

Among the 262 patients 184(70.23%) were treated surgically. This finding is not correlated with the study of Hanif et al who showed surgically treated patient about 80% in their series[6]. This dissimilarity may be due to referral to other hospital as lack of NICU in our settings. Out of 184 cases, 174(94.57%) had uneventful recovery and 12(6.52%) patients developed postoperative complications. Among 20(7.63%) deaths, 2(10%) patients did not recover from anaesthesia. Seventy eight (29.67%) patients were treated conservatively, out of which 70(89.74%) were improved and 8(10.26%) died. Presentation, diagnosis and treatment modalities of this study are more or less consistent with the other studies[8,9]. Prematurity, gross fluid electrolyte imbalance, metabolic acidosis, hypoglycaemia, hypothermia results from inadequate warming during examination and/or negligence, respiratory distress, septicemia,

associated malformations and postoperative complications are the leading cause of morbidity and mortality. This is also consistent with other studies[10,11].

In conclusion, Pediatric surgeons definitely improved the neonatal surgical cares and contributing significantly in reducing infant as well as neonatal mortality rate and thus help in achieving MDG4. For neonatal surgery full work up is required for the baby at birth and timely surgical intervention is important. Early referral and presentation and provision of NICU should improve the outcome. Surgical outcomes are generally good, the patient can look forward to a full and healthy life.

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Juvenile nasopharyngeal angiofibroma - Excision through lateral rhinotomy and sublabial approach - a case report.

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Introduction

Juvenile angiofibroma is a rare hypervascular, locally aggressive benign tumour which is exclusively found in the nose and paranasal sinuses of male adolescents. The definitive treatment for this tumour is complete surgical excision. Different surgical approaches are used for complete excision. Most recent development is excision of the tumour using endoscopes. But in certain cases with large size and different extensions, open transfacial approaches are the choice for complete removal and for less operative bleeding, which are the main challenges for surgical excision of this tumour.

Case Report

A 16 yr old male patient admitted in the male ward of ENT & HNS, SOMCH with the complaints of bilateral progressive nasal obstruction with recurrent bouts of epistaxis since last one and half yr, voice change since last 1yr. On clinical examination right cheek swelling is noticed which was firm on palpation just below the right malar eminance (fig-1).

Anterior rhinoscopy reveals a reddish mass in the right nasal cavity, almost fixed and firm on probbing. Post nasal space examination shows a similar looking huge reddish mass involving the whole of the nasopharynx with bulging of the soft palate. X-ray PNS done which shows opacity in the right maxillary antrum and night nasal cavity region. A CT of axial (fig-2) and coronal plane (fig-3) shows a huge isodense shadow involving the nasopharynx, right nasal cavity, right maxillary antrum, right pterygopalatine fossa and right infratemporal region. Routine exam of blood, urine, CXR, ECG reveals no abnormality. Based on clinical findings and radiological evaluations it was diagnosed as a case of juvenile nasopharyngeal angiofibroma and planed for surgical excision under GA through right lateral rhinotomy and sublabial approach.

After getting written informed consent and sufficient pre-operative measures, including 4 units of fresh blood in hand, the patient was operated using hypotensive anaesthesia, in supine and 15^0 head end up position. Through right lateral rhinotomy (fig-4) and sublabial incision (fig-5) the tumour was approached by medial maxillectomy with exposure of right maxillary antrum and right sphenopalatine foramen region, from where the tumour has originated. Through the sublabial approach, after blunt dissection, the check extension was reached and with digital pressure and dissection it is pushed into the nasopharynx along with sub-periosteal dissection of the main mass. Then the whole mass (fir-6) was removed along with its extensions per orally with help of a Boyle-Davis mouth gag. Per-operative bleeding was average, no injury to adjoining structures occurred and no part of the tumour was left, in gross eye vision. The newly formed whole cavity was packed with Ribbon pack mixed with antibiotic ointment. Both the lateral rhinotomy and sublabial incision was closed in layers and dressed in proper way. The pack was removed per nasally after 48 hours. No bleeding occurred at that time but there was some inflammatory soft tissue swelling seen in right check (Fig-7). No vision

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problem and ephiphora seen in right eye. After removing the skin stitches the patient was discharged after 10 days of operation.

Discussion

Juvenile nasopharyngeal angiofibroma, which accounts for less than 0.5% of all head-neck tumours is a rare, benign, non-encapsulated tumour arising usually from the superior margin of the sphenopalatine foramen or the pterygopalatine fossa at the aperture of the vidian canal[1]. It has a high rate of recurrence.

The tumour is most common in northern India, although the reasons for these are unknown[2]. Clinical examinations often shows a tumour in the nasal cavity and nasopharynx, but CT and MRI best demonstrates the extent of the tumour and its accompanying bony erosions. Angiography is rarely indicated. Biopsy should be avoided unless clinical and radiological examinations are not diagnostic, because of the risk of bleeding.

The tumour grows submucosally along the roof of the choana to reach the posterior border of the septum and then expands further to present in the nasal cavity and nasopharynx. The tumour can further extend to the pterygopalatine fossa, infratemporal fossa, temporal fossa and orbit and can also grow intracranially[3].

Surgical excision is the treatment of choice. The approach to the tumour can be transpalatal, transantral, lateral rhinotomy, midfacial degloving, maxillary swing, transzygomatie, transmandibular, transhyoid, or via craniofacial resection or the natural orifices, depending upon the tumour's extension. The other modalities of treatment are radiotherapy, hormone therapy, cryotherapy, electro-coagulation, sclerotherapy and chemotherapy; these are considered as adjuncts to the surgical treatment of extensive tumours. Primary radiation therapy for angiofibroma at doses of 3000-3500 cGy, has been considered in few centres[4]. Recent advancement in technology and techniques have made endoscopic excision of angiofibroma possible. Based on the experience of endoscopic sinus surgery and transnasal endoscopic vidian neurectomy, Kamel first suggested endoscopic transnasal surgery for angiofibroma in 1996[5]. Endoscopic exposure and excision is considered to be the first choice of surgical approach in cases of limited angiofibroma involving the posterior part of the nasal cavity, nasopharynx, sphenoid sinus, and pterygopalatine fossa. Endoscopes can also be used to complement conventional surgery, enabling endoscope-assisted surgery for extensive lesions.

Generally tumour removal from the infratemporal and pterygomaxillary regions can be supplemented by sublabial and buccolabial incisions. The tumour should be excised in the submucosal and subperiosteal planes, displaced and then finally delivered either transnasaly or transorally. New tumours can be excised en-block by blunt dissection and recurrent tumours can be excised with the help of a laser, microdebrider, image guidance system and frozen section pathological analysis.

Surgical managament of angiofibroma can be complicated by excessive haemorrhage and persistent of residual lesion. These complications are always reduced if the tumour is extirpated with its roots.

The ideal surgical approach should enable direct access to the origin and extensions of the tumour. The transpalatal approach has been recommended for lesions of less than 5cm, but it gives exposure to only the inferior surface, without any direct visualization of the superior attachments. The lateral rhinotomy and other transfacial approaches give excellent exposure of the roots and extensions of the tumour, but leave a facial scar. The endoscopic approach has the distinct advantage of direct access to the tumour origin and extension areas without any facial scar, reduced bleeding and lower incidence of rasidual lesion. In addition this approach has the advantage of reduced morbidity, shorter hospital stay and avoidance of the problems of open surgery i.e. epiphora, dysaesthesia, pain and the possible effects on facial growth[6].

To reduce peri operative haemorrhage some authors recommended pre-operative embolization of the tumour through external carotid catheters[7].

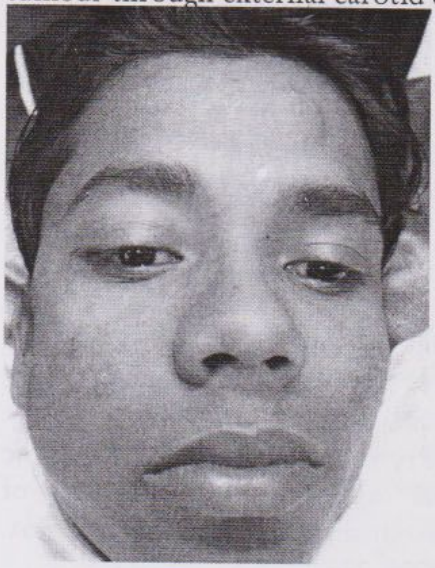

Figure - 1: Preoperative photograph with right cheek swelling.

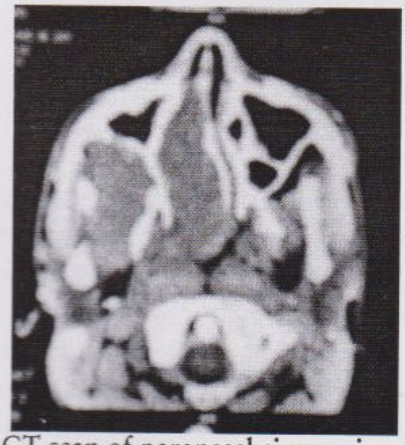

Figure-2: CT scan of paranasal sinuses in axial plane.

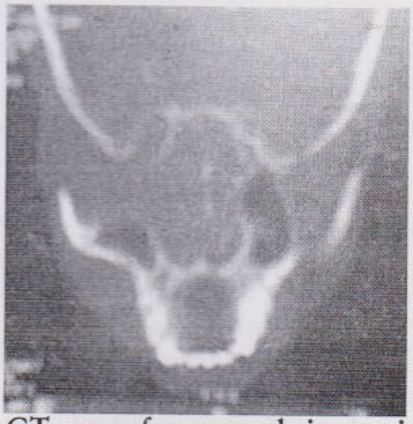

Figure-3: CT scan of paranasal sinuses in coronal plane.

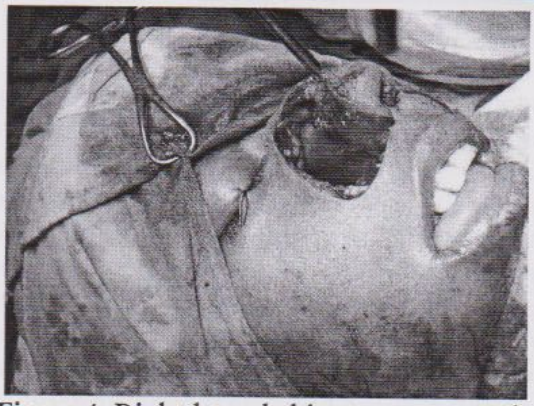

Figure-4: Right lateral rhinotomy approach.

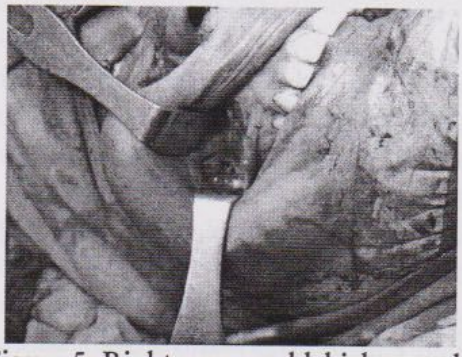

Figure-5: Right upper sublabial arrpach.

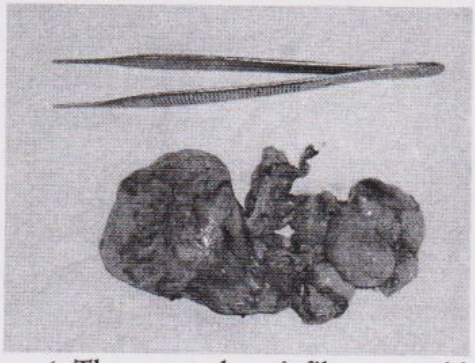

Figure-6: The resected angiofibroma en-block.

Figure-7: Post operative photograph (7th POD) with inflammatory righ cheek swelling.

Conclusion

Endoscopic resection is a feasible and safe treatment for angiofibroma. But it has some limitations. Open approaches like lateral rhinotomy and sublabial routes are also appropriate in some cases based on extensions. Main disadvantages for these routes are remaining of a facial scar and greater patient morbidity. Above all, in addition to advantages and disadvantages of different procedures of tumour resection, the main aim of surgery is complete removal and reduced bleeding during surgery.

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Immunoproliferative small intestinal disease (IPSID) - A Case Report.

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Introduction

Immunoproliferative small intestinal disease (also known as alpha heavy chain disease) is a form of lymphoma that arises in small intestinal mucosa-associated lymphoid tissue (MALT)[1] and is associated with the expression of a monotypic truncated immunoglobulin a
heavy chain without an associated light chain. We describe herein a patient with Immunoproliferative small intestinal disease (IPSID), who had been having chronic diarrhea, low grade fever, abdominal pain and significant weight loss for 2 ½ years, possibly the first documented case of Immunoproliferative small intestinal disease (IPSID) in M.A.G. Osmani Medical College Hospital, Sylhet.

Case Report

A young man of 20 years, Habibur Rahman, hailing from Muslimbag, Sreemongol, Moulvibazar admitted into Gastroenterology unit with 2 ½ years history of loose motion, low grade fever, occasional vomitting, abdominal pain and significant weight loss. He passes stool 6/8 times a day, consistency ranging from watery to semi solid, occasionally mucous mixed but not with blood. He also suffers from occasional low grade fever not associated with chills or rigor. He has occasional vomiting, peri-umbilical pain and significant weight loss. He gave no history of cough, chest pain, haemoptysis, contact with TB patient, food intolerance (milk, wheat or flour), palpitation, tremor,polyuria, needling, traveling abroad and exposure.

With above complaints he consulted GP and medicine specialist and taken various drugs like Tetracyclin ,Ciprofloxacin, Metronidazol, Meverine citrate several times.He noticed partial improvement after taking tetracycline.

On examination patient looks ill, mildly anaemic with a below average body built. His pulse 80/min, B.P. 110/70 mm of Hg, temperature 98.40 F. Jaundice, oedema, palpable L.N., Koilonychia, leukonychia, clubbing, skin pigmentation absent. Thyroid gland is not enlarged.

On examination of G.I.T. abdomen looks scaphoid. There is mild peri-umbilical tenderness. No other abnormality detected.

Other system reveals normal.

Investigation revealed his HB was65 %, ESR 120 mm in 1st hour, TC of WBC 9500/cmm, differential count N-56 ,L-38%,M -03% E-03%,B-00%, Platelet count-250000,). Stool routine examination revealed no abnormality. Stool for OBT was Negative. RBS: 95 mg/dl, Urine R/E: NAD, Chest X ray P/A view: NAD, Serum Total protein: 7.4 gm/dl, Albumin: 2.5 gm/dl. Tuberculin test: Induration 5 mm after 72 hrs, USG of W/A: Normal, Thyroid profile: Normal. H.I.V: Negative.Enteroclysis: Thickening of the mucosal fold specially at the jejunum.

Endoscopy of upper G.I.T.: Mucosal nodularity in 2nd part of duodenum. Biopsy taken from 2nd part of duodenum .Colonoscopy: Mucosal nodularity seen at terminal ileum, mucosa not ulcerated. Biopsy taken from terminal ileum

Histopathology Report: The villi are almost flat. Lamina propria are packed with plasma cells and lymphocytes.

Comment: **Immunoprolliferative small intestinal disease (IPSID) .**

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In view of the presence of above clinical features and investigations report diagnosis of **Immunoproliferative small intestinal disease (IPSID)** was made. He was treated with Tetracycline 500mg b.i.d. for 6 months.

Evaluation after 6 months shows much symptomatic improvement of the patient with weight gain. Tetracycline was continued but after 3 months he began to deteriorate. Chemotherapy was the planned but patient did not come for follow-up. After someday, attendant of the patient inform us over telephone that he had died while taking some homeopathic and endogenous remedies.

Discussion

Immunoproliferative small intestinal disease (IPSID) is a malabsorption disease classified as a subtype of mucosa-associated lymphoid tissue (MALT) lymphoma and is now the term used to include Mediterranean lymphoma and alpha chain disease (alpha-CD).[2] It was first described in 1965.[3] In 1978 the World Health Organization recommended the term Immunoproliferative Small Intestinal Disease for the syndrome associated with Mediterranean lymphoma because at that time it was felt that the disease in its early stages "does not appear to be truly malignant lymphoma".[4] Prevalence is unknown but the incidence of IPSID is decreasing, probably as a result of improving socioeconomic status and sanitary conditions in developing countries.

The majority of IPSID cases were reported from Israel, Northern Africa, and other Middle Eastern and Mediterranean countries but cases have also been described from the Indian subcontinent, the Far East, Central and Subsaharian Africa, and Central and South America.[5] IPSID mainly affects adults classically presents in the second or third decade of life. It is uncommon in extremes of age. Male to female ratio nearly equal.[4]

The etiology of this disease remains unclear, although various environmental, infective, genetic, and toxic mechanisms have been proposed. There is a significant association with poor hygienic standards. Environmental exposures early in life may be particularly important; for instance, IPSID is less prevalent in Jews born in Israel than in Jews born in Africa who had immigrated later to Israel, where living standards are higher[6]

Endemic parasitic infestation, and infantile infectious enteritis plays a role.[7]. Chronic stimulation from bacterial or parasitic antigenic particles may cause an over proliferation of the intestinal lymphoid system, eventually developing into a monoclonal proliferation once frank lymphoma occurs .[8] Monoclonal gene rearrangements in early disease suggest to some that IPSID is neoplastic from the outset .[9]

Genetic factors are likely to play a role. There is a possible association between IPSID and human leukocyte antigen types Aw19, B12, and A9 [10], as well as with blood group B [11]. One study has shown high concordance rates of this condition among blood relatives, even when living apart. [10]. In addition, unusually high levels of serum alkaline phosphatase from intestinal sources are found both in patients and in healthy first degree relatives .[10]

IPSID manifests itself as chronic intermittent nonbloody diarrhea, abdominal pain, nutrient malabsorption, weight loss of months' to years' duration. [12, 13] The diarrhea appears to be caused by loss of absorptive surface, disordered intestinal motility, and bacterial overgrowth. There is often anemia associated with iron, folate, or vitamin B12 deficiency. There may be digital clubbing. Fistula formation, fever, ascites, hepatosplenomegaly, and peripheral lymphadenopathy are rare.Recurrent intestinal obstruction has not been reported to be a major symptom, except as a consequence of ileal lymphoma.[14]

The diagnosis of IPSID depends on radiographic and endoscopic studies of bowel and an extensive analysis of the intestinal histology. Radiographs reveal a serrated pattern at the edge of mucosal folds, especially in the presence of lymphomatous involvement . [15]

Upper gastrointestinal endoscopy shows abnormalities in the second, third, and fourth parts of the duodenum and upper jejunum in all patients except those with very early disease. Thickened mucosal folds, nodules, ulcers, mosaic pattern are also noted .[16, 17]

Although the clinical, laboratory, and radiologic findings are pathognomonic, the final diagnosis of IPSID depends on endoscopic biopsies and/or

laparotomy. IPSID is characterized by a dense, band like lymphoplasmacytic infiltrate in the mucosa and submucosa of the entire small intestine, particularly the distal duodenum and proximal jejunum, as well as the mesenteric lymph nodes. Plasma cells with the least atypia are usually located in the superficial mucosa, whereas more atypical cells are confined to the deeper muscular layers. Lymphoid aggregates are often present. Invariably, destruction of crypts and blunting of villi lead to obliteration of the orderly crypt villus architecture .[5]

Up to 50% of IPSID patients will be found to have a concurrent intestinal lymphoma at the time of initial diagnosis and most of the remaining patients develop frank lymphoma within a few years. So, if per oral biopsy is positive, a staging exploratory laparotomy is mandatory to examine the mesenteric lymph nodes. Although many IPSID patients progress to high grade indeterminate-type lymphoma within a few years, there have been occasional reports of long term survival without lymphomatous conversion .[5]

Diagnosis is confirmed by characteristic findings on peroral biopsy; if positive, a staging exploratory laparotomy should be done to examine the mesenteric lymph nodes because of the frequent discrepancies between intestinal and mesenteric lymph nodes with regard to lymphomatous foci .[12, 18]

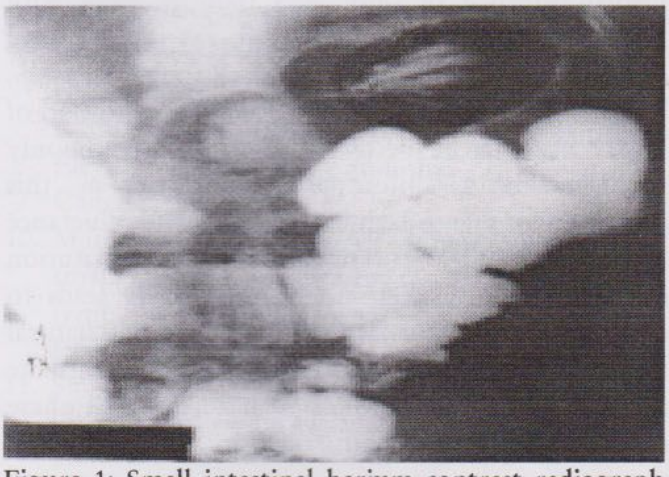

Figure 1: Small intestinal barium contrast radiograph showing marked asymmetric dilation, possible sacculation, and loss of the normal cross-markings of the intestinal folds

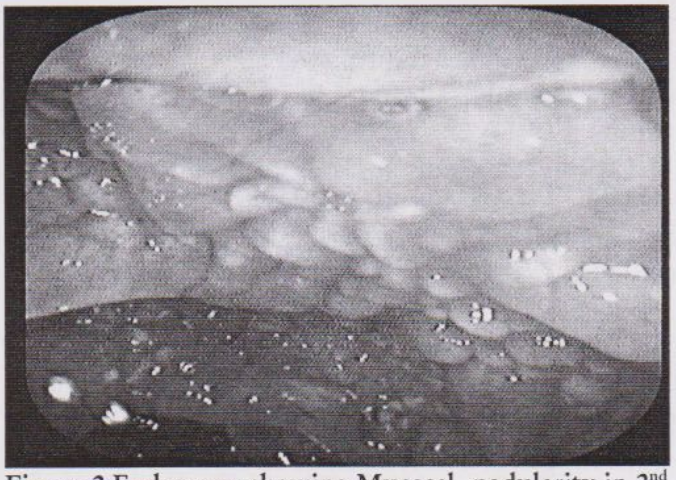

Figure 2:Endoscopy showing Mucosal nodularity in 2nd part of duodenum.

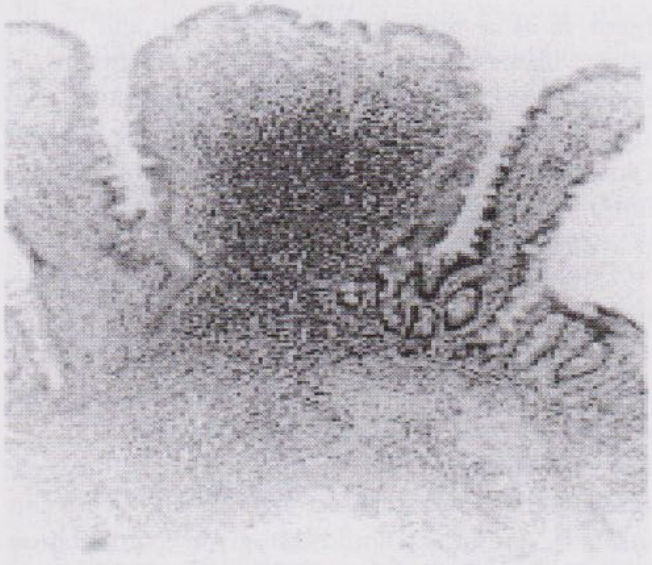

Figure 3: Jejunal mucosa, revealing villus widening and dense lymphoplasmocytic infiltrate of the lamina propria extending into the basal muscularis. Preservation of the columnar shape and scalloping of the enterocyte layer are notable (magnification ×100).

The differential diagnosis usually includes chronic parasitic infestations, celiac sprue, tropical sprue, AIDS enteropathy, Whipple's disease and lymphomas other than IPSID, because all of these can be associated with villus changes and increased infiltration of the lamina propria with round cells .[8, 19] But there are subtle but distinct differences in the

histology between these diseases when interpreted in the light of clinical information.

Staging for IPSID has not been uniformly defined, although

the most commonly used system consists of early benign (stage A), late benign (stage B), and lymphomatous categories (stage C). Once malignancy develops, IPSID lymphoma can be divided into four stages of involvement: I) the intestine or the mesenteric lymph nodes, II) intestine and the mesenteric lymph nodes, III) retroperitoneal extra-abdominal lymph nodes and IV) noncontiguous non lymphatic structures .[5]

Because of the unclear etiology of this illness, therapy has been empirical and only indifferently successful. The experts who approach IPSID as an infectious disease recommend antibiotics; others regard it as a premalignant condition and prefer cancer chemotherapy .[5] Early treatment is recommended to control the symptoms and hopefully slow or prevent progression of the disease[20]

Tetracycline (1 g/day) has been reported to induce clinical, histological, and immunological remission in up to 40% of patients with prelymphomatous IPSID. [6,13,21] Some add metronidazole and/ ampicillin with tetracycline.[4] The more atypical the histology, the less the likelihood of a response to antibiotics.. Prednisone may be useful in early stages, but cyclophosphamide appears to be ineffective.[5]

Patients without marked improvement after a 6-month course of antibiotic or complete remission within 12 months should be given combination regimens that usually were similar to those used at the time for other forms of non-Hodgkins lymphoma with CHOP (cyclophosphamide, vincristine, doxorubicin, and prednisone) or COPP (cyclophosphamide, vincristine, procarbazine,and prednisone), MOPP (mustine, vincristine, prednisone, and procarbazine) chemotherapy [20,22] Chemotherapy was also recommended up front together with antibiotics for patients with advanced disease at presentation. The average overall complete remission (CR) rate using this regimen was around averaged 50 -64%.

Relapses of the low-grade IPSID may be controlled by antibiotics alone [28]. Whether maintenance antibiotic is necessary for a long period of time is not established. Lifelong suppression of antigenic stimulus has been proposed. In addition to clinical improvement and histologic tumor regression by serial jejunal biopsies, response can be roughly quantitated by estimating the serum level of HC protein.[20] Surgery is usually reserved for a palliation of obstructing tumor masses or as a diagnostic and staging procedure. [5]

Total abdominal radiation has been recommended in bulky abdominal disease with some reported remissions .[23] Unresponsive disease progresses relentlessly at a variable pace and most patients die of malnutrition, sepsis, intestinal obstruction, and other disabling complications secondary to massive involvement of the bowel and abdominal cavity by tumor. Intensive chemotherapy and autologous bone marrow transplantation was recommended for patients with advanced or refractory disease, but to our knowledge there are no reports in the literature demonstrating the utility of bone marrow or hematopoietic cell transplantation in IPSID[20].

In general, the prognosis, even in stage A, is poor and morbidity is high; unless the patient is one of the fortunate few who respond dramatically to antibiotics, lymphomatous conversion followed by death usually occurs within a few years. In general, in stage C patients, some small studies have shown a median survival of only 10.5 months, even with aggressive chemotherapy. Overall, the 3-yr survival rate for all stages is around 65% .[5]

The realincidence and the geographic distribution of IPSID need to be better defined. It is commonly misdiagnosed as intestinal tuberculosis in this subcontinent due to lack of awareness and reluctance to obtain small bowel biopsies. Empirical institution of anti-tubercular chemotherapy not only leads to delayed diagnosis but also possibly alters the natural history of the disease, resulting in an intermediate phase of amelioration followed by a terminal phase of lymphomatous transformation. The disease is therefore usually diagnosed at an advanced stage and hence is associated with a relatively poor outcome. We believe that further investigations of IPSID can yield additional information contributing to the understanding of the molecular biology as well as clinical aspects and managements of this disease in general.

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