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Nano-drugs: Perspectives and challenges

AKM Mosharrof Hossain

Solubility status ,sustained and targeted delivery to site of action , fluctuation of plasma drug concentration are main pharmacokinetic obstacles in pharmacotherapy. These challenge can overcome by new drug delivery system through fabrication of nanostructures involving nanotechnology.[1] Nanotechnology developed involving nanoparticles characterized by size with at least one dimension ranging from 100 to 500 nano metre in length (one billionth of metre).Optimum size of nanoparticles is 100nm.Nanotechnology applied in medicine (nanomedicine) could revolutionize path to detect and treat disease. Application of nanotechnology in medicine enable accurate and rapid diagnosis, targeted and effective drug delivery to site of action[2]. The nanopharmacology involve application of nanotechnology to improve pharmacodynamics and pharmacokinetic profiles of a drug.

Nanoparticles would revolutionize drug delivery allowing drug to be targeting hosts cell, like viruses, tumor cells ,leaving healthy tissue intact. Nanoparticle based drug formulation yielded scope to address and treat challenging diseases like AIDS, cancer. Through manipulation of molecular size and surface properties of nanoparticles, delivery of drug for longer period of time with less frequent dosing is targeted3.An ideal nanoparticle drug delivery system should reach, recognize ,bind and deliver loaded drug to specific pathological tissue , avoiding drug-induced damage to healthy tissue[3]. Nanoscale therapeutic system developed with aim to enhance permeability, bioavailability and plasma half life.[4,5]

Bypassing biological barriers such as biomembrane, blood brain barriers allow delivery of high drug concentration in target tissue in tumor site, ischemic tissue, organ inflamed areas[3,6].Targeted and sustained drug delivery would decrease drug toxicity and increase patient compliance as well provides advancement in diagnostic technique[3]. Small size, large surface area of nanoparticles yield increased solubility, thereby bioavailability, can cross biomembranes e.g. blood brain barrier, pulmonary system, tight junction of skin endothelium[3]. Nanomaterial- based immunotherapy represents a novel approach in diagnostic testing, nutraceutical delivery ,treatment of AIDS, cancer, autoimmune diseases.[7,8] Lipid-and polymer-based nanocarriers contain biodegradable and biocompatible nanomaterials used for delivery of cancer drugs , genes . Nanoparticles will also be able to deliver heat, light or other substances to specific types of cells, such as cancer cells. Carbon nanotubles inserted into cancer cells emit infrared laser light resulting heating up, selectively kill cancer cells, while leaving healthy cells intact.

Nanoparticles of polymer, useful in transport of wide range of anticancer drug, geneticmaterials, peptides, proteins.Liposomes, spherical vesiclescomposed of phospholipid or cholesterol deliver both lipo- and hydrophilic substances.Liposomes drug delivery system usually target directly to tissue .It can be applied in delivery of vaccine, antibodies,nucleic acid ,anticancer drugs.Liposome also improve receptor -mediated anticancer drugs. PEGylated liposomes make liposomes less vulnerable to immune system,render pharmaceutical advantages[10]. Taken orally nanoparticles can pass through intestinal lining to reach bloodstream allowing administration of drug like insulin , vaccine without use of needles.

Nanoparticles demonstrated significant advancement in potential oral delivery of insulin .Encapsulated lipid-polymeric nanopartices provide insulin stability and transportation through intestinal mucosa . Sponge like nanomaterial surrounds an insulin core, which expands and contract in response to blood sugar level to release insulin as needed[11]. Nanodrugs are also potential to be used as diagnostic imaging agent ,implantable materials ,tissue regeneration[10] They have 'theranostic' capabilities (used for both diagnostic and therapeutic purposes .Silver nanoparticles are used as dental plaque ,biofilm, treatment of infected wound, catheter dressing for their antimicrobial properties[12]. Nanoparticle-based delivery system attempt for respiratory, oral, blood brain barrier crossing system developed to allow a targeted and controlled release of drug .Through manipulation of molecular size and surface properties of nanoparticles, delivery of drug for longer period of time with less frequent dosing is targeted[3].

Nanomaterial based biosensors have been developed for early detection of neurodegenerative diseases, cardiovascular diseases, cancer . It might be an ultimate solution to growing a global threat for resistance to antibiotics and cancer chemotherapy. Nanoparticles are potentially toxic. Nanomaterials can enter body through

many portals as skin, respiratory tract, gastrointestinal tract , through injection routes[13]. Nanopharmacological products might exhibit nanotoxiciy and environmental risk. Nanoparticles crosses blood brain barrier may cause brain tissue toxicity. Titanium used as dental implant , cardiac stent may provoke, reactive oxygen species generation with inflammatory responses[10], immuntoxicity and genotoxicity[14]. Nanomaterials may change epigenetic regulatory mechanism involved in pathogenesis of cancer[15]. Superparamagnetic iron oxide nanoparticles (SPIONs) used as MRI diagnostic agent , drug carrier appears as epigenetic toxic[16]. Nanoparticles may adversely affect blood platelet function and vascular hemostasis[17]. Organic biodegradable nanoparticles would confer lesser concern compared to inorganic non-biodegradable nanoparticles. It is early to comment on risk and safety aspect with use of nano-pharmaceuticals.

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ORIGINAL ARTICLE

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Antimicrobial Resistance of ESBL producers and non-producers in Urinary Isolates of Escherichia coli & Klebsiella species in a Tertiary Care Hospital of Sylhet.

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Abstract

Antimicrobial resistance is a mounting threat and most important challenge to the control of infectious diseases both globally as well as locally in Bangladesh. There have been significant changes in the antimicrobial resistance patterns of uropathogens over the years including resistance due to extended-spectrum ?-lactamase (ESBL) producing strains. But published data on the existence and magnitude of ESBL production in urinary pathogens in local setting is limited. This study was carried out to determine the prevalence of antimicrobial resistance among ESBL producers and non-producers of Escherichia coli and Klebsiella species isolated from urine samples obtained from outdoor and indoor patients at Sylhet MAG Osmani Medical College Hospital, Sylhet, Bangladesh from 1st January to 31st December 2016. A total of 200 clinically suspected urinary tract infection patients aged 16-85 years were included in this study. Out of 58 isolates, ESBL producing organisms were detected in 34 (58.6%). ESBL-producing Escherichia coli strains were significantly more resistance to all the antibiotics used in this study except amikacin (95.5%), ciprofloxacin (86.4%) and cotrimoxazole (81.8%) than strains that did not produce ESBL. The antibiotic ampicillin and cefuroxime were 100% resistant to both ESBL-producing and non-producing Escherichia coli and Klebsiella species. Moreover, both ESBL producing and non-producing Klebsiella species showed highest resistance (100%) to all the 3rd generation antibiotics (cefotaxime, ceftriaxone, ceftazidime) and cotrimoxazole. But, non-ESBL-producing Klebsiella species were more resistant to all the antibiotics than ESBL-producing strains except imipenem (85.7%), nitrofurantoin (71.4%) and ciprofloxacin (42.7%)($p<0.001$). Almost all the ESBL-producing and non-ESBL-producing isolates were multidrug resistant making available therapeutic choices very difficult. We recommend continued antibiotic resistance surveillance as well as comprehensive multi-center studies to address the emerging problem of ESBL-associated infections in order to preserve the continued usefulness of most antimicrobial agents.

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Introduction

Antimicrobial resistance from selective pressure of antimicrobial agents can spread by virtue of the rapid replication rates of microorganisms and the efficient transfer of antimicrobial resistant genes via the process of conjugation whereby plasmids are exchanged among microbes[1,2]. The link between inappropriate use of antimicrobials and development of antimicrobial resistance has been acknowledged in different scientific studies and global proceedings.

In Bangladesh, prescribers generally diagnose microbial infection on clinical judgment and select antimicrobials on empirical basis, which adversely affects the sensitivity pattern of microbes[3]. Urinary Tract Infections (UTIs) are one of the most common bacterial infections, both in the community and in hospital settings with almost 150 million diagnosed cases each year. From a microbiologic perspective, UTI exists when pathogenic microorganisms are detected in the urine, urethra, bladder, kidney, or prostate. In most instances, growth of 105 organisms per milliliter from a properly collected midstream "clean-catch" urine sample indicates infection[4]. Typical organisms causing UTI in the community include Escherichia coli derived from the gastrointestinal tract (about 75% of infections), Proteus species, Pseudomonas species, streptococci and Staphylococcus epidermidis.

In hospital, Escherichia coli still predominates, but Klebsiella or streptococci are more common[5]. There have been significant changes in the antimicrobial resistance patterns of uropathogens over the years including resistance due to extended-spectrum lactamase (ESBL)-producing pathogens[6-7]. The increasing prevalence of infections caused by antibiotic- resistant bacteria makes empirical treatment of these infections difficult.

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Antibiotic resistance varies according to geographic locations and is directly proportional to the use and misuse of antibiotics[8,9]. Emergence of resistance to lactam antibiotics began even before the first lactam, penicillin, was developed. The lactamase was first identified in Escherichia coli prior to the release of penicillin for use in medical practice. Many genera of Gram-negative bacteria possess a naturally occurring, chromosomally mediated lactamase.

The first plasmid-mediated lactamase in Gram negatives, TEM-1, was described in the early 1960s. The TEM-1 enzyme was originally found in a single strain of Escherichia coli isolated from a blood culture of a patient named TEMoniera in Greece, hence the designation TEM[10,11]. Another common plasmid-mediated lactamase found in Klebsiella pneumoniae and Escherichia coli is SHV-1 (for sulphydryl variable). The SHV-1 lactamase is chromosomally encoded in the majority of isolates of Klebsiella pneumoniae but is usually plasmid-mediated in Escherichia coli11.[11] Over the last 20 years, many new lactam antibiotics have been developed that were specifically designed to be resistant to the hydrolytic action of lactamases. One of these new classes was the oxyimino-cephalosporins, which became widely used for the treatment of serious infections due to Gram-negative bacteria in the 1980s[11]. Because of their increased spectrum of activity, especially against the oxyimino-cephalosporins, these enzymes were called extended-spectrum lactamases (ESBLs).

Today, more than 200 different types of ESBLs have been reported around the world; they were often identified in Enterobacteriaceae family[10,11,12] Extended-spectrum lactamases producing bacteria produce ESBL enzymes that mediate resistance to extended-spectrum (third generation) cephalosporins (e.g., ceftazidime, cefotaxime, ceftriaxone etc.), and monobactams (aztreonam) by hydrolysis of these antibiotics but do not affect cephamycins (e.g., cefoxitin & cefotetan) or carbapenems (e.g., meropenem & imipenem) and which are inhibited by lactamase inhibitors such as clavulanic acid, sulbactam and tazobactam. [10,11,13] The appearance of antibiotic resistance caused by ESBLs in the management of UTIs is a serious public health issue, particularly in the developing world where there is high prevalence of questionable quality drugs in circulation as well as irrelevant use of antimicrobial agents.

Therefore, treatment of a UTI patient with an antibiotic to which the organism is resistant results in high rates of microbiological and clinical failure and leads to additional morbidity and costs. In order to have adequate information for treatment of bacterial infections especially ESBL-producing isolates, it is crucial to find the trends in the antibiotic resistance pattern, occurrence and their geographical spread. Considering these above backgrounds, this study was designed to determine the antimicrobial resistance of ESBL-producers and non-producers isolated from patients with UTI in a tertiary care hospital.

Materials & Methods

This was a prospective and cross sectional study conducted at Department of Microbiology, Sylhet MAG Osmani Medical College, Sylhet from 1st January to 31st December 2016. The protocol was approved by the Ethical Review Committee of Sylhet MAG Osmani Medical College, Sylhet, Bangladesh and informed written consent was taken from patients before collection of their sample. A total of 200 consecutive clean-catch midstream and/or catheter-catch urine samples were collected from clinically suspected patients of UTI of different age and sex either visited the outpatient department (OPD) or admitted in inpatient department (IPD) of the hospital was the study population during this period. Patients were advised to collect clean-catch midstream or catheter-catch urine into a sterile wide mouth container with all aseptic measures.[14]

Culture of urine

Culture of urine: The specimens were inoculated on the labeled Blood agar and MacConkey agar media (Himedia, Mumbai, India) plates by using calibrated wire loop of holding 0.004 ml of well mixed un-centrifuged urine. Culture plates were incubated aerobically at 37°C for 18-24 hours. A growth of ?105 colony forming units per ml of one type of organism was considered as significant bacteriuria. Identification of Escherichia coli and Klebsiella species isolates was done by observing colony morphology on Blood and MacConkey agar media. Lactose-fermenting colonies were further identified performing standard biochemical tests as described by Collee et al.[15]

Antimicrobial Susceptibility Test

Samples which showed significant colony count were taken into consideration and sensitivity pattern of the isolated Escherichia coli and Klebsiella species was tested for antimicrobial susceptibility by the modified Kirby-Bauer disc diffusion technique as described by CLSI[16] (Clinical and Laboratory Standards Institute, former NCCLS). As per CLSI guidelines susceptibilitywas noted as sensitive (S), intermediate sensitive (I) and resistant (R) based on the diameter of zone of inhibition. The following first and second line antibiotic

discs (Himedia, Mumbai, India) were used in the testing: cotrimoxazole (25 µg), ampicillin (10 µg), gentamicin (15µg), amikacin (30µg), ceftazidime (30µg), cefotaxime (30µg), ceftriaxone (30µg), cefuroxime (30µg), imipenem (10µg), ciprofloxacin (5µg), netilmicin (30µg) and nitrofurantoin (300 µg).

Reading & interpretation

After overnight incubation, each plate was examined and diameter of the complete zones of inhibition was measured in mm with the help of scale placed under surface of the Petri dish. Zone of inhibition was measured in two directions of right angles to each other through the center of each disc and the average of the two readings were taken and compared with standard. The zone of inhibition in growth produced by each antimicrobial agent on the test organisms were compared with that produced on the control organisms.[16]

Detection of ESBL

A) Primary ESBL Screening Test (Phenotype): Escherichia coli and Klebsiella species isolates which were resistant to first line antibiotics (Ampicillin, Cotrimoxazole, Gentamicin, Amikacin, Nitrofurantoin) and 3rd generation cephalosporins (ceftriaxone, cefotaxime and ceftazidime) were suspected to be ESBL producers. Isolates with reduced susceptibilities to ceftriaxone (zone diameter of <25 mm), and/or cefotaxime (zone diameter of <27 mm) and/or ceftazidime (zone diameter of <22 mm) were provisionally regarded as ESBL-producing pathogens according to guidelines for laboratory detection of ESBL from Clinical and Laboratory Standards Institute. Every isolate that showed resistance to at least one of the screening agents was tested for ESBL production. The use of more than one of these agents for screening improves the detection of sensitivity.

B) Phenotypic Confirmatory Disc Diffusion Test (PCDDT): All the strains which screened out for the ESBL production were subjected to confirmation by using the PCDDT, as recommended by the Clinical and Laboratory Standards Institute. In this test, cefotaxime (30 µg) and ceftazidime (30 µg) discs alone and in combination with clavulanic acid (cefotaxime + clavulanic acid, 30/10µ g and ceftazidime + clavulanic acid, 30/10µg) discs (Himedia, Mumbai, India), were applied onto a plate of Mueller Hinton Agar (MHA) which was inoculated with the test strain. An increase of 5 mm in the zone of inhibition of the combination discs in comparison to that of the cefotaxime and ceftazidime disc alone were considered to be a marker for ESBL production.[16]

Quality control

As per manufacturer's instruction, the discs were stored in refrigerator between temperatures 2-80C up to date of expiry. Discs from each batch was standardized first by testing against reference strain of Escherichia coli ATCC 25922 (non-ESBL producer) used as negative control and Klebsiella pneumoniae ATCC 700603 (ESBL producer) used as positive control collected from BSMMU, Shahbag, Dhaka.

Statistical analysis

All Data were processed and analyzed with the help of SPSS (Statistical Package for Social Sciences) Version 23.0. Qualitative data were analyzed by frequency and percentage and comparisons were performed by Pearson's Chi square (χ^2) test. A probability value ($p<0.05$) was considered statistically significant.

Results

During the study period, a total of 58 isolated and indentified Escherichia coli and Klebsiella species were further tested to observe the production of ESBL. Of 58 isolates, 34 (58.6%) isolates were ESBL producers and 24 (41.4%) were non-ESBL producers (Figure 1). ESBL producer were tested for their susceptibility to third generation cephalosporin. ESBL-producing Escherichia coli were significantly more resistant to ceftazidime (96.3%), cefotaxime (92.6%) and ceftriaxone (77.8%) than non-ESBL producing strains ($p < 0.001$).The antibiotic ampicillin and cefuroxime were 100% resistant to both ESBL-producing and non-producing Escherichia coli. Non-ESBL-producing Escherichia coli showed more resistance to amikacin, ciprofloxacin and cotrimoxazole (95.5%, 86.4% & 81.8%) than ESBL-producing strains (11.1%, 70.4%, 70.4%).

Resistance to imipenem was significantly higher in ESBL-producing Escherichia coli strains than non-ESBL producing strains (59.3% vs. 31.8%, $p < 0.001$) as showed in figure II. Both ESBL producing and non-ESBL-producing Klebsiella species showed highest resistance (100%) to ampicillin, cotrimoxazole, cefuroxime, and 3rd generation antibiotics (cefotaxime, ceftriaxone, ceftazidime). Klebsiella species showed least resistance to netilmicin (11.1%) and that was non-ESBL producer. Non-ESBL-producers Klebsiella species were significantly more resistant to all the antibiotics used in this study than ESBL-producer strains except amikacin and gentamicin ($p<0.001$) as depicted in figure III.

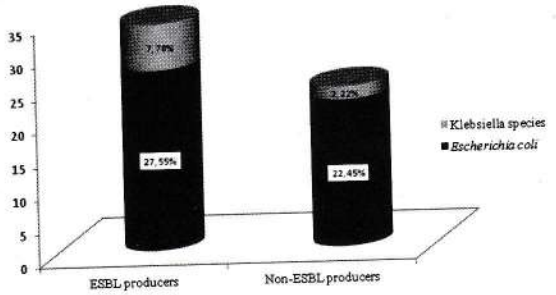

Figure I: Frequency of ESBL producers and non-producers organisms.

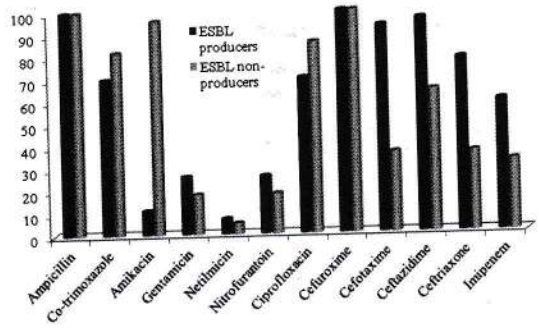

Figure II: Antimicrobial resistance of ESBL producers and non-producers of Escherichia coli.

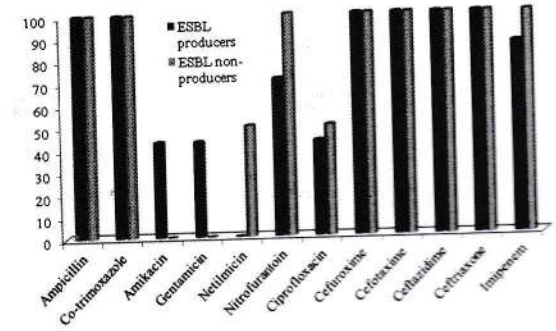

Figure III: Antimicrobial resistance of ESBL producers and non-producers of Klebsiella species.

Discussion

Satisfactory information on local antimicrobial resistance patterns among urinary isolates is vital not only in guiding clinicians to prescribe appropriate antibiotics but also for evidence-based recommendations in empirical antibiotic treatment of UTI. In this study, the antimicrobial resistance rate of ESBL producers and non-producers of isolated Escherichia coli and Klebsiella species was found to be very high to ampicillin, cefuroxime, cotrimoxazole and ciprofloxacin. High resistance to first line drugs found in the current study is similar to other studies in developing countries [17,19]. The observation may be due to wide empirical use, excessive and injudicious use of these drugs because they are relatively cheap and being oral antibiotics easy to administer.

Surprisingly, it was observed that rate of resistance towards cefuroxime in ESBL producers & non-producers of both isolated Escherichia coli and Klebsiella species was absolutely high. In the year 2015, another study by Haque et al.[20] recorded 78.8% & 63.6% respectively of these urinary isolates resistant to cefuroxime whereas, present study yielded that value of 100% in both isolates. This finding is supported by the study of Davi and Rajkumar (2013)[21] and Ndugulile et al. (2005)[19] who showed 94% and 100% of urinary isolates were resistant to cefuroxime respectively. Carelessness misuse, erratic use and improper use of this drug for a long period in our country would have been thought as the cause of this rapid emergence of absolute cefuroxime resistance.

Urinary isolates of Escherichia coli of the present study showed low resistance (22.5%) against nitrofurantoin. Although the value was slightly higher compared to Haque et al. (2015)[20] (16.1%) but still it remains as most sensitive drug and similar results were also reported from others studies [22,23]. The reason behind this might be due to low use of this drug for long period considering its toxicity and side effects. With sensitivity rate of 74.1% for ESBL-producing isolates nitrofurantoin might be the only useful oral antibiotic in the treatment of uncomplicated UTI and prophylaxis in the context of gradually decreasing susceptibility of the most of the comparatively cheaper anti-UTI drugs.

In the present study, isolated Escherichia coli showed second highest sensitivity (77.5%) against gentamicin though ESBL producers were found more resistant (25.9%) than non ESBL producers (18.2%). This finding was similar with the study done by Moyo et al[24]. (2010). Moreover, Gajamer et al. (2015)[17] and Masud, Afroz and Fakruddin (2014)[25] recorded 67.7% and 79.5% sensitivity respectively in their studies. Although our study did not found same values as compared to the above mentioned studies but trend of effectiveness of gentamicin towards Escherichia coli is similar.

The explanation for this sensitivity would be due to the fact that gentamicin is available only in injectable form and three times daily dose schedule. So, its use especially in community by rural practitioners is somehow restricted due to low acceptability of injection to the

patients and dose inconvenience. This minimal use might have caused lowering of resistance. ESBL-producing Escherichia coli and Klebsiella species showed significantly high resistance to ciprofloxacin (77.6% & 44.4% respectively). These findings are similar to the result of Sarkar et al. (2015) [26] who found similar resistance pattern (78.9% & 64% respectively). Besides, there are more studies [26,27] with similar results indicating high level resistance to ciprofloxacin. This increased resistance may be due to widespread indiscriminate use, their oral route of administration, easy availability and affordability of ciprofloxacin over the country. So, physicians should prescribe this drug with caution to preserve its effectiveness.

In our setting, netilmicin was the most sensitive antibiotic (resistant rate 6.12% & 11.1% respectively) for both ESBL-producing & non-producing Escherichia coli and Klebsiella species to treat the UTI patients. As increased amikacin resistance showed in this study by 49%, netlimicin may be an alternative parental drug for the treatment of complicated UTI in the local setting, at least in a tertiary health facility [28]. ESBL-producing Escherichia coli and Klebsiella species in this study showed a significantly high rate of resistance to non-beta-lactam antibiotics. These findings are similar to those reported by others [19, 29].

This observation may be explained by the fact that ESBL are plasmid-mediated enzymes which are transferable between one bacterium to another and such transferable plasmids also code for resistance determinants to antimicrobial agents other than beta-lactams [30]. In our setting, we found imipenem had lost its sensitivity (40.7% & 14.3% respectively) in both Escherichia coli and Klebsiella species. Our result in ESBL positive Klebsiella species regarding resistance pattern of imipenem is similar with the works done in India and Iran [31,32] where incidences of carbapenem-hydrolyzing enzymes amongst Enterobacteriaceae has been reported. Carbapenems are used to treat life threatening infections caused by MDR bacterial pathogens and antibiotics in this class represent the last line of therapy in treatment options against very serious infections such as those caused by ESBLs. However, carbapenem-resistance has also been reported elsewhere as an increasing public health problem that should be dealt with holistically [32,33]

The resistance of ESBL-producing Enterobacteriaceae (including Escherichia coli and Klebsiella pneumoniae) to carbapenems (as predicted in our study) is worrisome and of clinical and microbiological importance because such pathogens are usually resistant to a host of beta-lactam antibiotics and they may also carry genes that confer on them co-resistance to non-beta-lactam antibiotics as well. Reduced imipenem susceptibility has been described in Escherichia coli with CTX-M type ESBL [34]. Therefore, further studies are needed for molecular characterization of ESBL isolates circulating in our setting. Recently, the co-existence of both AmpC beta-lactamase and ESBL in some Gram-negative bacilli has also been reported. This could be due to plasmid-mediated AmpC beta-lactamase has been disseminated among the Enterobacteriaceae, sometimes in combination with ESBL[18]. Such strains may give false negative tests in the detection of ESBL. In our setting, we observed that in Escherichia coli, some non-ESBL-producers were more resistant than ESBL producer strains and in Klebsiella species, ESBL-producers were less resistant than non-ESBL-producers ($p>0.05$). These similar findings also observed in a study done by Dalela et al. (2012)[35].

Conclusions

High prevalence of ESBL-producing Escherichia coli and Klebsiella species strains was found among inpatients and complicated UTI patients. Antibiotic resistance is becoming an emerging problem for the public health which threatens the lives of hospitalized individual as well as those with chronic condition. It is quite alarming to note that almost all the ESBL producer and non-producer isolates in this study were found multidrug resistant making available therapeutic choices very difficult. Therefore, routine screening of extended-spectrum β-lactamase (ESBL) detection should be mandatory in all tertiary care hospitals. Regular antibiotic surveillance and comprehensive multi-center studies should be conducted to address the emerging problem of ESBL-associated infections in order to preserve the continued usefulness of most antimicrobial agents. Further studies should be made to evaluate the molecular characteristics of ESBL isolates to guide appropriate and judicious antibiotic use.

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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 16 Number 2

Doppler ultrasound and clinical evaluation of Peripheral Arterial Diseases in Sylhet region of Bangladesh.

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Abstract

Doppler ultrasound scan is a non-invasive and cheap tool that complements the roles of computed tomography (CT), magnetic resonance imaging (MRI) and angiography in the screening, diagnosis and follow-up of many vascular diseases. Purpose of this study was to determine the usefulness in the exploration of peripheral arterial disease with the help of Doppler ultrasound. All the findings of peripheral arterial Doppler ultrasound examinations were performed at Radiology and imaging Dept. of Sylhet MAG Osmani Medical College Hospital and two other non-government diagnostic clinics during a period of 18 months (July 2013 to December 2014) were reviewed. The findings of 90 patients (62 male and 28 female) within age range (21-90 years) having suspicion of peripheral arterial disease were reviewed. Diabetic foot disease intermittent claudication, gangrene and limb swelling were the most common indication for arterial Doppler examination, constituting 28.6%, 37.7%, 14.4% and 15.5% respectively. Total luminal occlusion, significant luminal stenosis, insignificant stenosis were the frequent findings, constituting 26.6% 28.8%, 18.8% respectively. 12.2% cases showed normal. Below knee arteries & femoro-popliteal arterial segment were commonly involved by these abnormalities. Incidental findings includes venous thrombosis, arterio-venous malforamation (AVM) hemangioma and popliteal cysts. Diabetes, hypertension, hyperlipidaemia and smoking were the frequents associated problems of these patients. Doppler ultrasound has a high diagnostic yield in depicting abnormalities in patients with clinical features of peripheral arterial disease.

[OMTAJ 2017; 16 (2)]

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Introduction

The diagnosis of diseases involving peripheral arteries can usually be made on the basis of a thorough history & physical examination[1]. Additional testing is usually required for further characterization and/or quantification of the pathologic process. Ultrasound scan is noninvasive and cheap tool for vascular examination of the peripheral arteries. It is currently competing and complementing the roles of computed tomography (CT), magnetic resonance imaging (MRI) and angiography. Compare to angiography duplex imaging was able to detect arterial disease within over all sensitivity of 92%, specificity of 99% positive predictive value of 91% and negative predictive value of 100%.[2]

In addition to determination of structural anatomical lesion, application of Doppler modes allows determination of functional status of the vessels by measuring the flow velocities & extent of vascular compliance.[3] Symptoms of peripheral arterial disease are becoming more important due to rising incidence of the disease & the risk factors, such as diabetes, hyperlipidaemia, smoking and sedentary life styles. Clinical indication for peripheral arterial color duplex imaging are intermittent claudication, limb rest pain, abnormal peripheral pulses, arterial trauma & gangrene or tissue necrosis, as well as follow up therapeutic intervension4. As a result of limited availability of other diagnostic tool such as CT, MRI and angiography in many developing countries, ultrasound is gaining importance.[4]

Therefore, this early experience describes the spectrum of abnormalities detectable by color Doppler examination of peripheral arteries at radiology and imaging department of Sylhet MAG Osmani Medical College Hospital and two other non-government diagnostic clinics, Sylhet. We also analyzed the clinical presentation of the patients with their corresponding findings on Doppler sonography.

Materials and Methods

It was a prospective longitudinal study. The study was carried out Radiology & imaging Department of Sylhet MAG Osmani Medical College Hospital and two other non-government diagnostic clinics in Sylhet city from

July 2013 to December 2014. During the review period a total 245 scans were conducted in the hospital & clinics, among the 90 cases were selected which have specific request for peripheral arterial examination. The records of the socio-demographic characteristics of the patients, the clinical symptoms and risk factors for the development peripheral arterial disease, site of the examination and the source of the patients were documented on the data collection sheet. There after examination of relevant lower limb (right or left) were done with the patient lying supine or prone position using 7.5 MHz linear transducer connected to LOGIC p5 ultrasound imaging system (GE Co. Ltd, USA) and VOLUSION p8 machine, occasionally 3.5 MHz convex transducer of the same machine was used (to optimise the depth) in obese patients and those with severe subcutaneous oedema.

Following application of water soluble gel, ultrasound scan was started with grey scale mode to demonstrate clarity of the lumen, presence or absence of plaques and calcification. Color Doppler scans were done to the arteries to document the presence or direction of the blood flow. Spectral Doppler measurements were done on each of the major arteries, obtained following the application of angle-corrected sampling gate at the centre of the color map of the artery. Further more, lowest possible filter, highest gain below noise level and the smallest scale were selected to avoid aliasing.

The height of the Doppler waveforms was maximized to facilitate measurement. After obtaining contiguous spectral tracing automatic velocity measurement peak systolic velocity (PSV), end diastolic velocity (EDV) and corresponding resistive indices were obtained using in-built electronic calipers. The scan was considered normal if the artery showed normal caliber, uniform color flow & consistent typical triphasic waveform. (Fig I) The artery was considered to have a haemodynamically significant stenosis in the presence of either (or combination) of the followings : Luminal diameter reduction by at least 50%, sudden marked increase in PSV (of more than 100% of the expected) at the area of narrowing and presence of "parvus tardus" pattern in the distal run-off arteries as illustrated in (Fig 2). The artery was considered to be totally occluded if there was no demonstrable blood flow with power Doppler mode (Fig III)

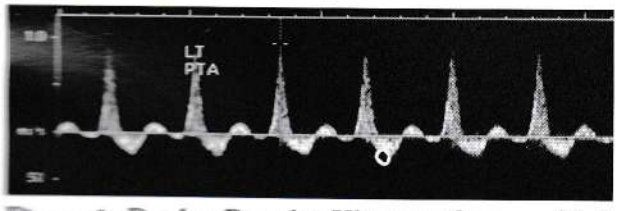

Figure 1: Duplex Doppler Ultrasound scan of left posterior tibial artery with normal triphasic flow.

The examination was also extended to external iliac arteries. In addition, complementary corresponding venous examinations were conducted on each limb to detect asymptomatic incidental abnormalities such as deep venous thrombosis (DVT) & abnormal dilatation of superficial venous channels (varicosity). All examination were performed (by at least a consultant radiologist) with patient lying calmly on the examination table & each examination was conducted over a minimum 20 min or more. The informed verbal consent was taken from the patients and their confidentiality was maintained. The study protocol was reviewed by the Ethical Committee of Sylhet MAG Osmani Medical College.

Results

Distribution of vascular ultrasound examination at radiology and imaging Department of Sylhet MAG osmani Medical College Hospital and two other non-government diagnostic clinics.

During review period a total of 245 scans were conducted, Among them 90 cases were selected which show specific request for peripheral arterial examinations (Table 1) making up 36.7% of all vascular examination and constitute the sample of the study. Others include 110 peripheral venous scan (44.8%), scrotal scan 30 (12.2%) carotid 10 (4.08%) and renal Doppler 05 (2.04%)

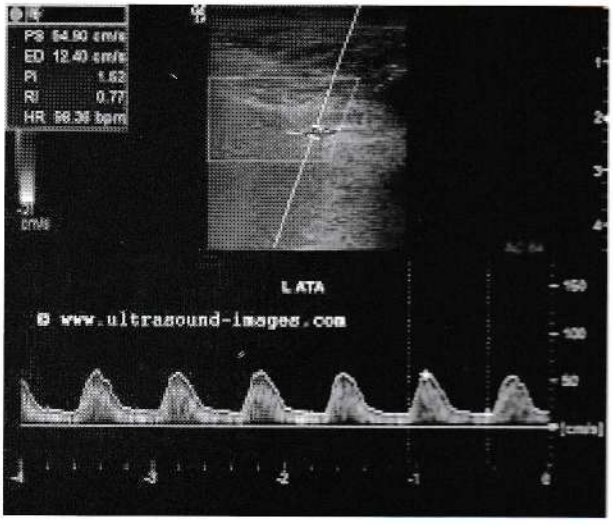

Figure- III: Doppler ultrasound scan of left anterior tibial artery showing Tardas parvus waveform due to proximal obstruction.

Table I : The distribution of vascular ultrasound examinations.

Examination	Frequency	Percentage
Peripheral venous	110	44.8%
Peripheral Arterial	90	36.7%
Scrotal/testicular	30	12.2%
Carotid	10	4.08%
Renal	05	2.04%
Total =	245	100

Demographic and clinical characteristics of the patients :

Their ages ranged from 21 to 90 years. They consist of 62 male (68.8%) and 28 female (31.2%). Maximum number of patients are within the age ranged of 50-70 years with mean age of 55.6 yr which constitute about 57.7%. The incidents are lower in the early age between 21-30 years which constitute 6.6%. (Table 2) As shown in Table 3, The frequency of indication of diabetic foot syndrome with non-healing ulcer 25 (28.6%), Intermittent claudication 34 (37.7%), limb pain swelling 14 (15.5%), Gangrene 13 (14.4%), others 04 (4.4%). Others include, trauma and a clinical suspicion of peripheral vascular disease.

Table II : The distribution of the patient according to their age : (n= 90)

Age	No of patient	Percentage
21 -30 yrs	06	6.6%
31 -50 yrs	21	23.3%
50 -70 yrs	52	57.7%
70 -90 yrs	11	12.2%
Total =	90	100

Table III: The clinical data necessitating the Doppler scan (n= 90).

Clinical History	Frequency	%
Diabetic foot disease	25	28.6%
Intermittent Claudication	34	37.7%
Limb pain & swelling	14	15.5%
Gangrene	13	14.4%
Others	04	4.4%
Total =	90	100

Relationship of Doppler ultrasound findings with risk factors :

Multifactorial (diabetes, hyperlipidaemia, hypertension) risk factors is the most common cause for developing peripheral arterial disease constitute 32 (35.5%), single common most risk factors was smoking 15 (16.6%) is revealed in Bangladesh for peripheral arterial disease. Incidental findings were deep venous thrombosis (DVT) 03 (6.66%) was found in this study. Other incidental findings were (AVM) 02 (2.22%), haemangioma 05 (5.55%) and popliteal cyst 02 (2.22%). About 20 cases were found had no positive risk factors. Trauma also cause a risk factors for peripheral arterial disease. (Table 4).

Table IV : The relationship Doppler ultrasound findings with risk factors (n =90)

Risk Factors	PAD	VT	AVM	PC	H	N	T
Multi factors	32						32
Diabetes	12	03					15
Hyperlipidaemia	06						06
Smoking	15						15
Trauma	02						02
None			02	02	05	11	20
Total =	67	03	02	02	05	11	90

PAD : Peripheral Arterial Disease, **VT :** Venous Thrombosis, **AVM :** Arterio-venous malformation, P. C : Popliteal cyst, **H :** Haemangioma, **N :** Normal, **T :** Total.

Doppler Ultrasound Findings

The findings of the arterial Doppler examination are show in Table 5.

It revealed total luminal occlusion 24 (26.6%) with 26 patient having signification stenosis (28.8%) insignificant stenosis 17 (18.8%), while 11 (12.2%) patient showed normal findings. Other findings include arterio-venous malformation (AVM), haemangioma, popliteal cyst which collectively constitute (13.3%). The territorial of arterial involvement are illustrated in Table 6. Multiple below knee arteries constitute 26 (28.8%), Isolated superficial femoral artery occlusion 18 (20%) popliteal artery 18 (20%) Iliofemoral 05 (5.5%) and normal in all arteries is 11 (12.2%).

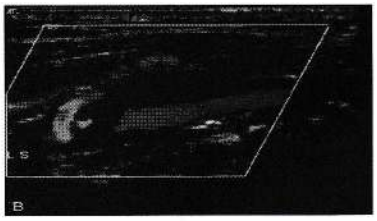

Fig III: Duplex ultrasound scan showing complete luminal occlusion of superficial femoral artery.

Table V : The spectrum of Doppler ultrasound findings in these patients

Doppler findings	Frequency	Percentage
Total Occlusion	24	26.6%
Significant Stenosis	26	28.8%
Insignificant Stenosis	17	18.8%
AVM	02	2.22%
Haemangioma	05	5.5%
Popliteal Cyst	02	2.22%
Venous Thrombosis	03	3.33%
Normal	11	12.2%
Total =	90	100

Table VI : The frequency of arterial territorial involvement

Arterial segment	Frequency	%
Iliofemoral	05	5.5%
superficial femoral artery	18	20%
Popliteal Artery	18	20%
Multiple below knee arteries	26	28.8%
Normal	11	12.2%
Others	12	13.3%
Total =	90	100

Discussion

Color duplex sonography is useful to identify, localize and grade the arterial luman narrowing due to peripheral vascular disease. This study include 90 scan out of 245 scan requisition for color duplex study, which constitute about 36.7% of all vascular ultrasound examination.

The mean age of 55.6 years in these patients peripheral arterial disease This is as demonstrated by Shaheen and Shoail5 in their review of 100 diabetes with peripheral arterial disease of about 55.5 yrs. Ascher et al[6] also documented the mean age of 55 years in their review of 68 patients with acute lower limb arterial ischaemia.

As shown in this review, the relative high frequency of diabetic foot disease, intermittent claudication and frank gangrene underscores the magnitude of these problems in the arena of peripheral vascular disease in our environment.

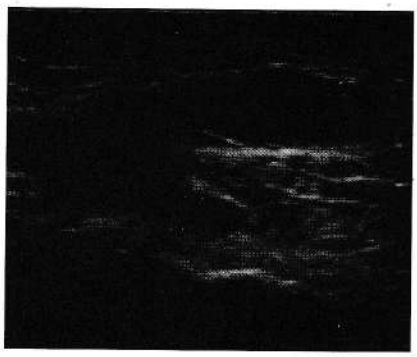

Fig IV: Color Doppler sonogram shows incidental findings of popliteal cyst.

Doppler evidence of vascular abnormalities was found in 74.4% with clinical suspicion of peripheral arterial disease, while 13.3% showed other vascular problems and 12.2% were normal. This is mild higher than the study done by Shaheen and Shohail[5], they showed 62%. This disparity may be from the differences in the experiences of the radiologists may also increase the sensitivity of ultrasound results as well as differences in the characteristics of the study subjects.

On the other hand, this disparity may imply a possible higher prevalence of peripheral vascular disease in our local environment compared to theirs. This study showed complete luminal stenosis (26.6%), significant luminal stenosis (28.8%) and no gender preponderance. This findings agree with those of Collins et al[7] in their study on gender and peripheral arterial disease, found no significant difference by gender in the prevalence of peripheral arterial disease. Though they did not use of Doppler ultrasound in their research. As shown our result multiple below knee arteries 28.8%, femoro popliteal arteries 45.5% were involved. This pattern slightly differ from the report of Guo et al.[8] on 162 diabetics with arterial lesions, they showed below knee arteries preponderance is higher than femoro popliteal segment arteries.

Nevertheless their study uses diagnostic angiography while this study was done with Doppler ultrasound. The findings showed multifactorial risk factors (eg diabetes hyperlipidaemia, hypertension) cause high magnitude of peripheral arterial disease of about 55.5% corresponds of typical patients with peripheral arterial disease. While smoking is the single most common risk factors 16.6% is revealed in Sylhet, north east, Bangladesh. This findings support the works done by Edith et al[9], they found in peripheral arterial disease (PAD) 2.6 factors higher in smokers than the nonsmokers. The emphasis on diabetes in peripheral arterial disease by the fact that diabetes important contributor of foot ulcer and gangrene leading to lower extremity amputation.[10,11] The high percentage

of significant luminal stenosis in claudicating patients showed the relative high sensitivity of Doppler ultrasound in detecting the arterial lesions.

As illustrated by Aly et al[2] duplex imaging can detect arterial disease with an overall sensitivity of 92% specificity of 99% positive predictive value of 91% and negative predictive value of 100% when compared with angiography. In conclusion Doppler ultrasound examination in experience hand proves to be highly effective modality for the diagnosis of peripheral arterial disease, having claudicating limb pain, swelling, foot ulcer and gangrene. It is noninvasive, nonionsing and cheap tool for the patients prior to go angiography, stenting or surgery. Our study showed high diagnostic yield of Doppler ultrasound in depicting abnormalities in patients with clinical features of peripheral arterial disease.

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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 16 Number 2

Laparoscopic Hernia Repair versus open herniotomy in Children - A randomized controlled study.

Md Shamsur Rahman[1], Md Sirazul Islam[2], Md Ibrahim Khalil [3], Sayed Sharif Ul Alam[4]

Abstract

Laparoscopic inguinal hernia repair in children was started over two decades ago and it has been gaining popularity day by day. There were several emerging laparoscopic techniques with trends toward extracorporeal suturing and knotting technique, single-port access technique as well. In this study A prospective randomized controlled study was carried out in the Pediatric Surgery department of Sylhet M A G Osmani Medical College Hospital and two other private hospitals in Sylhet, Bangladesh from July 2015 to June 2017. One hundred and twenty-four patients with Inguinal Hernia (IH) were randomized into two equal groups by a random-number table sequence after taking a written informed parental consent . Group A (n = 62) was subjected to laparoscopic assisted inguinal hernia repair by Spinal Needle (20 G) and Group B (n = 62) was subjected to open herniotomy (OH). Results were satisfactory in Group-A. So laparoscopic inguinal hernia repair by Needle assisted extracorporeal knotting technique can be an alternative of open herniotomy in children.

[OMTAJ 2017; 16 (2)]

Introduction

Inguinal hernia is one of the most common surgical conditions in infants and children. Over the past few decades, inguinal exploration with clear dissection of the hernial sac off the vas deferens and spermatic vessels and secure high ligation of the patent processus vaginalis (PPV) herniotomy, has remained the gold standard treatment. There are controversies regarding the management strategy for a possible contralateral patent processus vaginalis (20%) that may develop into a subsequent hernia. Recently, many centers routinely perform laparoscopic hernia repair in children and there have been numerous reports describing various laparoscopic techniques rather than the traditional open approach[1,2,3,4]

Laparoscopic hernia repair also allows contra-lateral patent process vaginalis (PPV) hernias to be defined and repaired in the same operation[5,6,7] . Routine exploration of the contra-lateral side, as has been adopted by some workers, may result in a significant proportion of un-necessary inguinal explorations, along with the potential complications. Randomized control study of laparoscopic hernia repair versus OH in pediatrics is rare in the literature[8,9,10] . This paper presents a big series and describes a new technique which is the use of Spinal Needle in laparoscopic hernia repair in comparison with OH. To the best of our knowledge, this technique has not been reported before in our country.

So, this prospective randomized controlled study was conducted to compare laparoscopic assisted hernia repair by Spinal Needle with OH in infancy and childhood as regards operative time, hospital stay, postoperative hydrocele formation, recurrence rate, iatrogenic ascent of the testis and cosmesis.

Pathophysiology

The processus vaginalis is an outpouching of peritoneum attached to the testicle that trails behind as it descends retroperitoneally into the scrotum. Failure of obliteration of the processus vaginalis causes inguinal hernia. In case of children there is always indirect inguinal hernia occurs because the contents passes through the deep inguinal ring and exit through superficial inguinal ring (Figure 1A & 1B).

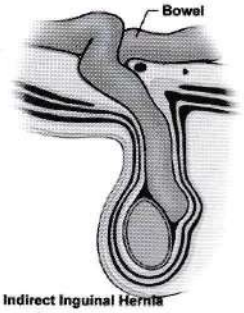

Figure : I A

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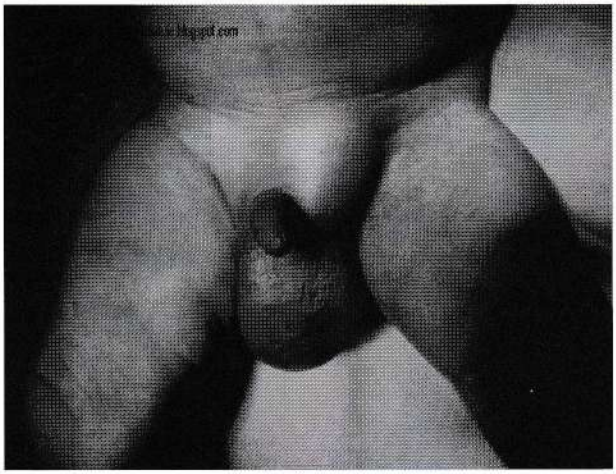
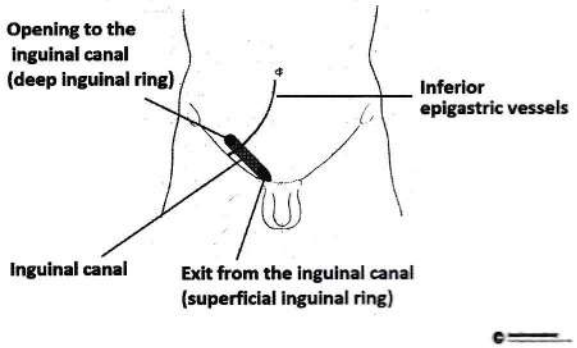


Figure : IB

In the female embryo, the ovaries descend into the pelvis but do not leave the abdominal cavity. The upper portion of the gubernaculum becomes the ovarian ligament, and the lower portion becomes the round ligament, which travels through the inguinal ring into the labium majora. If the processus vaginalis remains patent, it extends into the labium majora and is known as the canal of Nuck. Failure of obliteration of canal of Nuck causes hernia.

Anatomy of inguinal canal in children



Specialty of Inguinal ring in children

In the newborn child, the deep ring lies almost directly posterior to the superficial ring so that the canal is considerably shorter at this age

Incidence

Incidence of inguinal hernia in infant and children is about 1-5%.Indirect hernias are more common on the right side because of delayed descent of the right testicle. Right sided inguinal hernias are common (60%) than left side(30%). Incidence of bilateral inguinal hernia is about 10% and male to female ratio is 8:1.

Patients and Methods

A prospective randomized controlled study was carried out in the Pediatric Surgery department of Sylhet M A G Osmani Medical College Hospital and two other private hospitals in Sylhet, Bangladesh over two years period. One hundred and twenty-four patients with IH were randomized into two equal groups by a random-number table sequence after taking a written informed parental consent . Group A (n = 62) was subjected to laparoscopic assisted inguinal hernia repair by Spinal Needle (20 G) and Group B (n = 62) was subjected to open herniotomy. The demographic data were matched between both groups (Table 1).

Table I: The demographic data for the two groups.

Groups	Group-A	%	Group-B	%	Total	p-value
Sex: Male	47	75	53	85	100 (80%)	0.48**
Female	15	25	09	15	24 (20%)	
Age/months :						
i.1-12	08	12.9	16	25.8	24 (19.3%)	
ii. 12-24	22	35.4	20	32.2	42 (33.8%)	0.80**
iii.>24	32	51.6	26	41.9	58 (46.7%)	
Presentation						
i.Unilateral	32	51.6	45	72.5	77(62%)	
ii. Bilateral	20	32.2	06	9.6	26 (20.9%)	
iii.Recurrent	01	1.6	01	1.6	02 (1.6%)	
iv.Inguinal hernia with umbilical hernia.	02	3.2	06	9.6	08 (6.4%)	0.18**
v.Inguinal hernia with questionable other side.	07	11.2	04	6.4	11(8.8%)	

** Insignificant.

All children were subjected to full history taking, thorough clinical examination, routine laboratory investigations, and inguino-scrotal U/S.

The main outcome measures were operative time, hospital stay, postoperative hydrocele formation, recurrence rate, iatrogenic ascent of the testis and cosmesis. All operations were done by the first author, and a senior resident holds the camera. In group A, after induction of general endo-tracheal tube anesthesia, the patient was placed supine in Trendelenburg's position. Insertion of the main umbilical port was accomplished by the open method. Pneumo-peritoneum was established to a pressure of 8 to 12 mm Hg.

Laparoscopy was used for initial visualization of the pelvis and internal inguinal rings (IIRs) on both sides. Laparoscopic Needle assisted hernia repair was done according to standard technique described in literatures[11] A 3mm Maryland forceps was inserted into the abdomen with trocar at the lateral border of the rectus muscle just above the level of the umbilicus.

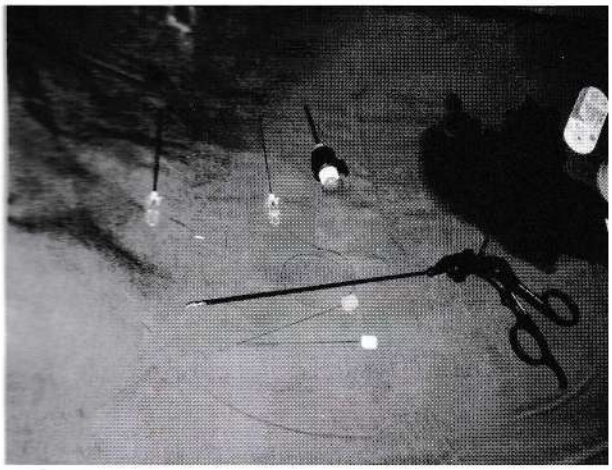


Figure IIA

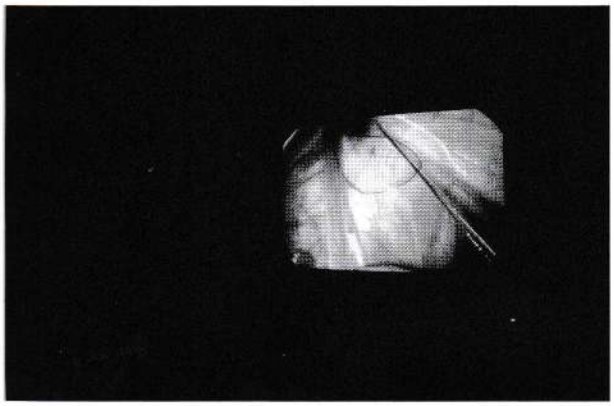


Figure IIB

Insertion of Needle on the right side

A stab incision of the skin was done just above the internal inguinal rings on the right side, and also at the same level on the left side when required . A 3/0 prolene suture was anchored with the 1st Spinal needle (Figure-IIA) and then the needle was manipulated to pierce the skin and fascia over the internal inguinal rings and was advanced to pass through the lower margin of internal inguinal rings under the peritoneum and in front of the spermatic vessels and vas to pierce the peritoneum.

Care was taken to avoid injury of the spermatic vessels, and vas by grasping and lifting the peritoneum with Maryland forceps. The loop of prolene was hold by Maryland forceps and the needle was withdrawn backward in the same path. Then the 2nd Spinal Needle was loaded with 3/0 vicryl and inserted at the previous stab incision site, advanced along the upper margin of the IIR beneath the peritoneum and fascia transversales to come into the peritoneal cavity through previous entry point. Prolene loop was spread into the peritoneal cavity, short end of the thread was inserted (Figure-IIB), needle was withdrawn and vicryl was pulled outside the abdominal cavity along with prolene loop for extracorporeal suture tie. Before tightening the knot, the scrotum was squeezed and the intra-peritoneal pressure was released to expel the gas from the hernial sac.

A contra-lateral internal ring with a patent processus vaginalis (more than 2mm) was regarded as a possible cause of developing clinical hernia and repaired at the same time. The skin incisions were closed with Steri-strips. All patients were followed up in the out-patient clinic after 7 days, 2 weeks and 3 months. Parents were advised to contact with the department of pediatric surgery, if there were any concerns in the immediate postoperative period. All patients resumed normal activities within 6 hours after surgery. All patients had uneventful postoperative recoveries and were discharged on the 1st post-operative day.

Statistical Analysis

The collected data were organized, tabulated, and statistically analyzed using Statistical Package for Social Science (SPSS) version 16 (SPSS Inc., USA). Qualitative data, frequency, and percent distribution were calculated and Chi square test was used for comparison between groups. Quantitative data, mean, standard deviation (SD), and range were calculated, and for comparison between two groups, student's (t) test was used. For interpretation of results, $P < 0.05$ was considered significant.

Results

One hundred and twenty four patients with inguinal hernia were operated upon by 2 different techniques. Group A (n = 62) was subjected to laparoscopic assisted inguinal hernia repair by Spinal Needle and Group B (n = 62) was subjected to open herniotomy. There were 100 males and 24 females. The youngest was 5 months and the oldest was 96 months, given an overall mean age of 61.56 ± 28.32 months.

All procedures of group A were completed laparoscopically without any conversion. No intra-operative complications occurred during this study.

In group A the patients resumed normal activities within 6 hours after surgery, whereas in patients of group B they resumed normal activities within 08 hours. All patients had uneventful postoperative recoveries and were discharged on the 1st post-operative day. The mean hospital stay was 12 ± 3.23 hours after operation with no significant difference between both groups. There is

significant statistical difference between the studied groups as regards operative time (Table II).

Table II: Distribution of operative time in studied group

Groups	Group-A	Group-B	P-value
Unilateral	7.6 +3.5 min	12.8+4.5 min	<0.001*
Recurrent unilateral	9.2+4.6 min	14.3+3.6 min	<0.001*
Bilateral	11.4+2.7 min	21.9+7.2 min	<0.001*

*Significant

One patient developed hydrocele in the early postoperative follow-up period in group A, while in group B, postoperative hydrocele was reported in 2 cases. However, all cases responded well to conservative management within 2 weeks (Table 3).

Table III: Post-operative complications in studied groups.

Groups	GroupA	%	GroupB	%	P value
Hydrocele	01		02		0.52**
Recurrence	01		01		o.31**
Iatrogenic ascent of the testes	00		02		o.049*
Ugly scar	00		03		0.024*

*Significant, ** Insignificant.

Over a mean follow-up period of 24 months (range of 16-30 months), the recurrence rate was 1.6% (one case) in each group (Table 3). In group A, there were no cases of iatrogenic ascent of the testis, while in group B, 2 cases (3.22%) developed iatrogenic ascent of the testis.
The early cosmetic results for bilateral cases were excellent in group A(Figures 3(A) and 3(B)). At a follow-up examination more than 6 months later, there were practically no visible scars in group A, while in group B 3 cases had ugly scars as reported by parents (Figure 4). The umbilical scars were not visible in all of the patients of group A.

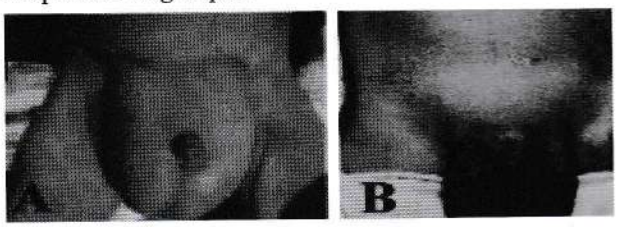


Figure: IIIA and IIIB

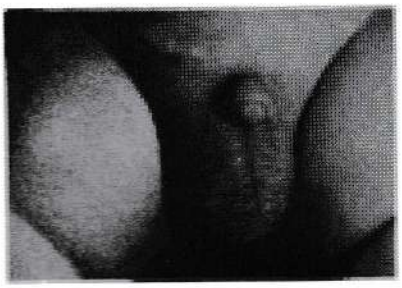


Figure: IV

Discussion

In children, the standard surgical treatment of IH is limited to division and ligation of the hernial sac at the IIR without narrowing the ring[5] . Open herniotomy is an excellent method of repair in the pediatric population. However, it has the potential risk of injury to the spermatic vessels or vas deferens, hematoma formation, wound infection, iatrogenic ascent of the testis, testicular atrophy, and recurrence of hernia. It also carries the potential risk of tubal or ovarian damage which may cause infertility [12,13,14]

Laparoscopic approach is rapidly gaining popularity with more and more studies validating its feasibility, safety, and efficacy [5,15]. Laparoscopic hernia repair in children is known to take longer operative time than OH. Many reports showed that it ranged from 20 to 74 minutes [5,17,18,19]. However, the operative time is reduced with experience.

In laparoscopic surgery, approaching the hernial defect from within the abdomen, makes the area of interest bloodless, and the magnification renders anatomy very clear, making surgery precise.[13,15,20] In our series the operative time is less than that reported in the literature as we use an easy simple and rapid technique for repair of IH using Spinal Needle which can be done within a very short time. Also, we used the extracorporeal suture ligation which is less time consuming[21]

Open herniotomy in children has been reported to have recurrence rates of 0.8-3.8%[8]. While in laparoscopic hernia repair it is ranged from 0.7% to 4.5%. That is may be due to the presence of skip areas during placement of purse-string sutures as well as the tension resulting from intracorporeal knotting particularly in closure of large defects. The critical steps of hernia sac neck transaction at the IIR were not achieved in many laparoscopic procedures unlike during OH. Thus, transient or persistent hydrocele was unavoidable after these laparoscopic techniques .

The natural history of the PPV in infants remains a controversial topic. Prior studies indicate that 40% of PPVs close spontaneously by two months of age and 60% by 2 years of age; however, the risk of incarcerationis highest during infancy, while insome other series PPVs

less than 2mm were not closed[6]. Our approach has been to ligate all PPVs to avoid the development of metachronous hernia. However, more studies are needed to clarify this point. five-millimeter and 3 mm incisions in group A were indeed cosmetically more appealing compared with 2 cm incisions during OH in group B. All parents were satisfied with the cosmetic results of group A.

The potential risks of open herniotomy in Males are injury to the spermatic vessels or vas deferens, Hematoma formation, wound infection, Iatrogenic ascent of the testis, testicular atrophy and recurrence (0.8 - 3.8%) And that of Female are, tubal or ovarian damage which may cause infertility. Advantage of laparoscopic hernia repair are excellent visual exposure, the ability to evaluate the contra lateral side, minimal dissection and avoidance of access trauma to the vas deferens and testicular vessels, less chance of Iatrogenic ascent of the testis and less operative time .

Conclusion

The result of conventional open herniotomy is similar to that of laparoscopic hernia repair. Laparoscopic assisted inguinal hernia repair is feasible, safe and rapid technique which reduces operative time , recurrences , testicular atrophy, iatrogenic ascent of the testis and ensure cosmesis .Contra-lateral Patent processus vagainalis found in 20% cases & best option for detection and repair of CPPV is Laparoscopy. Long-term follow-up is needed to determine the validity of this technique.

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ORIGINAL ARTICLE

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Efficacy and Safety of Topical 1% Butenafine Cream in Tinea Corporis: An Open clinical Trial

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Abstract

This open clinical trial was conducted among 60 patients, diagnosed clinically to have localized tinea corporis and confirmed on KOH examination, were assigned to butenafine once daily for 2 weeks. Follow-up was done at 1, 2, 4 weeks (2 weeks after the cessation of treatment). Clinical assessment score at each visit and KOH examination were performed at 2 and 4 weeks. Fifty one patients completed 2 weeks treatment with 30 (58.8%) male and 21 (41.2%) female. Mean age was 33.47 ± 10.5 years. The mean clinical assessment score was declined from 6.69 ± 1.13 at baseline to 3.96 ±1.15 at week one, 0.80 ± 1.13 at week 2 and 0.35 ± 0.80 at week 4 which was statistically significant (p<0.001). The improvement of clinical score was from baseline to 41.46 ± 7.70 percent at week one; 91.36 ± 13.06 percent at week 2 and 95.29 ± 9.55 percent at week 4 which was statistically significant (p<0.001). Clinical cure rate was 68.6% at 2nd week and 84.3% at 4th week. Mycological cure was 96.1% at 2nd week and 98.0% at 4th weeks. Recorded side effect was transient burning sensation in 4 (7.8%) cases. In conclusion single daily application of butenafine cream is highly effective and a favourable safety profile in the treatment tinea corporis. Key words: Tinea corporis, butenafine, efficacy, safety.

[OMTAJ 2017; 16 (2)]

Introduction

Dermatophytoses is a geographically widespread group of fungal infections caused by dermatophytes.[1] Predominance of type depends on the organism, its hosts, and local factors. Infection may occur through contact with infected humans and animals, soil, or inanimate objects.[2] Its prevalence is much higher in developing than in industrialized countries.[3-5] The most common factors affecting the distribution and transmission of dermatophyte infections are climatic conditions, general hygiene, and animal contact.[6,7]

Tinea corporis and tinea cruris are the commonest varieties of dermatophytosis, followed by tinea pedis, capitis, barbae, unguium and manuum in a descending order of frequency. Several antimycotic agents, including the imidazoles and triazoles, have been used for tropical treatment of dermatomycoses.[8] The ideal topical therapeutic agent for localized superficial fungal infections should have broad-spectrum fungicidal activity, efficacy at low concentration, convenient dosing, keratophilic and lipophilic properties, a reservoir effect in stratum corneum, high mycological and clinical cure rates, lack of development of fungal resistance, low relapse rates, low incidence of adverse effects, and should be economically viable.[9]

Butenafine and the allylamines act at an earlier stage in the ergosterol biosynthesis pathway and do not inhibit the cytochrome p450-dependent enzymes which have an interaction with the azoles; therefore, butenafine would not be expected to manifest some of the adverse events reported with the oral azoles, for example an effect on adrenal corticosteroid production reported at the higher doses of ketoconazole.[10] Butenafine cream 1% was approved in Japan in 1992 for the treatment of some superficial mycoses. It was later approved in the USA in 1996 for the treatment of tinea pedis, tinea cruris and tinea corporis.

For these indications butenafine cream has high efficacy with a favorable adverse-effects profile[11-13] . Efficacy of topical 1% butenafine once daily for 2 weeks and 1% clotrimazole twice daily in tinea cruris and tinea corporis exhibited higher clinical cure as compared with clotrimazole recipients at the end of 1 week (26.5% vs 2.9%) as well as higher mycological cure (61.7% vs 17.6%).[9] The efficacy of topical 1% butenafine in tinea corporis is not extensively done in our country. So, this study was designed to evaluate the efficacy of topical 1% butenafine in tinea corporis.

Materials and Methods

The study was an open clinical trial conducted in the Department of Dermatology and Venereology, Sylhet M

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A G Osmani Medical College, Sylhet from January 2017 to September 2017. Sixty patients with localized tinea corporis aged 18 years or above were included. The clinical diagnosis was confirmed by the presence of branched, septate fungal hyphae on microscopic examination of lesional skin scrapings in 10% KOH. Pregnant and lactating females, patients with extensive (>20% of skin surface) tinea, concurrent skin diseases which could interfere with the clinical evaluation on subsequent visits, or with other severe systemic diseases were excluded from the study.

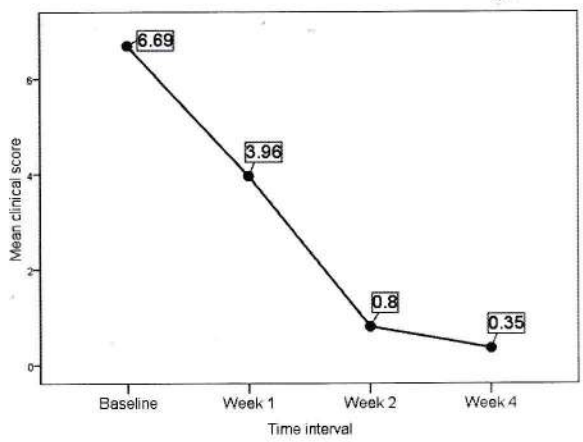
Informed written consent was obtained from the patients after full explanation of the details of the disease process, options of treatment, ultimate outcome and possible side effects. At the initial visit, all the study patients underwent detailed physical and cutaneous examination. All clinical details were recorded on a predesigned proforma. The severity of signs and symptoms of tinea corporis such as pruritus, erythema and burning were graded on a scale ranging from 0-3 where 0.0 (absent); 1.0 (mild); 2.0 (moderate) and 3.0 (severe).[8] The individual symptom scores were added and a total score (clinical assessment score) was recorded, with a maximum additive score of 9. Lesional skin scraping in 10% KOH was performed to confirm the presence of fungal hyphae.

All patients were instructed to apply butenafine 1% cream once daily for 2 weeks. Patients were followed up after 1, 2 and 4 weeks (2 weeks after the cessation of treatment). At each visit, clinical examination was carried out, any adverse events were recorded clinical assessment score was calculated, and KOH smear was repeated at 2nd week and 4th week. Microscopic examination (10% potassium hydroxide) of a skin scraping from the same site of the lesion was performed at baseline and at scheduled follow up.

Assessment of drug efficacy was based on 10.0% KOH reading at the end of the study period and was defined as follows: (1) mycologic cure pathogen conversion Negative on 10.0% KOH reading and (2) mycologic failure Positive on 10.0% KOH reading.[8] Clinical efficacy was categorized as (1) cure (disappearance of all baseline signs and symptoms of infection; negative 10.0% KOH reading) (2) improvement (improvement in or partial disappearance); (3) failure (no change or worsening); or (4) relapse (improvement or cure followed by reappearance or worsening).[8] During the course of treatment and follow up 9 patients were lost. Results were analysed as per protocol using SPSS (Statistical Package for Social Science) version 22. The p-value was calculated using the repeated measure ANOVA. The level of significance was set to 0.05.

Results

The age of the patients ranged from 18 to 60 years with the mean age of 33.47 ± 10.5 years; 19 (37.3%) patients in the age group of 21-30 years, 16 (31.3%) patients in the age group of 31-40 years, 7 (13.7%) patients in the age group of 41-50 years, 6 (11.8%) patients in the age group of 18-20 years and 3 (5.9%) patients in the age group of 51-60 years. There were 30 (58.8%) male and 21 (41.2%) female with a ratio of male to female was 1.4:1. The mean clinical assessment score was declined from 6.69 ± 1.13 at baseline, to 3.96 ±1.15 at week one, 0.80 ± 1.13 at week 2 and 0.35 ± 0.80 at week 4. Clinical assessment score declined from baseline to end of the treatment period was statisticallysignificant ($p<0.001$) (Figure-1). The improvement of clinical score was from baseline to 41.46 ± 7.70 percent at week one; 91.36 ± 13.06 percent at week 2 and 95.29 ± 9.55 percent at week 4. Improvement of clinical score from baseline to end of the treatment period was statistically significant ($p<0.001$) (Figure-2). Clinical cure rate was 68.6% at 2nd week and 84.3% at 4th week. Mycological cure (negative KOH) was 96.1% at 2nd week and 98.0% at 4th week (Table-I). Recorded side effect was transient burning sensation at the application site of butenafine in the first week in 4(7.8%) which resolved on continuation of treatment and did not require discontinuation of therapy.



Repeated measure ANOVA was employed to analyse the data.

Figure I: Clinical assessment score at different interval (n=51)

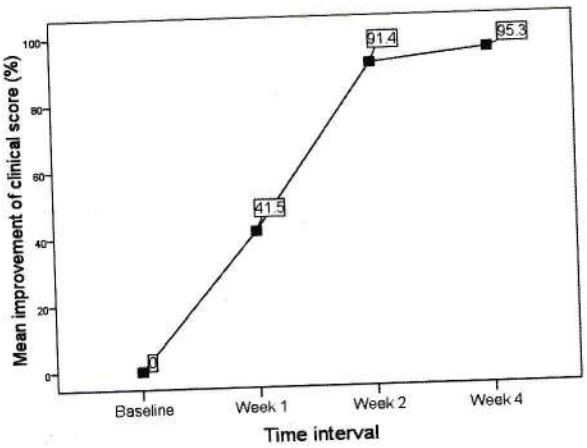


Figure II: Improvement at different time interval (n=51)

Table I: Efficacy of treatment measured at 2nd week and 4th week (n=51)

Efficacy	Week 2	Week 4
Clinical		
Cure	35 (68.6%)	43 (84.3%)
Improvement	16 (31.4%)	8 (15.7%)
Mycological		
Cure	50 (98.0%)	50 (98.0%)
Failure	1 (2.0%)	1 (2.0%)

Discussion

Superficial fungal infections (Dermatophytosis) of the skin are the most common among infectious diseases. These are more prevalent in tropical areas because of high temperature and relative humidity. The increasing prevalence of superficial fungal infections worldwide demands prompt attention and adequate treatment measures. The main classes of antifungal currently employed in the topical treatment of superficial fungal infections include the polyenes, the azoles, and the allylamines.[14] In this open clinical the efficacy of topical 1% butenafine in tinea corporis was evaluated. The age of the patients ranged from 18 to 60 years with the mean age of 33.47 ± 10.5 years. This result was supported by Pakshir and Hashemi,[15] in which mean age of the patients with dermatophytosis was 32 years.

This study also recorded 19 (37.3%) patients in the age group of 21-30 years, 16 (31.3%) patients in the age group of 31-40 years, 7 (13.7%) patients in the age group of 41-50 years, 6 (11.8%) patients in the age group of 18-20 years and 3 (5.9%) patients in the age group of 51-60 years. This result was in accordance with the study of Patel et al.[16] in which the commonest age group involved was 21-30 years in 58 (29.30%). There were 30 (58.8%) male and 21 (41.2%) female with a ratio of male to female was 1.4:1. Higher incidence of dermatophytes in male than in females has been reported both in India and abroad. Singh and Beena,[17] found male to female ratio of 1.75:1. Higher incidence in males could be due to greater physical activity and increased sweating. The lower incidence in females may be due to that female are less attended the hospitals due to the prevailing social stigma.

In the present study reduction of clinical assessment score from baseline to end of the treatment period was statistically significant ($p<0.001$) and the improvement of clinical score from baseline to end of the treatment period was statistically significant ($p<0.001$) were recorded in this study. This result was consistent with study of Singal et al.[9] This study revealed that clinicalcure rate was 68.6% at 2nd week and 84.3% at 4th week. Mycological cure (negative KOH) was 96.1% at 2nd week and 98.0% at 4th week. This result was consistent with the study of Singal et al.[9] The efficacy of topical 1% butenafine in the treatment of superficial fungal infections has been demonstrated in many studies. Butenafine was better than vehicle in treating interdigital tinea pedis,[11,13,18] as well as tinea corporis.[19]

Butenafine recipients had significantly higher rates of mycological cure at day 7 (64% vs 9%) with continued improvement through day 42 (88% vs 17%)[19]. The results of another study indicated that 1% butenafine applied once daily for 2 weeks is safe and effective in the treatment of tinea cruris and the proportion of patients cured increased between the end of treatment and 4 weeks post treatment.[12] The recorded side effect was transient burning sensation at the application site of butenafine in the first week in 4 (7.8%) but it resolved spontaneously and did not require discontinuation of therapy.

Similar things happened in other study in which 5.9% patients complained burning sensation at the site of application of butenafine at initial week, which resolved spontaneously while continued treatment and did not require discontinuation of therapy.[9] Limitations of the study were (1) single centre study and (2) sample size was small. In conclusion single daily application of butenafine cream is highly effective and a favourable safety profile in the treatment tinea corporis. However a large scale multicentre randomized control clinical trial was warranted.

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ORIGINAL ARTICLE

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Conjunctival Autograft Fixation using Autologus Blood Versus Sutures in Pterygium Surgery.

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Abstract

Various surgical procedures are used to treat pterygium. The excision of a pterygium with bare sclera was widely practiced because it was believed to be safe and simple but associated with unacceptably high recurrence rate ranging from 24% to 89%. During the past decade, pterygium surgery was centered on sutures and fibrin glue to affix the conjunctival graft but recent introduction of patient's own blood (autologous blood) for fixation of conjunctival flap has proven to be better over the previous two approaches. To see the outcome of conjunctival auto graft fixation using autologous blood and sutures in pterygium surgery. This prospective comparative study was conducted in the Department of Ophthalmology, Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from 1st January 2015 to 31st December 2016. After obtaining approval from the institutional review board and the ethics committee total 112 patients with primary pterygium, aged older than 18 years and both sex were included. Patients with corneal ulceration, corneal edema, uveities, pseudopterygium, pingueculum, recurrent pterygium, glaucoma, retinal pathology requiring surgical intervention, history of previous ocular surgery or trauma and those who have bleeding disorder were excluded. They were divided by random allocation into group-A and group-B each consisting 56 patients by odd number and even number respectively. The patients of group-A were treated with excision of primary pterygium with conjunctival auto graft fixation using autologous blood and that of group-B with excision of primary pterygium with conjunctival auto graft fixation using sutures. All surgical procedures were done under local anesthesia and done under a microscope. An attempted follow-up of cumulative 6 months (at postoperative 1 day, 1 week, 1 month, 3 months, and 6 months) was done to every patient. At each postoperative visit, thorough slit lamp examination, and any recurrence, complication(s), or any complaints were recorded. Statistical analysis of the data was performed. The mean age of the patients was 41.11 (SD 13.21) years in group-A and 39.68 (SD 13.54) years in group-B, difference was not significant ($p>0.05$). There were 44 (78.6%) male and 12 (21.4%) female in Group A; whereas 43 (76.8%) male and 13 (23.2%) female in Group B; difference was not significant ($p>0.05$). Operation time was 29.45 (S3.88) minutes in group-A and 37.68 (SD 2.35) minutes in group-B; significantly shorter in group-A than that of group-B ($p<0.001$). Subconjunctival haemorrhage, conjunctival congestion, loose graft, graft oedema and graft retraction at first postoperative day and at one week did not differ statistically significant between group-A and group-B ($p>0.05$). Conjunctival congestion was found significantly more in group-B than that of group-A at 1 month but not significant at 3 and 6 month of follow up. Granuloma formation did not differ significantly between group-A and group-B at 1 and 3 months but significantly higher in group-B than group-A at 6 months of follow up. No recurrence in any groups at 1 month, but recurrence at 3 month and at 6 month was 2 (3.6%) and 3 (5.4%) respectively in group-A; and 3 (5.4%) 4 (7.1%) respectively in group-B. The recurrence did not differ significantly between two treatment groups ($p>0.05$ each) at 3 and 6 months. Autologus blood used for autologous conjunctival graft fixation in pterygium surgery did not differ significantly compared to conventional sutures in pterygium surgery in terms of complications and recurrence.

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Introduction

A pterygium is a triangular fibrovuscular subepithelial ingrowth of degenerative bulbar conjunctival tissue over limbus onto the cornea[1]. Several hypotheses have been described to its etiology. Currently it is believed that

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the pterygium is a growth disorder characterized by conjunctivalization of the cornea due to localized ultraviolet produced damage to limbal stem cells[2]. Destructive pterygial fibroblasts are also responsible for corneal invasion[3]. Pterygium is more seen in men than in women. It is usually seen within the intrapalpebral fissure and most often from the nasal side[4]. The prevalence rate of primary pterygium varies from 0.7 to 31% in various populations around the world [5].

In early stage it is asymptomatic except some cosmetic blemish. Visual disturbance occur when it encroaches upon visual axis or induces corneal astigmatism[6]. The indications for surgery include reduced vision due to encroachment of visual axis and irregular astigmatism, chronic irritation, recurrent inflammation and restriction of ocular motility and cosmesis [2]. A pterygium is best left alone unless it is progressing towards the pupillary area cause excessive astigmatism, restriction of ocular motility, disfiguring, chronic irritation and cosmesis. Medical treatment consists of anti-inflammatory drugs and lubricants to minimize the patients discomforts but do not cure the disease.

Surgical removal is the treatment of choice. Surgical treatment options are (1) Simple excision with keeping bare sclera (2) Simple excision with Conjunctival autograft fixation (3) Simple excision with use of Mitomycin-C [7]. Simple excision has a recurrence rate of 24% to 89%. To overcome this, last two surgical techniques develops to minimize the recurrence. Conjunctival autograft fixation has been shown recurrence rate ranging from 2% to 39% after pterygium surgery.[7]

Use of patients own autologous blood was based on clotting mechanism of blood coagulation, but should be used before fibrinolysis occurs as blood clots naturally, was developed with all the drawbacks eliminated[8]. Auto blood no longer problem because puncture vessels leads to ooze if quantity of clot is inadequate, with this technique no mismatch, uncomplicated, easy availability, faster rehabilitation to patient[2]. The purpose of this study was to assess the outcome of conjunctival auto graft fixation by using autologous blood compared to that of sutures in pterygium surgery.

Methodology

This prospective comparative study was conducted in the Department of Ophthalmology, Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from January 2015 to December 2016. After obtaining approval from the institutional review board and the ethics committee, total 112 patients with primary pterygium, aged older than 18 years and both sex were included. Patients with corneal ulceration, corneal edema, uveities, pseudopterygium, pingueculum, recurrent pterygium, glaucoma, retinal pathology requiring surgical intervention, history of previous ocular surgery or trauma and those who have bleeding disorder were excluded. The following points were observed as under name, age, sex, address, occupation, history, general examination, local examination. Informed consent was taken from the patient before performing the surgery.

They were divided by random allocation into group-A and group-B each consisting 56 patients by odd number and even number respectively. The patients of group-A were treated with excision of primary pterygium with conjunctival auto graft fixation using autologous blood and that of group-B with excision of primary pterygium with conjunctival auto graft fixation using sutures.

Surgical procedure

All surgical procedures were done under local anesthesia and done under a microscope. After all aseptic precautionary, eyelid was separated by a speculum, and sub-conjunctival and subpterygial 0.5 ml lignocaine solution (xylocaine 2%) was injected. Gentle massage over the lesion was applied by cotton-tipped applicator for few seconds. The neck of the pterygium was then lifted up with the help of finetoothed forceps, while the head of the pterygium was gently avulsed from the cornea by placing closed tips of a curved corneal scissors. Gentle dissection was then carried out in-between the conjunctiva and the sclera with the help of crescent knife.

Neither cautery nor saline irrigation was used throughout the surgery, except active bleeding, with bi-polar cautery whenever required to check excess hemorrhage. The size of the bare sclera defect was then measured with Castroviejo calipers. Corneal care was taken by applying wet cotton throughout the procedure. Now, approximately 0.5 ml xylocaine 2% was used to balloon up a conjunctival flap. Corneal scissor was used to make a fine film of 0.5 mm oversized, free conjunctival graft, carefully avoiding inclusion of tenon, or making buttonhole within it.

The graft was then laid over the bare sclera ensuring same limbus to limbus orientation. We waited for 5 to 10 min for haemostasis to occur in group A patients. And fours end free conjunctival flap were sutured by 10/0 nylon in group B patients. All eyes were then patched for 24hrs with Chloramphenecol eye ointment. The eye was assessed for symptom, graft adherence, or any complication(s) under slit lamp. Postoperatively, patient was put on topical antibiotic and steroid combination for first 2 weeks thereafter tapered over

next 4wks. Thereafter, an attempted follow-up of cumulative 6 months (at postoperative 1 day, 1 week, 1 month, 3 months, and 6 months) was done to every patient. At each postoperative visit, thorough slit lamp examination, and any recurrence, complication(s), or any complaints were recorded. Statistical analysis of the data was performed.

Results

Table I: Showing Distribution of the Respondents According to Age (n= 112)

Age	Study Group		p-value
	Group-A(56) No (%)	Group-B(56) No (%)	
18-20 years	2 (3.6)	6 (10.7)	
21-30 years	10 (17.9)	13 (23.2)	
31-40 years	21 (37.5)	9 (16.1)	>0.05
41-50 years	11 (19.6)	18 (32.1)	
51-60 years	9 (16.1)	8 (14.3)	
>60 years	3 (5.4)	2 (3.6)	
Mean (SD)	41.11 (SD 13.21)	39.68 (SD 13.54)	> 0.05

The mean age of the patients was 41.11 (SD 13.21) years (range, 18 to 75 years) in group-A and 39.68 (SD 13.54) years (range, 34-68 years) in group-B. The difference was not differ significant (Z=0.565; p>0.05). Age distribution of the respondents was shown in table-I. In group-A 21 (37.5%) patients were between 31 to 40 years, 11 (19.6%) patients were between 41 to 40 years, 10 (17.9%) patients were between 21 to 30 years, 9 (16.1%) patients were between 51 to 60 years, 3 (5.4%) patients were above 60 years and 2 (3.6%) patients between 18 to 20 years. It was 9 (16.1%), 18 (32.1%), 13 (23.2%), 8 (14.3%), 6 (10.7%) and 2 (3.6%) respectively in group-B. There was no statistically significant difference of age of patients between group-A and group-B when categorized if different age group (2 =11.273; p>0.05).

Table II: Showing Distribution of the Study Subjects According to Sex (n=112)

Sex	Study subjects		*p-value
	Group-A(56) No (%)	Group-B(56) No (%)	
Male	44 (78.6)	43 (76.8)	>0.05
Female	12 (21.4)	13 (23.2)	
Total	56 (100.0)	56 (100.0)	

p- value is significant when p>0.05

Sex distribution of the study subjects was shown in table-II. In Group A, 44 (78.6%) patients were male and 12 (21.4%) patients were female. Whereas in Group B43 (76.8%) patients were male and the rest 13 (23.2%) patients were female. There was no statistically significant difference between group-A and group-B in respect to sex of the patients (χ^2=0.051; p>0.05).

Table III: Showing Recurrence Rate of Pterygium after Surgery (n= 112)

Recurrence		Study group		* p-value
		Group-A(56) No (%)	Group-B(56) No (%)	
At 1 month	Yes	0 (0.0)	0 (0.0)	
	No	56 (100.0)	56 (100.0)	
At 3 month	Yes	2 (3.6)	3 (5.4)	>0.05
	No	54 (96.4)	53 (94.6)	
At 6 month	Yes	3 (5.4)	4 (7.1)	>0.05
	No	53 (94.6)	52 (92.9)	

p- value is significant when p<0.05

Recurrence rate of Pterygium after surgery was shown in table IX. After 1 month, no recurrence of pterygium was found in any groups. At 3 months, recurrence of Pterygium was observed in 2 (3.6%) patients in group-A and 3 (5.4%) cases in group-B. The recurrence of Pterygium at 3 months did not differ significantly between two treatment groups (p>0.05). At 6 months, recurrence of Pterygium was recorded in 3 (5.4%) patients in group-A and 4 (7.1%) cases in group-B. The recurrence of Pterygium at 3 months did not differ significantly between group-A and group-B (p>0.05).

Table IV: Showing Distribution of Complications at First Post Operative Day (n= 112)

Complications at first post operative day	Study group		p-value
	Group (56) No (%)	Group (56) No (%)	
Subconjunctival haemorrhage	2(3.6)	0 (0.0)	>0.05
Conjunctival Congestion	56 (100.0)	56 (100.0)	
Loose graft	2 (3.6)	1 (1.8)	>0.05
Graft Oedema	12 (21.4)	15 (26.8)	>0.05
Graft retraction	5 (8.9)	6 (10.7)	>0.05
Scleral necrosis	0 (0.0)	0 (0.0)	
Abscess formation	0(0.0)	0 (0.0)	
Dalen formation	0 (0.0)	0 (0.0)	
Granuloma formation	0 (0.0)	0 (0.0)	
Conjunctival cyst	0 (0.0)	0 (0.0)	

p- value is significant when p<0.05

At first post operative day, all patients of both group showed conjunctival congestion. Recorded subconjunctival haemorrhage [2 (3.6%) versus 0 (0.0%), χ^2=2.036; p>0.05]; loose graft [2 (3.6%) versus 1 (1.8%); χ^2=0.343; p>0.05], graft oedema [12 (21.4%) versus 15 (26.8%), χ^2=0.493; p>0.05] and graft retraction [5 (8.9%) versus 6 (10.7%), χ^2=0.101; p>0.05] did not differ statistically significant between group-A and group-B. Distribution of complications at first post operative day was shown in Table IV.

Table V: Showing Distribution of Complications at One Week (n= 112)

Complications at one week	Study group		*p-value
	Group-A(56) No (%)	Group-B(56) No (%)	
Subconjunctival haemorrhage	0 (0.0)	0 (0.0)	
Conjunctival Congestion	56 (100.0)	56 (100.0)	
Loose graft	3 (5.4)	2 (3.6)	>0.05
Graft Oedema	3 (5.4)	6 (10.7)	>0.05
Graft retraction	3 (5.4)	0 (0.0)	>0.05
Scleral necrosis	0 (0.0)	0 (0.0)	
Abscess formation	0 (0.0)	0 (0.0)	
Dalen formation	0 (0.0)	0 (0.0)	
Granuloma formation	0 (0.0)	0(0.0)	
Conjunctival cyst	0 (0.0)	0 (0.0)	

p- value is significant when p<0.05

At 1 week, all patients of both group showed conjunctival congestion. Loose graft [3 (5.4%) versus 2 (3.6%); χ^2=0.209; p>0.05]; graft oedema [3 (5.4%) versus 6 (10.7%), χ^2 =1.087; p>0.05]; and graft retraction [3 (5.4%) versus 0 (0.0%), χ^2=3.083; p>0.05] did not differ statistically significant between group-A and group-B. Distribution of complications at 1 week was shown in table V.

Table VI: Showing Distribution of Complications at One Month (n= 112)

Complications at one month	Study group		p-value
	GroupA(56) No (%)	Group-B(56) No (%)	
Delayed healing	0 (0.0)	0 (0.0)	
Conjunctival Congestion	7 (12.5)	36 (64.3)	<0.01*
Dalen formation	0 (0.0)	0 (0.0)	
Granuloma formation	1 (1.8)	4 (7.1)	>0.05
Conjunctival cyst	0 (0.0)	0 (0.0)	
Haematoma formation	0 (0.0)	0 (0.0)	

* p- value is significant when p<0.05

At 1 month conjunctival congestion [7 (12.5%) versus 36 (64.3%), p<0.01] was found significantly more in group-B than that of group-A. But granuloma formation [1 (1.8%) versus 4 (7.1%), p>0.05] differ significantly. Whereas none of the patients had delayed healing, dalen formation, conjunctival cyst and haematoma formation. Distribution of complications at one month was shown in table-VI.

Table VII: Showing Distribution of Complications at 3 Month (n= 112)

Complications	Study group		p-value
	Group-A(56) No (%)	Group-B(56) No (%)	
Delayed healing	0 (0.0)	0 (0.0)	
Conjunctival Congestion	3 (5.4)	7 (12.5)	**>0.05**
Haematoma	0 (0.0)	0(0.0)	
Dalen formation	0 (0.0)	0 (0.0)	
Granuloma formation	1 (1.8)	5 (8.9)	**>0.05**
Conjunctival cyst	0 (0.0)	0 (0.0)	

At 3 month conjunctival congestion [3 (5.4%) versus 7 (12.5%), ?2=1.575; p>0.05] and granuloma formation [1 (1.8%) versus 5 (8.9%), ?2=2.818; p>0.05] did not differ significantly between group-A and group-B. Whereas none of the patients had delayed healing, dalen formation, conjunctival cyst and haematoma formation in either group. Distribution of complications at 3 month was shown in table VII.

Table VIII: Showing Distribution of Complications at 6 Month (n= 112)

Complications at 6 month	Study group		p-value
	Group-A(56) No (%)	Group-B(56) No (%)	
Delayed healing	0 (0.0)	0 (0.0)	
Conjunctival Congestion	3 (5.4)	4 (7.1)	**>0.05**
Haematoma	0 (0.0)	0 (0.0)	
Dalen formation	0 (0.0)	0 (0.0)	
Granuloma formation	1 (1.8)	7 (12.5)	**<0.05***
Conjunctival cyst	0 (0.0)	0 (0.0)	

* p- value is significant when p<0.05

At 6 month conjunctival congestion [3 (5.4%) versus 4 (7.1%), χ^2=0.152, p>0.05] did not differ significantly between two groups; but granuloma formation [1 (1.8%) versus 7 (12.5%), χ^2=4.846; p<0.05] significantly higher in group-B than group-A. Whereas none of the patients had delayed healing, dalen formation, conjunctival cyst and haematoma formation in either group. Distribution of complications at 6 month was shown in table VIII.

Table IX: Showing Distribution of Patients According to Operation Time (n= 112)

Operation time	Study group		*p-value
	Group-A(56) No (%)	Group-B(56) No (%)	
23- 30 minutes	39 (69.6)	1 (1.8)	
31- 40 minutes	17 (30.4)	53 (94.6)	<0.01*
41- 43 minutes	0 (0.0)	2 (3.6)	
Mean	29.45 (SD 3.88)	37.68 (SD 2.35)	<0.01*

* p- value is significant when p<0.05

Operation time ranged from 23-40 minutes with the mean of 29.45 (S3.88) minutes in group-A; whereas operation time ranged from 30-43 minutes with the mean of 37.68 (SD 2.35) minutes in group-B. The operation time of the group A was significantly shorter than that of group-B (Z=-13.567; p<0.001). Table-III shows the distribution of patients according to operation time. In Group-A, operation time was 23-30 minutes in 39 (69.6%) patients and 31-40 minutes in 17 (30.4%); whereas in Group-B, operation time was 23-30 minutes in 1 (1.8%) patient, 31-40 minutes in 53 (94.6%) and 41-43 minutes in 2 (3.6%) patients. The operation time significantly differed between two groups (χ^2=56.614; p<0.01).

Table V: Showing Distribution of Complications at One Week (n= 112)

Complications at one week	Study group		*p-value
	Group-A(56) No (%)	Group-B(56) No (%)	
Subconjunctival haemorrhage	0 (0.0)	0 (0.0)	
Conjunctival Congestion	56 (100.0)	56 (100.0)	
Loose graft	3 (5.4)	2 (3.6)	>0.05
Graft Oedema	3 (5.4)	6 (10.7)	>0.05
Graft retraction	3 (5.4)	0 (0.0)	>0.05
Scleral necrosis	0 (0.0)	0 (0.0)	
Abscess formation	0 (0.0)	0 (0.0)	
Dalen formation	0 (0.0)	0 (0.0)	
Granuloma formation	0 (0.0)	0(0.0)	
Conjunctival cyst	0 (0.0)	0 (0.0)	

p- value is significant when p<0.05

At 1 week, all patients of both group showed conjunctival congestion. Loose graft [3 (5.4%) versus 2 (3.6%); χ^2=0.209; p>0.05]; graft oedema [3 (5.4%) versus 6 (10.7%), χ^2 =1.087; p>0.05]; and graft retraction [3 (5.4%) versus 0 (0.0%), χ^2=3.083; p>0.05] did not differ statistically significant between group-A and group-B. Distribution of complications at 1 week was shown in table V.

Table VI: Showing Distribution of Complications at One Month (n= 112)

Complications at one month	Study group		p-value
	GroupA(56) No (%)	Group-B(56) No (%)	
Delayed healing	0 (0.0)	0 (0.0)	
Conjunctival Congestion	7 (12.5)	36 (64.3)	<0.01*
Dalen formation	0 (0.0)	0 (0.0)	
Granuloma formation	1 (1.8)	4 (7.1)	>0.05
Conjunctival cyst	0 (0.0)	0 (0.0)	
Haematoma formation	0 (0.0)	0 (0.0)	

* p- value is significant when p<0.05

At 1 month conjunctival congestion [7 (12.5%) versus 36 (64.3%), p<0.01] was found significantly more in group-B than that of group-A. But granuloma formation [1 (1.8%) versus 4 (7.1%), p>0.05] differ significantly. Whereas none of the patients had delayed healing, dalen formation, conjunctival cyst and haematoma formation. Distribution of complications at one month was shown in table-VI.

Table VII: Showing Distribution of Complications at 3 Month (n= 112)

Complications	Study group		p-value
	Group-A(56) No (%)	Group-B(56) No (%)	
Delayed healing	0 (0.0)	0 (0.0)	
Conjunctival Congestion	3 (5.4)	7 (12.5)	**>0.05**
Haematoma	0 (0.0)	0(0.0)	
Dalen formation	0 (0.0)	0 (0.0)	
Granuloma formation	1 (1.8)	5 (8.9)	**>0.05**
Conjunctival cyst	0 (0.0)	0 (0.0)	

At 3 month conjunctival congestion [3 (5.4%) versus 7 (12.5%), ?2=1.575; p>0.05] and granuloma formation [1 (1.8%) versus 5 (8.9%), ?2=2.818; p>0.05] did not differ significantly between group-A and group-B. Whereas none of the patients had delayed healing, dalen formation, conjunctival cyst and haematoma formation in either group. Distribution of complications at 3 month was shown in table VII.

Table VIII: Showing Distribution of Complications at 6 Month (n= 112)

Complications at 6 month	Study group		p-value
	Group-A(56) No (%)	Group-B(56) No (%)	
Delayed healing	0 (0.0)	0 (0.0)	
Conjunctival Congestion	3 (5.4)	4 (7.1)	**>0.05**
Haematoma	0 (0.0)	0 (0.0)	
Dalen formation	0 (0.0)	0 (0.0)	
Granuloma formation	1 (1.8)	7 (12.5)	**<0.05***
Conjunctival cyst	0 (0.0)	0 (0.0)	

* p- value is significant when p<0.05

At 6 month conjunctival congestion [3 (5.4%) versus 4 (7.1%), χ^2=0.152, p>0.05] did not differ significantly between two groups; but granuloma formation [1 (1.8%) versus 7 (12.5%), χ^2=4.846; p<0.05] significantly higher in group-B than group-A. Whereas none of the patients had delayed healing, dalen formation, conjunctival cyst and haematoma formation in either group. Distribution of complications at 6 month was shown in table VIII.

Table IX: Showing Distribution of Patients According to Operation Time (n= 112)

Operation time	Study group		*p-value
	Group-A(56) No (%)	Group-B(56) No (%)	
23- 30 minutes	39 (69.6)	1 (1.8)	
31- 40 minutes	17 (30.4)	53 (94.6)	<0.01*
41- 43 minutes	0 (0.0)	2 (3.6)	
Mean	29.45 (SD 3.88)	37.68 (SD 2.35)	<0.01*

* p- value is significant when p<0.05

Operation time ranged from 23-40 minutes with the mean of 29.45 (S3.88) minutes in group-A; whereas operation time ranged from 30-43 minutes with the mean of 37.68 (SD 2.35) minutes in group-B. The operation time of the group A was significantly shorter than that of group-B (Z=-13.567; p<0.001). Table-III shows the distribution of patients according to operation time. In Group-A, operation time was 23-30 minutes in 39 (69.6%) patients and 31-40 minutes in 17 (30.4%); whereas in Group-B, operation time was 23-30 minutes in 1 (1.8%) patient, 31-40 minutes in 53 (94.6%) and 41-43 minutes in 2 (3.6%) patients. The operation time significantly differed between two groups (χ^2 =56.614; p<0.01).

Discussion

Surgical removal of pterygium is the treatment of choice but no single technique is universally successful due to high recurrence rate. There are numerous adjunctive measures described to reduce the recurrence rates after pterygium excision but they are also associated with severe, sometimes sight threatening complications. Numerous adjunctive measures have been described to reduce the recurrence rates after its excision. These may be broadly classified as medical methods, beta irradiation and surgical methods[9]. Limbal-conjunctival autograft is currently the most popular surgical procedure as it has been suggested that including the limbal stem cells act as a barrier to the conjunctival cells migrating onto the corneal surface[9].

The most common method of autograft fixation is suturing, with drawbacks of prolonged operating time, postoperative discomfort, prolonged wound healing, infection and fibrosis. Subsequent local ocular-surface complications like pyogenic granuloma which usually requires a second operation for removal. Others like symblepharon formation, forniceal contracture, ocular motility restriction, diplopia, scleral necrosis, and infection are much more difficult to manage and can end up in sight-threatening lesions[10]. Replacing sutures with tissue adhesives may shorten the operating time, improve postoperative comfort, and avoid suture related complications. However, the major concern of the commercial fibrin glue is the cost and the potential risk of transmitted infection.[11]

In this study the age of the patients ranged from 18 to 75 years with the mean age of 41.11 (SD 13.21) years in group-A; whereas the age of the group-B ranged from 34 to 68 years with the mean age of 39.68 (SD 13.54) years. The mean age of the patients in both groups did not differ significantly ($p>0.05$). This result was similar to the study of Rashid, Hossain, Islam, et al. that the mean patient age at the time of pterygium surgery was 41.9 SD 8.1 years ranged from 30 to 60 years[12]. This result was also supported by the study of Goswami, Chatterjee, Goswami, et al. that the mean age of patients with pterygium was 44.75 SD 11.2 years (range, 21 years to 62 years)[13]. Foroutan, Beigzadeh and Ghaempanah, et al. found that the mean age of the patients was 37.26 SD 12.61 years (range 23-60).[14]

This result was almost similar to the study of Sangole and Kose, that the mean age of the patient in group A (autologous conjunctival graft with patient's own blood) was 49.21 years and in group B (autologous conjunctival graft with suture fixation) was 47.54 years[15]. In their study Alp, Yanyali, Ay, et al. found that the age of their Pterygium patients ranged from 34 to 70 years with the mean age of 52.8 SD 10.5 years[16]. and Fernandes, Sangwan, Bansal, et al., (2005) found that mean age of their patients was 50.6 SD 13.5 years[17]. The present study also showed that 21 (37.5%) patients were between 31 to 40 years, 11 (19.6%) patients were between 41 to 40 years, 10 (17.9%) patients were between 21 to 30 years, 9 (16.1%) patients were between 51 to 60 years, 3 (5.4%) patients were above 60 years and 2 (3.6%) patients between 18 to 20 years in patients of group A. It was 9 (16.1%), 18 (32.1%), 13 (23.2%), 8 (14.3%), 6 (10.7%) and 2 (3.6%) respectively in group-B. There was no statistically significant difference of age of patients between group-A and group-B when categorized if different age group ($p>0.05$). This result was supported by Fisher JP that It was uncommon for patients to present with pterygia prior to age 20 years.[18]

Patients older than 40 years had the highest prevalence of pterygia. Rashid, Hossain, Islam, et al., (2014) found that 38% of patients with pterygium were aged between 30 to 40 years, 34% of patients were aged between 41 to 50 years and 28% of patients were aged between 51 to 60 years[12]. In this study 44 (78.6%) patients were male and 12 (21.4%) patients were female in Group A; whereas 43 (76.8%) patients were male and the rest 13 (23.2%) patients were female in Group B. There was no statistically significant difference between group-A and group-B in respect to sex of the patients ($p>0.05$). This result was consistent with the study of Foroutan, Beigzadeh and Ghaempanah, et al[14]. and Majumder CS[19]. Foroutan, Beigzadeh and Ghaempanah, et al. reported that Pterygia was more frequent in male (76.9%) than that of female (23.1%)[14], Majumder CS was found that Pterygia was more frequent in male (72.3%) than that of female (27.7%)[19]. This result was also supported by Fisher[18]. That Pterygia were reported to occur in males twice as frequently as in females. Male being the major working group in our society and thus are more consistently exposed to the external environment that may be the cause of male predominance.

In the present study operation time ranged from 23-40 minutes with the mean of 29.45 (S3.88) minutes in group-A; whereas operation time ranged from 30-43 minutes with the mean of 37.68 (SD 2.35) minutes in group-B. The operation time of the group A was significantly shorter than that of group-B ($p<0.001$). The operation time was 23-30 minutes in 39 (69.6%) patients and 31-40 minutes in 17 (30.4%) in Group-A; whereas operation time was 23-30 minutes in 1 (1.8%) patient, 31-40 minutes in 53 (94.6%) and 41-43 minutes in 2 (3.6%) patients in Group-B,. The operation time significantly differed between two groups ($p<0.01$). This result was almost similar to the study of Sangole and

Knse that the duration of surgery in group A (Patient's own blood) (19.71 SD 5.13) minutes was significantly less as compared to group B (Suture fixation) (31.48 SD 6.85) minutes (p <0.001)[15]. Gajjar and Pandey, were found that the mean surgical time was 14 (1.4) minutes for fixation of in autologous conjunctival graft using autologus blood.[20]

In this study recorded complications at first postoperative day such as subconjunctival haemorrhage, lose graft, graft oedema and graft retraction did not differ statistically significant between group-A and group-B (p>0.05). Dulani and Dulani were found that graft loss occurred in two eyes in the immediate postoperative day of autologus blood fixation group[21]. In this study conjunctival congestion [7 (12.5%) versus 36 (64.3%), p<0.01] was found significantly more in group-B than that of group-A at 1 month. But granuloma formation [1 (1.8%) versus 4 (7.1%), p>0.05] did not differ significantly. Whereas none of the patients had delayed healing, dalen formation, conjunctival cyst and haematoma formation. This study revealed that conjunctival congestion [3 (5.4%) versus 7 (12.5%), p>0.05] and granuloma formation [1 (1.8%) versus 5 (8.9%), p>0.05] did not differ significantly between group-A and group-B; whereas none of the patients had delayed healing, dalen formation, conjunctival cyst and haematoma formation in either group at 3 month of follow up.

The present study showed that conjunctival congestion [3 (5.4%) versus 4 (7.1%), p>0.05] did not differ significantly between two groups; but granuloma formation [1 (1.8%) versus 7 (12.5%), p<0.05] significantly higher in group-B than group-A. whereas none of the patients had delayed healing, dalen formation, conjunctival cyst and haematoma formation in either group at 6 month of follow up. Shinde, evaluated the efficacy of autologus fibrin glue for attachment of conjunctival autograft in primary pterygium surgery and found that two eyes developed graft retraction (12.5%) which responded to continued patching for two more days.[22]

One eye developed complete dehiscence (6.25%) which needed suturing of the graft with 10-0 nylon suture. None of the patient showed any other complication like corneal ulcer, sclera melting, conjunctivitis, symblepheron formation. Recurrence is a common complication of pterygium surgery; and the success of this surgery is based on avoiding this complication. Recurrence rates vary in the literature, based on the surgical expertise, the surgical technique, and the adjunctives used. Conjunctival autografting, regardless of the material used, following pterygium surgery has been associated with lower recurrence rates of 2% to 9 % (Uy, Reyes and Flores[23]. In this study no recurrence of pterygium was found in any groups at on 1 month follow up.

But recurrence of Pterygium at 3 month and at 6 month of follow was observed in 2 (3.6%) and 3 (5.4%) patients respectively up in group-A; and 3 (5.4%) cases 4 (7.1%) cases respectively in group-B. The recurrence of pterygium at 3 month and at 6 month did not differ significantly between two treatment groups (p>0.05 each).

Gajjar and Pandey[20]. found no recurrence of Pterygium after conjunctival autograft in pterygium surgery using autologus blood. Mitra[24] also reported none of the pterygium recurred in the study's six month of follow up. Dulani and Dulani[21] found that recurrence occurred in one eye, which was probably due to inadequate dissection of pterygium tissue rather than autoblood fixation of the graft and it was detected after one - month postoperative follow up examination. Shinde[22]. evaluated the efficacy of autologus fibrin glue for attachment of conjunctival autograft in primary pterygium surgery and found no recurrence at 12 month of follow up. Results of transplant of a free conjunctival autograft show a fewer recurrence rate and is associated with fewer complication.

The most common method of conjunctival autograft fixation is suturing with the drawback of prolonged surgical time, postoperative discomfort, suture abscess, granulaloma formation which are reported. Commercial fibrin glue is useful in attaching the conjunctival autograft. Koranyi, Seregard and Kopp[25] in a randomized controlled trial reported that fibrin glue could be used to attach the conjunctival graft instead of sutures with reduced operating time and postoperative discomfort. The safety record of fibrin glue is of considerable importance because commercial fibrin glue is made from the pooled blood product. The main issue in using the fibrin glue, despite of viral inactivation techniques, is transmission of viral infection. Therefore autologus fibrin glue in comparison with commercial product eliminates the potential risk of transmission of infection and hypersensitivity reaction.

Conclusion

From the findings of the present study it may be concluded that conjunctival autografting by patients own blood is better than 10/0 nylon sutures in terms of less subconjunctival haemorrhage, subconjunctival congestion, granuloma formation but recurrence rate did not differ significantly with 10/0 nylon suture in pterygium surgery.

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ORIGINAL ARTICLE

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Short Term Outcome of Multiple Births in a Tertiary Care Hospital

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Abstract

Multiple-birth is one of the important cause of premature and low birth weight babies in all over world. A significant increase in the multiple births has occurred recently due to widespread availability of ovulation inducing agents, assisted reproduction techniques and delayed child bearing by women. Multiple births newborns are at risk of adverse outcome. This prospective observational study was carried out to observe and record the short term outcome of multiple births newborn admitted within 24 hours of age into the department of Paediatrics of Sylhet MAG Osmani Medical College Hospital, Sylhet between November, 2015 and October, 2016. Sampling method was convenient purposive. The data was processed and analyzed both manually and by using SPSS version 21.0. For statistical analysis, mean and standard deviations was used for quantitative data and percentage (%) was done for qualitative data. Out of 33 multiple births newborn majority (93.7%) was twin and 6.3% was triplet, almost two thirds (65.6%) patients belonged to gestational age 34 - <36 weeks, 56.3% patients had birth weight of 1500-2499 gm. Early neonatal survival rate was 84.85% among them 54.55% survived without any complication and 30.30% survived with morbidities. Early neonatal death was 15.15%. Neonatal morbidities observed among multiple births were neonatal sepsis 15.2% followed by neonatal jaundice 12.0%, congenital anomalies 6.0%, necrotizing enterocolitis 6.0%, intraventricular haemorrhage 3.0% and respiratory distress syndrome 3.0%. Most of the multiple births newborn were twin, premature and low birth weight. Most of the early neonatal deaths were very preterm (< 30 weeks) and extreme low birth weight. Neonatal sepsis was most common morbidity followed by neonatal jaundice among multiple births. Multiple births, Prematurity, Low birth weight, early neonatal survival, Early neonatal death.

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Introduction

Multiple births have a great impact on perinatal and neonatal outcome. The incidence of multiple births has shown a significant increase over the last decades and the twin birth rate increased by 52%.[1] The overall incidence is increasing due to widespread availability of ovulation inducing agents, assisted reproduction techniques and delayed child bearing by women.[2] A multiple births refer to the birth of twins, triplets or more.[3] The reported incidence of spontaneous twinning is highest among blacks and East Indians, followed by northern European whites, and is lowest in the Asian races.[4]

Normal incidence of twins is 1 in 90 pregnancies and of triplets 1 in 8,100 pregnancies.[5] Preterm infants are at risk for developing complications that result from anatomic or functional immaturity. The complications seen most frequently among preterm and LBW babies are hypothermia, respiratory distress syndrome, apnoea of prematurity, patent ductus arteriosus, intracranial hemorrhage, hypoglycemia, necrotizing enterocolitis, infection, chronic lung disease, and retinopathy of prematurity.[6] There is extensive evidence that twins and higher order multiple births worldwide are associated with a substantially-higher risk of maternal and perinatal mortality and morbidity compared to singletons.[7]

One study in Bangladesh by Sultana M et al found nearly two-thirds (64%) of the twin pregnancies had preterm deliveries and, 10% of the babies had congenital anomalies. They also shown that very low birth weight babies were 32%, low birth weight babies were 60% and perinatal mortality rate was 11%.[8] The main causes of adverse neonatal outcome in multiple pregnancies are related to prematurity, fetal growth restriction and low birth weight.[3] Another study by Hong R et al.[9] in Bangladesh

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showed that children born with multiple births had six times more chance of death than those born with singleton. our study was designed to explore the short term outcome of multiple births.

Materials and Methods

This prospective observational study was done among 33 multiple births newborn admitted within 24 hours of age into the department of Paediatrics of Sylhet MAG Osmani Medical College Hospital, Sylhet between November, 2015 and October, 2016. Sampling method was convenient purposive sampling and data were collected by preformed structured data collection sheet. By taking details history, thorough physical examinations of the study population and necessary investigations (cranial USG, septic screening, chest x-ray etc) were done. Gestational age was estimated from history of LMP, review of antenatal USG report and by using NBS.

Daily follow up was given up to 7th day of age of each multiple births newborn. The data was processed and analyzed manually and by using SPSS version 21.0. For statistical analysis, mean and standard deviations was used for quantitative data and percentage (%) was done for qualitative data. In all cases informed written consent from the parents of the baby was taken. Ethical permission was taken from the Ethical Committee of Sylhet MAG Osmani Medical College, Sylhet.

Observation and Results

Out of 33 multiple births newborn almost two thirds (65.6%) patients belonged to gestational age 34-<36 weeks, 18(56.3%) patients had birth weight of 1500-2499 gm, 13(40.6%) was small for gestational age, 30(93.7%) was twin and 3(6.3%) was triplet (Table-I).

Table I: Distribution of the study patients by baseline characteristics (n=33)

Variables	Number of patients	Percentage
Gestational age by NBS system (weeks)		
<34	3	9.4
34-36	22	65.6
>36	8	25.0
Birth weight (grams)		
<750	1	3.1
750 - 999	2	6.2
1000 - 1499	8	25.0
1500 - 2499	18	56.3
>2500	4	12.5
Small for gestational age	13	40.6
Pattern of multiple births		
Twin	30	93.7
Triplet	3	6.3

Majority 11(68.7%) of the mothers belonged to age 20 - 30 years and the mean age was 25.3±4.1 years and 12 (75%) mothers were multipara during their pregnancy (Table II).

Table II: Maternal demography and maternal illness during pregnancy (n=16)

Variables	Number of patients	Percentage
Age of the Mother (in years)		
<20	4	25.00
20-30	11	68.70
>30	1	6.30
Mean±SD	25.3±4.1	
Range(min,max)	17,35	
Parity of the mother		
Primipara	4	25.00
Multipara	12	75.00

Early neonatal survival rate was 84.85% among them survived without any complication 18(54.55%), 10(30.30%) was survived with morbidities, however, 5(15.15%) had early neonatal death (Table-III).

Table III: Outcome of study patients on 7th day of age (n=33)

Outcome	Number of patients	Percentage
Early neonatal survival	28	84.85
Survival without any complication	18	54.55
Survival with morbidities	10	30.30
Early neonatal death	5	15.15

Neonatal morbidities of multiple births within 7 days of age were observed neonatal sepsis 5(15.2%) followed by neonatal jaundice 4(12.0%), congenital anomalies 2(6.0%), necrotizing enterocolitis, 2(6.0%) intraventricular haemorrhage 1(3.0%) and respiratory distress syndrome 3.0% (Table IV).

Table IV: Distribution of the study patients by neonatal morbidities of multiple births (n=33)

Neonatal morbidities	Number of patients	Percentage
Neonatal sepsis	5	15.20
Congenital anomalies	2	6.00
Neonatal jaundice	4	12.00
Necrotizing enterocolitis	2	6.00
Intraventricular haemorrhage	1	3.00
Respiratory distress syndrome	1	3.00

Discussion

Multiple births are no longer considered as a rare event. Twin represents 2-3% of all live births.[10] Multiple gestations have a large impact on perinatal complications and these account for adverse neonatal outcomes. The most common and profound implications is preterm delivery with low birth weight which is second leading cause of infant death.[11] This prospective observational study was carried out with an aim to record the rate of early neonatal death, prematurity, low birth weight,

intrauterine growth restriction and to record the common morbidities (RDS, Neonatal sepsis, NEC, congenital anomalies etc.) among multiple births.

A total of 33 multiple births cases of 24 hours old newborn were included in this study. Among them 30 (93.7%) was born as twin and 3 (6.3%) was born as triplet. In this current study it was observed that two third (65.6%) patients belonged to gestational age of 34 - <36 weeks. In a study by Chowdhury found gestational age < 37 weeks 58.5%.[12] Simailrly Dolgun et al.[13] found gestational age varied from 25 - 36 weeks. These previous studies support our study findings. In this present study it was observed that majority (56.3%) patients had birth weight of 1500-2499 grams. Chauhan et al.[14] found 60.0% of the twins delivered as preterm and weighed <2500 grams, which is comparable with the current study findings.

In this current study it was observed that majority (68.7%) of the mothers belonged to age 20 - 30 years. The mean age was found 25.3±4.1 years varied from 17 -35 years which is similar to the study of Spellacy et al.[15] Dolgun et al.[13] also found the mean age was 28.8±6.4 years, which is comparable with the current study findings. Regarding the outcome of multiple births on 7th day of age it was observed in our study that 54.55% babies survived without any complication, 30.30% survived with morbidities and early neonatal death was 15.15%. Chowdhury[12] found 11.3% perinatal mortality in his study which was corresponded with the present study. Twin perinatal mortality was found approximately in 10-15%.[16] Therefore findings in our study about neonatal mortality are comparable to the reports published by previous authors.

Regarding the neonatal morbidities of multiple births in this present study it was observed that neonatal sepsis was more common (15.2%) followed by 12.0% neonatal jaundice, 6.0% congenital anomalies, 6.0% necrotizing enterocolitis, 3.0% intraventricular haemorrhage and 3.0% respiratory distress syndrome. Schimmel et al.[17] reported that the risk of congenital malformations, mortality and neonatal morbidities (respiratory distress syndrome, necrotizing enterocolitis, intraventricular hemorrhage and bronchopulmonary dysplasia) were associated with multiple births. Several studies have demonstrated that multiple births are still independently at an increased risk of neonatal sepsis, neonatal jaundice, congenital anomalies, necrotizing enterocolitis, intraventricular haemorrhage and respiratory distress syndrome.[17] Therefore neonatal morbidities of multiple births in our study are similar to previous studies published by different authors.

Conclusion

Most of the multiple births newborn were twin, premature and low birth weight. Most of the early neonatal deaths were very preterm (< 30 weeks) and extreme low birth weight. Neonatal sepsis was the most common morbidity followed by neonatal jaundice among multiple births newborn.

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ORIGINAL ARTICLE

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Comparison of A Seven Day Treatment of Cefixime And Ciprofloxacin In Acute Uncomplicated Urinary Tract Infections In Women

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Abstract

Urinary tract infection (UTI) represents one of the most common diseases encountered in medical practice today. Although fluoroquinolones remain the most reliable urinary antimicrobial, resistance rates have increased and effective fluoroquinolone-sparing antimicrobials are needed. Cefixime, with its broad spectrum of antimicrobial activity, would provide a useful alternative to fluoroquinolones for the treatment of uncomplicated UTI if demonstrated to be similar in efficacy to fluoroquinolones with negligible adverse effects. A prospective randomized comparative study was carried out in Sylhet M A G Osmani Medical College Hospital, Sylhet with a view to evaluate the efficacy and safety of a seven day therapy of cefixime and ciprofloxacin in acute uncomplicated urinary tract infections in women. After collection of urine sample for culture empirical treatment was given.

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The patients were treated with either Cefixime 200 mg or Ciprofloxacin 500 mg 12 hourly for 7 days. Thirty-eight women had negative cultures at day 3 of which 18 in the cefixime- group and 20 in the ciprofloxacin-group. Thirteen women in the cefixime-group and 24 in the ciprofloxacin-group were resistant to cefixime and ciprofloxacin respectively. Culture negative and resistant group of patients were excluded from the study. Two women in the cefixime-group and single in the ciprofloxacin-group were lost from follow-up by the 7-day visit; 4 women in the cefixime group and 3 in the ciprofloxacin group were lost from follow-up by the 30th -day visit. Finally 39 patients of cefixime group and 28 patients of ciprofloxacin group included in the study for analysis.

The isolated microorganisms of uncomplicated UTI were Escherichia coli (82.2%) followed by Staphylococcus saprophyticus (7.6%), Proteus spp (4.2%), Klebsiella spp (3.4%), and Pseudomonas aeruginosa (2.5%). There was no statistically significant difference between the isolated microorganisms in cefixime-group and ciprofloxacin-group (p=0.961). In cefixime group 78.3% of patients were sensitive and 21.7% of patients were resistant to cefixime; while 58.6% of patients were sensitive and 41.4% of patients were resistant to ciprofloxacin (p=0.021).

Clinical cure rate was 97.8% and 93.9% in cefixime and ciprofloxacin treated group respectively. Microbiological cure 95.6% in cefixime group and 93.9% in ciprofloxacin group. There is no difference in clinical cure (p=0.384) and Microbiological cure (p=0.749).In cefixime group 4.2% and in ciprofloxacin group 18.2% patients experienced adverse effect at day 7. In cefixime group 2.6% of patients experienced recurrence at 30th day, while no recurrence was observed in ciprofloxacin group (p=0.393). None of patients experienced adverse effect at 30th day in cefixime treated group while 3.6% of patients experienced adverse effects in ciprofloxacin group (p=0.234).

Susceptibility of cefixime to uropathogen in uncomplicated UTI in female was significantly higher and adverse effect was fewer than that of ciprofloxacin; while clinical and microbiological cure rate; recurrence and late adverse effect were almost similar with use both the drugs. Our study suggest that a 7-day treatment of cefixime is more effective and safer then ciprofloxacin in the treatment of acute uncomplicated UTI in females.

Introduction

UTI is the third most common infection experienced by humans after respiratory and gastro-intestinal infections[1] and are a major public health problem in terms of morbidity and financial cost, and incur the highest total health care cost among urological diseases, exceeding that of chronic renal failure even when renal dialysis and

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renal transplantation are included.[1,2] UTI represents one of the most common diseases encountered in medical practice today with an estimated 150 million UTIs per annum worldwide.[3]

An uncomplicated infection is an episode of cysto-urethritis following bacterial colonization of the ureteral and bladder mucosae. This type of infection is considered to be uncomplicated because sequelae are rare and exclusive due to the morbidity associated with reinfection in a subset of women.[1]

Although UTIs occur in both men and women, clinical studies suggest that the overall prevalence of UTI is higher in women. Uncomplicated UTIs in healthy women have an incidence of 50/1000/year (De Backer et al., 2008) An estimated 50% of women experience at least one episode of UTI at some point in their lifetime and between 20% and 40% of women have recurrent episodes.[4] Approximately 20% of all UTIs occur in men[5]. Current management of UTIs are usually empirical, without the use of a urine culture or susceptibility testing to guide therapy. However, as with many community acquired infections, antimicrobial resistance among the pathogens that cause UTIs is increasing and is a major health problem in the treatment of UTI.[6] There is growing concern regarding antimicrobial resistance worldwide, particularly to E. coli which is the dominant causative agent of UTI in women.[7,8]

Fluoroquinolones have high rates of efficacy, high rates of susceptibility among pathogens causing uncomplicated urinary tract infection (UTI), and minimal adverse drug reactions. Indeed, recent surveys have found that fluoroquinolones are more commonly used than trimethoprim-sulfamethoxazole for uncomplicated UTI in women in the United States[9]. However, increasing rates of fluoroquinolone-resistant Escherichia coli are being reported worldwide, including areas within the United States and Canada, even among young women with uncomplicated cystitis.[10,11]

Cefixime a 3rd generation cephalosporin as far as activity against gram-negative micro-organisms is concerned. There is a paucity of data on the use of cefixime, for the treatment of uncomplicated UTI. Cefixime, with its broad spectrum of antimicrobial activity, would provide a useful alternative to fluoroquinolones for the treatment of cystitis if demonstrated to be similar in efficacy to fluoroquinolones and without adverse effects[12]. Distribution of uropathogens and their susceptibility to antimicrobials is variable regionally and geographically and at different locations within the same country due to different degrees of antimicrobial use. However a large proportion of uncontrolled use of a ntimicrobials has invariably resulted in development of antimicrobial resistance which in recent years has become a major problem worldwide.

As uropathogens and their antimicrobial resistance pattern is changingconstantly, identifying the uropathogens and monitoring their antimicrobial susceptibility is pivotal. It provides the information about the organism associated with UTI and reports about antimicrobial susceptibility pattern, thus helps in most appropriate empirical antimicrobial therapy and curtails the spread of antimicrobial resistance. Although fluoroquinolones are reliable urinary antimicrobials, resistance rates have greatly increased and effective fluoroquinolones sparing antimicrobials are needed.

Cefixime, an oral third-generation cephalosporin with broad spectrum of antimicrobial activity is used in the treatment of UTI in several studies. But there is paucity of data regarding the comparison of effectiveness of treatment of cefixime and ciprofloxacin in uncomplicated UTI. So, present study was designed to isolate and identify micro-organism and to compare efficacy and tolerability of cefixime and ciprofloxacin in acute uncomplicated UTI.

Materials and Methods

A prospective randomized comparative study was under taken in Department of Pharmacology and Therapeutics in collaboration with the Department of Microbiology; the Outpatient Department of Medicine and Obstetrics and Gynaecology, Sylhet MAG Osmani Medical College and Hospital, Sylhet, during the period from January 2012 to December 2012. A total number of 208 female patients, age ranged 15-49 years diagnosed as acute uncomplicated UTIs fulfilling the inclusion and exclusion criteria were the study population.

A total 156 women with UTIs were selected and were divided randomly into cefixime group and ciprofloxacin group. Randomization of two groups was done by even and odd number each consisting of 78 women with UTIs. Every odd number of patients was taken in cefixime group and even number of patient was taken in ciprofloxacin group. Cefixime group were treated with cefixime & ciprofloxacin group were treated with ciprofloxacin prior culture sensitivity test result obtained. Those were resistant to either one were excluded. Sensitive to either cefixime or ciprofloxacin were continued treatment for 7 days.

On day 30 the urine was cultured to record evidence of recurrence. Antibiotic susceptibility test was carried out by the Kirby Bauer disc diffusion technique and

interpretations were made for each bacterial isolate following interpretative criteria recommended by the National Committee for Clinical Laboratory Standards.[13]

After collection of urine sample and performing urine R/E empirical treatment was given to each of the patient. The patients were treated with either Cefixime 200 mg or Ciprofloxacin 500 mg 12 hourly for 7 days. On day 3 culture and sensitivity report was analysed and any adverse effect were noted. Growth of organism in urine culture and sensitive to the prescribed drug, treatment was continued for 7 days and were advised to come back on day 7 for second follow up. Growth of organism in urine culture and resistant to the prescribed drug, prescribed drug was stopped, alternate sensitive drugs was given. No growth of organism in urine culture was excluded from the study.

On day 7 the patients were clinically assessed for improvement of symptoms and signs of UTI; urine sample was collected for microcopy and culture and any adverse effect were noted. They were requested to come back at day 30 for 3rd follow up. At day 30 the patients were clinically assessed for recurrence of symptoms and signs of UTI and urine sample was collected for microcopy and culture to see the recurrence. Number of acute uncomplicated UTI patient were primary variable of this study, where clinical cure rate, microbiological cure rate, recurrence rate, adverse effect were the outcome variable of this study.

Results

A total 178 women with suspected uncomplicated UTIs were divided randomly into cefixime group and ciprofloxacin group. Every odd number of patient belonged to cefixime group and even number of patient to ciprofloxacin group. Thirty-eight women had negative cultures at day 3 of which 18 in the cefixime group and 20 in the ciprofloxacin group. Thirteen women in the cefixime group and 24 in the ciprofloxacin group were resistant to cefixime and ciprofloxacin respectively. Two women in the cefixime group and one in the ciprofloxacin group were lost to follow-up by the 7-day visit; 4 women in the cefixime group and 3 in the ciprofloxacin group were lost to follow-up by the 30th day visit.

The age of the patient ranged from 16 to 49 years with the mean age of 29.2 ± 6.7 years. One hundred and ten patients (93.3%) were married and 8 patients (6.7%) were unmarried with no statistical difference in groups (P=0.495). Table I shows distribution of microorganisms. The isolated microorganisms were Escherichia coli (82.2%) followed by Staphylococcus saprophyticus (7.6%), Proteus spp (4.2%), Klebsiella spp (3.4%), and Pseudomonas aeruginosa (2.5%). There was no statistical significant difference between the isolated microorganisms in cefixime treated group and ciprofloxacin treated group (X2=0.621; p=0.961). Distribution of patients by susceptibility of the microorganism was shown table II.

In cefixime treated group, 47 patients (78.3%) were sensitive and 13 patients (21.7%) were resistant to cefixime; while in ciprofloxacintreated group, 34 patients (58.6%) were sensitive and 24 patients (41.4%) were resistant to ciprofloxacin. There was a significant difference between the groups in respect to sensitivity pattern (X2=5.324; p=0.021). Table III shows distribution of patients according to efficacy of treatment on day 7. In cefixime treated group, clinical cure was observed in 44 patients (97.8%) and failure in 1 patient (2.2%); while in ciprofloxacin treated group, clinically cure was in 31 patients (93.9%) and failure in 2 patient (6.1%). There was no statistical significant difference between the treatment outcome of the patients in cefixime treated group and ciprofloxacin treated group (X2=0.758; p=0.384).

In cefixime treated group, microbiological cure was found in 43 patients (95.6%) and failure in 2 patients (4.4%); while in ciprofloxacin treated group, microbiological cure was in 31 patients (93.9%) and failure in 2 patients (6.1%). There was no statistically significant difference between the treatment outcome of the patients in cefixime treated group and ciprofloxacin treated group (X2=0.102; p=0.749). In cefixime treated group, 2 patients (4.2%) experienced adverse effect; while 6 patients (18.2%) in ciprofloxacin treated group experienced adverse effect. There was statistically significant difference between the groups in respect to the adverse effects (X2=3.903; p=0.046). The adverse effects were recorded as diarrhoea in one and angiooedema in one patient in patients of cefixime treated group; while the adverse effects observed in ciprofloxacin treated group were diarrhoea in one, urticaria in one, nausea in two, dizziness in one and vaginosis in one patients.

There was no statistically significant difference of the individual adverse effect between cefixime treated group and ciprofloxacin treated group (X2=8.000; p=0.238Recurence of UTI was monitored at day 30 of treatment. In cefixime treated group, recurrence was observed in 1 patient (2.6%); while no recurrence was observed in ciprofloxacin treated group. In cefixime treated group, none of patient experienced adverse effect; while in ciprofloxacin treated group, 1 patient (3.6%) experienced dizziness (adverse effects) at 30th day.

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Table I: Distribution of patients by isolated microorganisms in urine culture

Micro-organism	Study group			p-value
	Cefixime group (n=60)	Cipro-floxacin Gr(n=58)	Number (Percentage) (n=118)	
Escherichiacoli	49 (81.7)	48 (82.8)	97 (82.2)	
Staphylococcus	5 (8.3)	4 (6.9)	9 (7.6)	
Proteus spp	3 (5.0)	2 (3.4)	5 (4.2)	*p=0. 961
Peudomonas	1 (1.7)	2 (3.4)	3 (2.5)	
Klebseilla	2 (3.4)	2 (3.4)	4 (3.4)	
Total	60 (100.0)	58 (100.0)	118 (100.0)	

*χ^2 TEST

Table II: Distribution of patients by susceptibility

Susceptibility	Study group		p-value
	Cefixim Group (n=60)	Ciprofloxacin Group (n=58)	
Sensitive	47 (78.3)	34 (58.6)	
Resistant	13 (21.7)	24 (41.4)	*p=0.021
Total	60 (100.0)	58 (100.0)	

Figure in the parenthesis indicates corresponding percentage.* χ^2 test

Table III: Distribution of patients according to efficacy of treatment at day 7

Efficacy of treatment	Study group		p-value
	Cefixime Group (n=45)	Ciprofloxacin Group (n=33)	
Clinical			
Cure	44 (97.8)	31 (93.9)	*p=0.384
Failure	1 (2.2)	2 (6.1)	
Microbiologi			
Cure	43 (95.6)	31 (93.9)	
Failure	2 (4.4)	2 (6.1)	*p=0.749

Figure in the parenthesis indicates corresponding percentage.χ^2 Test .

Discussion

Uncomplicated UTI is one of the most common bacterial infections, a frequent presenting complaint in women visiting their family practitioners. Short courses of antibiotic therapy are generally adequate treatment, and starting empiric therapy without obtaining a urine specimen is recommended[14].The emergence of antimicrobial resistance in community-acquired Escherichia coli, however, requires continuing reevaluation of empiric antimicrobial therapy[15]. Widespread empiric use of antibiotics, potentially contributes to development of antimicrobial resistance[16]. The panel recommended that the fluoroquinolones, while highly efficacious, should be reserved for important uses other than acute uncomplicated UTI, and thus should be considered alternative antimicrobials for acute uncomplicated UTI.

The main concern regarding fluoroquinolone use in uncomplicated UTI is the possible promotion of fluoroquinolone resistance, not only among uropathogens but also other organisms causing more serious and difficult-to-treat infections at other sites. There also is concern about the association between fluoroquinolone use and increased rates of methicillin-resistant Staphylococcus aureus. [12,17,18] In this study the age of the patient ranged from 16 to 49 years with the mean age of 29.2 ± 6.7 years. The mean age of the patients in both groups was almost identical [29.6 ± 6.5 years (ranged 16-48 years) vs 28.9 ± 6.9 years (ranged 16-49 years); p=0.578]. Age range of the patient was consistent with to other studies [18,19] found the median age of their female uncomplicated UTI patients was 22 (ranged, 18-45) years in amoxicillin-clavulanate and also 22 (ranged, 18-45) years in the ciprofloxacin treated group.

The isolated microorganisms in our study were Escherichia coli (82.2%) followed by Staphylococcus saprophyticus (7.6%), Proteus spp (4.2%), Klebsiella spp (3.4%), and Pseudomonas aeruginosa (2.5%). There was no statistically significant difference isolated micro-organisms in cefixime group and ciprofloxacin group (p=0.961). This result was correlated with the study of Islam and Hasan [20] that Escherichia coli is the most common urupathogen (78.97%), followed by Staph. saphrophyticus (5.18%), Coliform (4.13%), KLebsiella spp. (3.44%), Enterococous (3.44%), Staph. aureus (1.72%), Streptococcus (1.72%) and Pseudomonas spp. (1.38%). Mazed et al [13] reported the commonest organisms isolated were Escherichia coli (66, 37.71%) and Klebsiella species (60, 34.29%) followed by Proteus species (17, 9.71%), Pseudomonas species (16, 9.14%)and others including Coagulase-negative

Staphylococcus(2.86%). Magliano et al[21] reported that overall Escherichia coli accounted for 67.6% of all isolates, followed by Klebsiella pneumoniae (8.8%), Enterococcus faecalis (6.3%), Proteus mirabilis (5.2%), and Pseudomonas aeruginosa (2.5%). Abdullah et al[22] found that E. coli (43.1%) was most frequent, followed by Klebsiella pneumoniae (22.4%) and Staphylococcus aureus (15.5%). 57.2% of the Gram-negative bacteria and 48.7% of the Gram-positive isolates were resistant to ciprofloxacin. More than 95% of urinary tract infections are caused by a single bacterial species.[23]

In the present study 78.3% of patients were sensitive and 21.7% were resistant to cefixime in cefixime treated group; while 34 patients (58.6%) were sensitive and 24 patients (41.4%) were resistant to ciprofloxacin in ciprofloxacin treated group (p=0.021). Islam and Hasan[20]. reported Escherichia coli is the most common uropathogen and showed sensitivity pattern to Ciprofloxacin (41.48%) and Cefixime (31.0%). There was statistically significant difference between sensitivity pattern of the patients in cefixime group and ciprofloxacin group (p=0.021). A high percentage of ciprofloxacin resistance Escherichia coli were observed in this surveillance study. Such resistance is reported by many other studies [21-24] reported that susceptibility of E. coli to oral antimicrobial agents was demonstrated to be as follows fosfomycin (72.9%), trimethoprim /sulfamethoxazole (72.9%), ciprofloxacin (76.8%), ampicillin (48.0%), and amoxicillin/clavulanate (77.5%).

The resistance rate to ciprofloxacin varies from one country to another and depends on local antibiotic prescription practice. Increased resistance in the ciprofloxacin against Escherichia coli may reflect the overuse of quinolones in treatment of UTI.[24] Cefixime resistant may be due to increasing use of this drug in any kind of fever and cefixime was used in primary health care level as OTC drugs in Bangladesh. In this study clinical cure was observed in 97.8% and failure in 2.2% in cefixime treated group; while clinically cure was in 93.9% and failure in 6.1% in ciprofloxacin treated group (p=0.384).

The overall clinical cure rate in ciprofloxacin treated group was 93% in cases of uncomplicated UTI reported by Hooton et al[18, 19]reported that overall clinical cure rate with ciprofloxacin was 77% in cases of uncomplicated UTI. Hsu and Chou reported that clinical cure rate of cefixime was in 100.0% of cases of uncomplicated UTI; while Dreshaj et al[26] reported that clinical cure rate of cefixime was 94%. Krcmery and Naber reported[27] that clinical cure or improvement with ciprofloxacin was achieved in 97.3% of those treated with 500 mg q.i.d. versus 95.5% of those treated with 250 mg b.i.d.. Ludwig[28]found excellent efficacy of cefixime in adults with urinary tract infections (UTI), with cure in 94%, improvement in 5%, and failure in 1%of patients. Microbiological cure in the present study was observed in 95.6% and failure in 4.4% in cefixime treated group; while microbiological cure was in 93.9% and failure in 6.1% in ciprofloxacin treated group (p=0.749).[18,19]

The microbiological cure rate of ciprofloxacin was 96% cases of uncomplicated UTI reported by Hooton et al reported that overall clinical cure rate of ciprofloxacin was 95% cases of uncomplicated UTI. Hsu and Chou[25] reported microbiological cure rate of cefixime was in 100.0% of cases of uncomplicated UTI. Ludwig[28] found very good efficacy of cefixime microbiologically with eradication in 90.1% isolates from patients with UTI. In this study 4.2% experienced adverse effect in cefixime treated group; while 18.2% in ciprofloxacin treated group experienced adverse effect at day 7.

There was statistically significant difference between the adverse effect of the patients in cefixime treated group and ciprofloxacin treated group (p=0.046). The adverse effects were diarrhoea and angiooedema in cefixime treated group; while the adverse effects were diarrhoea, urticaria, nausea, dizziness and vaginosis in ciprofloxacin treated group. There was no statistically significant difference of the individual adverse effect between cefixime treated group and ciprofloxacin treated group (p=0.238). Similar types of adverse effects of ciprofloxacin were reported in Hooton et al.[18,19]

In the present study 2.6% of patients in cefixime treated group experienced recurrence at 30th day, while no recurrence in ciprofloxacin treated group (p=0.393). Hooton et al18,19 reported no recurrence at 30th day in ciprofloxacin treated group. In this study no patient experienced adverse effect at 30th day in cefixime treated group; while 3.6% of patients experienced adverse effects in ciprofloxacin treated group (p=0.234). Hooton et al[18,19] reported no adverse effects after end of the treatment period inciprofloxacin treated group.

Conclusion

The present study; susceptibility of cefixime to uropathogen in uncomplicated UTI in female was significantly higher and adverse effect was fewer than that of ciprofloxacin; while clinical and microbiological cure rate; recurrence and late adverse effect were almost similar in both the drugs. So we conclude that a 7 days treatment of cefixime is more effective and safer in the treatment of uncomplicated UTI in female.

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ORIGINAL ARTICLE

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Tracheostomy in Head-Neck malignancy-A study of 50 cases.

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Abstract

Objectives of the study were to find out the frequency, indications and complications of tracheostomy in head and neck malignancy.It was an observational study carried out in the Department of Otolaryngology and Head-Neck surgery of Sylhet MAG Osmani Medical College Hospital. Fifty cases were included in this study (44 males and 6 females), between the ages of 25 years to 80 years who were treated in between July 2011 to December 2011. Study was based on history, clinical, radiological, endoscopical, laboratory and histopathological examination. The lowest age was 25 years and the highest was 80 years. Number of patients in 6th decade was highest (44%). Among the 50 patients 44 were male (88%) and 6 were female (12%). Male to female ratio was 7.4:1. Out of 50 cases poor group was seen to be the commonest group scoring to 70% and affluent group was least 2% only. The highest number of the study subjects were related to cultivator 30% followed by businessmen 24%, service holder 18%, day labourer 12%, housewives 8%, driver 4%, teachers 2%, fishermen 2%. Out of 50 cases 70% were smokers, 20% were chewing betel nuts and betel leaves, 4% were alcoholic, 6% were not habituated with any particular habit. Carcinoma larynx was most frequent 60%, carcinoma pyriform fossa 26%, carcinoma base of the tongue 4% and carcinoma of the tonsil and thyroid gland is 2% in each. Out of 50 cases of tracheostomy 94% cases were emergency and rest 6% were elective. Complications were 50% and the most common complication was surgical emphysema (18%). The other complications were hemorrhage 3 (6%), wound infection 2(4%), tube dislodgment 2(4%), tube blockage 2 (4%), casting 2 (4%), stomal recurrence, stomal stenosis and sub glottic stenosis were the complications observed in frequently. Tracheostomy was a lifesaving procedure and was done to relieve respiratory distress. There was high rate of complications may be due to most of the patients came to the hospital in state of severe respiratory distress and they became very much restless during emergency tracheostomy resulting in clumsy procedure. Most of the complications may be preventable by careful operating technique and meticulous post-operative management.

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Introduction

The term tracheostomy is used to make an opening in the anterior wall of the trachea. Tracheostomy is used when a formal opening or stoma is made[1]. It is a surgical procedure which is often life saving. Frequently it has long been used for acute respiratory tract obstruction regardless of the cause.[2] Asclepiads of Bithynia (2nd century AD) has the honor of being the first to perform the operation.[3] Tracheostomy was performed in ancient times and the recoding of such events has been documented by asclepiads, the Greek physician in hundred BC.

The development of tracheostomy has been divided into five periods. The "period of legends" dating from 2000 BC to AD 1546; the "period of Fear" from 1546 to 1833 during which the operation was performed only by a few, often at the risk of their reputation; the "period of drama" from 1833 to 1932 during which the procedure was generally performed only in emergency situation on acutely obstructed patient; the "period of enthusiasm" from 1932 to 1965 during which the adage, "if you think tracheostomy ..... do it" became popular and the "period of rationalization" from 1965 to the present[1]. Although this procedure has been used for many centuries, it was considered hazardous and rarely performed till the early part of nineteenth century.[4]

In 1909 Jackson, described the indications, instrument and technique of tracheostomy that are used today4. It is one of the operations which are most frequently done improperly and mismanaged in after carer[5]. In the past tracheostomy used to be reserved for severely ill patients with acute respiratory obstruction; the indications for tracheostomy have been widened to include tracheobronchial

toileting, intermittent positive pressure ventilation, protection against inhalation of foreign body and reduction of dead space[6]. Tracheostomy is thought as an important life saving procedure in many conditions and has now become a well established procedure with more specific indications. It was found that tracheostomy is safer alternative to intubations when a prolonged artificial airway is required[7].

Tracheostomy is a frequently performed procedure and historically has had a high rate of complications[7]. It is one of the life saving procedure. There is a very wise aphorism that if a tracheostomy comes into one's mind then it is the time to do it[9]. It has been found that in ICU approximately 13% of patients will have a tracheostomy at any one time[10]. In the recent years more and more airway problems are managed with either endotracheal intubation or percutaneous, endoscopically guides tracheostomy[10]. But the last one is not yet routinely practiced in our country. So, surgical tracheostomy is practiced here in vast majority of cases to manage airway problems.

Head and neck region is a frequent site of malignancy. Many of these malignancies arise in and around the upper aerodigestive tract. In advanced stages, these malignancies give rise to development of respiratory distress. A great number of patients with head and neck malignancy in our country do not present at early stages, due to ignorance, poverty, and lack of health care. They often present at advanced stages with respiratory distress. In this situation, only tracheostomy can save the life. Main indication of tracheostomy in our country particularly in adult is upper airway obstruction due to head and neck malignancy[11].

Tracheostomy is a very common operation in any otolaryngology and head neck surgery department. But even in this era of antibiotics and aseptic surgery, tracheostomy is not free from complications. Although these complications are usually not serious, but occasional serious complications may arise which may cause death of the patient. The study is expected to show the frequency, indications and complications of tracheostomy in head and neck malignancy. The aims and objectives were to find out the frequency of tracheostomy in head and neck malignancy, their indications and complications.

Materials and Methods

It was an observational study. Sampling size : 50 Period of study : July 2011 to December 2011 Place of study: Department of otolaryngology and head neck surgery of SOMCH Inclusion criteria: Exclusion criteria: This observational study was conducted in the Department of otolaryngology and head neck surgery of SOMCH done using consecutive sampling method. Patient having respiratory distress with head and neck malignancy were included in the study. Patient having respiratory distress due to causes other than head and neck malignancy were excluded. Detailed history and the clinical examination were done with special attention. Fifty patients were enrollment. Data was collected in a prescribed data sheet. Collected data was analyzed and presented in table in a very simplified manner.

Results

Table I: Age distribution (n-50)

Age in year	Numbers	Percentage
25-30	2	4%
31-40	5	10%
41-50	9	18%
51-60	22	44%
61-70	10	20%
71-80	2	4%

The lowest age was 25 year and the highest age was 80 year. Number of patients in 6th decade was highest (44%).

Table II: Sex distribution (n-50)

Sex	Number of cases	Percentage
Male	44	88%
Female	6	12%

Among the 50 patients, male is 88% and female is 12%. Male to female ratio was 7.33:1.

Table III: Socio economic condition (n-50)

Socio economic status	No of cases	Percentage
Poor class	35	70%
Middle class	14	28%
Higher class	1	02%

Most of the patients come from poor socio economic class and about 70%.

Table IV: Occupation (n-5)

Occupation	No of cases	Percentage
Cultivation	20	40%
Service	7	14.28%
Labor	7	14.28%
Business	4	8%
Housewife	3	6%
Teaching	3	6%
Shopkeeper	3	6%
Hawker	3	6%

The commonest occupation group was cultivator (40%)

Table V: Personal habit (n-50)

Personal habit	No of cases	Percentage
Smoking	35	70%
Chewing betel nut and leaf	10	20%
Alcohol	2	4%
None	3	6%

Smoking was the commonest (70%) personal habit. The other common personal habits were chewing betel nut and leaf (20%).

Table VI: indications of Tracheostomy (n-50)

Indications	No of cases	Percentage
Carcinoma larynx	33	66
Carcinoma pyriform fossa	13	26
Carcinoma of the tonsil	1	2
Carcinoma base of the tongue	2	4
Carcinoma of the thyroid gland	1	2

Out of 50 patients, most common indication for tracheostomy was carcinoma larynx (66%).

Table VII: Types of tracheostomy (n-50)

Types	Number	Percentage
Emergency	47	94%
Elective	03	6%

Out of 50 patients 94% were emergency tracheostomy.

Table VIII: Complications of tracheostomy (n-50)

Complications	Number	Percentage
Surgical emphysema	9	18%
Haemorrhage	3	6%
Wound Infection	2	4%
Tube dislodgement	2	4%
Tube blockage	2	4%
Crusting	2	4%
Stomal recurrence	1	2%
Stomal stenosis	1	2%
Subglotic stenosis	1	2%

Out of 50 cases, over all complications was 46%, and most common complication was surgical emphysema (18%).

Discussion

The age range of this study varied from 25 to 80 years, and highest frequency is in the age group 51-60 years. In study by Ahmed and Rahman, the highest frequency in the age group 45 to 60 years which is not similar to our study. Sex distribution of the study among 50 cases showed 44 cases were male and six cases were female. Male to female ratio was 7.35:1. In study by Ahmed and Rahman male to female ratio was 6.91:1 which was similar to our study. In this study 70% of cases came from poor socioeconomic group. But in Rahman et al's study it was 51.48%.

Most common occupational group was cultivators (30%), then businessman (24%), service holders (18%), day-labourer (12%), housewife (8%). Less common occupational group were drivers, teachers and fishermen. In study Rahman et al, cultivators were 28.40%, businessmen 18.34%, service holders 15.98%, day-labourer 11.24%, housewife 5.92% which was almost similar to our study. In this study, personal habits- 75% were smokers, 20% were chewing betel and betel leaf, 4% were alcoholic. In study by Ahmod K et al, 74% were smokers, 42% were betel leaf chewers which is almost similar to our study. The commonest indications of tracheostomy in head neck malignancy were laryngeal carcinoma (66%), followed by carcinoma of pyriform fossa (26%). Less common indications were carcinoma based of tongue (4%), carcinoma of the tonsil (2%) and carcinoma of the thyroid gland (2%).

In the study of Rahman et al (2001), carcinoma larynx was 65% which is similar to our study. In another study by Rahman et al, carcinoma larynx was 54.44% followed by advanced hypo-pharyngeal 8.88% which was almost similar to our study. In our study emergency tracheostomies were 47(94%) and elective tracheostomies were 3 case (6%). In previous study it was about 91% and 9% respectively which was similar to our study.

Complications of tracheostomy in our study were 46%. The most common complications were surgical emphysema (18%). The other complications included haemorrhage (6%), wound infection (4%), tube dislodgement (4%), tube blockage (4%). In study by Miller et al, incidence of complications range from 5 to 40%. It was 39.05% in the study of Rahman et al which is almost similar to our study. In this study surgical emphysema was the commonest complication 18%. In preview who studies carried out in our country it was found 9.47% and 21% respectively which was similar to the result of our study.

The second most complication was haemorrhage - it was 6%. In a previous study at Dhaka Medical College Hospital by Rahman SH et al and Ahmod K et al, it was 5% and 5.33% ,which was similar to our study. Haemorrhage is most commonly occur from anterior jugular vein and thyroid gland. Study by Edward et al, described haemorrhage as the most fatal complication. Out of 36 deaths due to direct complication of tracheostomy, 10 death were due to haemorrhage. But in this study the bleeding was minor and treated conservatively.

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ORIGINAL ARTICLE

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Lipid Profile in Preeclampsia

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Abstract

This comparative cross sectional study on lipid profile in preeclampsia was conducted in the Department of Obstetrics and Gynecology, Sylhet M.A.G Osmani Medical College Hospital during the period of January 2006 to December 2006. One hundred pregnant women were selected consecutively in third trimester.Fifty normotensive pregnant women were selected as controls and fifty preeclamptic women selected as cases. The age range was 20 to 40 years. There was no significant difference of mean age and mean gestational age between the study groups. Preeclampsia was diagnosed as sustained pregnancy induced hypertension with proteinuria. Serum lipid profile includes Total cholesterol (TC), Triglyceride (TG), High density lipoprotein cholesterol (HDL-C) and Low density lipoprotein cholesterol (LDL-C). Mean values of the findings were compared between the study groups. There were significant difference of serum TC, TG, HDL-C and LDL-C between the controls and cases. Serum lipid profile of control groups (normotensive pregnant women) were within normal levels except serum TG. Serum TG was markedly raised in cases (preeclampsia) than controls. Serum HDL-C was below normal range in cases. This study indicates that dyslipidemia particularly hypertriglyceridemia and decreased level of HDL-C is associated with preeclampsia.

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Introduction

Preeclampsia is a multisystem disorder of unknown etiology that is unique to human pregnancy[1]. It occurs in about 6% of the general population. The incidence varies with geographic location[2] .Maternal mortality and morbidity from hypertensive disorders of pregnancy including preeclampsia remains high world wide and is a troublesome area of modern perinatology[3] An estimated one third of maternal death occurs due to preeclampsia even in developed countries like Canada. This scenario is even worse in third world countries like Bangladesh where antenatal and postnatal care is insufficient[4].

There is no effective management strategy other than elective delivery and no therapeutic intervention has proven effective in preventing and ameliorating this disease[5]. Several studies have suggested that women who develop preeclampsia are at increased risk of cardiovascular complications and hypertension later in life. Indeed many risk factors and pathophysiological abnormalities of preeclampsia are similar to those of coronary artery disease[1]. The most widely accepted theory about the etiology of preeclapmsia is endothelial damage and dysfunction[6] . This endothelial damage is the key event in the pathogenesis of preeclampsia[7]. Endothelial dysfunction may result from disorders of lipoprotein metabolism[8] . The causes of endothelial dysfunction are probably multifactoria[6]

Women with preeclampsia demonstrate dyslipidemia [increased level of any one of the plasma total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and decreased level of high density lipoprotein cholesterol (HDL-C)] which contribute to endothelial cell dysfunction[6] . It has been suggested that abnormal lipid profile may have a role in the pathogenesis of preeclampsia[9]. Plasma lipids have a direct effect on endothelial function[10]. The endothelial dysfunction in preeclampsia could originate from dyslipidemia as well as oxidative stress[11]. The role of oxidative stress has been implicated in several studies to the progression of preeclampsia. The mechanism, by which oxidative stress mediates endothelial damage and ultimately vascular reactivity, is not fully understood[12]. The oxidant and antioxidant balance of normal pregnancy is tipped in favour of promoting oxidative stress in preeclampsia[13]. Lipid peroxidation is exacerbated in preeclampsia.Lipid alteration may promote oxidative stress and vascular dysfunction in preeclampsia[14]. Oxidative modification of LDL in the arterial wall is currently thought to be central to the development and

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progression of atherosclerosis [15]. Pregnancy is associated with pronounced physiological hyperlipidemia This feature is not atherogenic and is believed to be under hormonal control. The mechanism regulating physiologic hyperlipidemia may malfunction in preeclampsia[10]. Plasma lipids climb substantially above levels seen in normal pregnancies[16]. Oxidative stress of preeclampsia is associated with a distinct pathologic lesion of the decidual arteries known as acute atherosis.

This arteriopathy occurs in regions of spiral and myometrial arteries in which the physiologic transformational changes are absent [17]. Although numerous basic, clinical, epidemiologic studies have been conducted over the last century the cause and pathogenesis of preeclampsia is still elusive [18]. Many studies on lipid profile in preeclampsia have been done by different researchers in different parts worldwide. In Bangladesh few studies have been done but in Sylhet region no such study has been done yet. So this study was under taken to see the relationship between preeclampsia and lipid profile.

Materials and Methods

This Comparative cross sectional study was carried out in the Department of Obstetrics & Gynecology and Department of Biochemistry in Sylhet M.A.G Osmani Medical College from July 2006 to June 2007. From all the admitted preeclamptic women and normotensive pregnant women in third trimester in the Department of Obstetrics and Gynecology, Sylhet M.A.G Osmani Medical college Hospital. The sampling technique was consecutive and exhaustive. 50 normotensive pregnant women were taken as control (Group I) and 50 preeclamptic women were taken as case (Group II). Preeclampsia was diagnosed by using the current American College of Obstetricians and Gynecologists (ACOG) guidelines. These guidelines defined preeclampsia as sustained pregnancy induced hypertension with proteinuria.

Hypertension was diagnosed as sustained blood pressure readings of 140/90 mm of Hg (with readings taking place>6 hours apart) or a sustained 15 mm of Hg diastolic rise or a 30 mm of Hg rise in systolic blood pressure above 1st trimester blood pressure value. Based on ACOG criteria proteinuria was defined as urine protein concentrations of $\geq$30 mg/dl (or 1+ on a urine dipstick) on 2 or more random specimen collected $\geq$4 hours apart [19] Hypertension detected before 20 weeks of gestation, multiple pregnancy, chronic renal disease, diabetes mellitus, known case of lipid disorder and on current medication known to affect lipid metabolism were excluded from the study. Serum Total Cholesterol (TC) Serum triglyceride (TG), serum high density cholesterol (HDL-C) and serum LDL-C were dependent variables. Age, Gestational age, Blood pressure, Gravidity and BMI were independent variables. Data were collected through a pre-designed structured questionnaire. The study was approved by the ethical committee of Sylhet M.A.G Osmani Medical College. All participants gave informed consent.

After selection of subjects detail history was taken and clinical examination was done. Subjects were requested to fast over night (10-12hrs). Duration of pregnancy was diagnosed on the basis of history, clinical examination and ultrasound findings. Blood pressure was measured with a standard mercury manometer after resting for at least 5 minutes. Systolic blood pressure was recorded at the appearance of sounds and diastolic blood pressure was recorded at the disappearance of sounds (v-phase korotkov) [20]. Proteinuria was assessed by dip reagent strip method. By this method, approximate values of protein in urine were considered for analysis. (In dip strip '+' means 30 mg/dl, '++' means 100 mg /dl, '+++' means 300 mg/dl protein in sample urine). Body mass index (BMI) was calculated as weight (kilograms) divided by height squared (meters squared).

Fasting blood samples were collected from the subjects with aseptic caution. 4 ml of venous blood was collected after 10-12-hours overnight fast for measuring serum glucose, TC, TG, HDL-C and LDL-C. Serum was separated by centrifugation at the rate of 3000 rpm for 15 minutes and was taken into eppendorf. Estimations were carried out as early as possible. Whenever there was delay, sample was stored in a refrigerator at -200 C. The results were presented as Mean ± SD. Independent sample's t-test was used for statistical significance. A level of P <0.05 was accepted as statistically significant.

Results

Serum lipid profile, BP, urinary protein and BMI were measured in one hundred women in third trimester of pregnancy. The results were expressed as Mean ±SD. Fifty (50) women with normal BP were controls of the study, termed as Group-I. Fifty (50) preeclamptic women (Hypertension with proteinuria) were cases of the study, termed as Group-II. Table-I shows distribution of age, gestational age and BMI of the study subjects and compared. Age (years) was 26.08±5.51and 27.46±6.03 in Group-I and Group-II respectively. There was no significant difference (p=0.225) of maternal age between the study groups. BMI (kg/m^2) was 21.44±2.25 and 25.56±3.01 in Group-I and Group-II respectively. There was significant difference (p=<0.001) of BMI between the study groups. Gestational age (weeks) was 34.56±3.11 and 35.36±2.79 in Group-I and Group-II

respectively. There was no significant difference (p=0.179) of gestational age between the study groups.

Table I: Clinical characteristics of the study subjects

Parameters	Group-I (control) n=50	Group-II (case) n=50	t-valu	p-valu
Age (years) Mean ±SD	26.08±5.51	27.46±6.03	1.194	0.235
BMI (kg/m2) Mean ±SD	21.44±2.25	25.56 ±3.23	7.589	<0.001
Gestational age (weeks) Mean ±SD	34.56±2.79	35.36±3.11	1.352	0.179

Table-II shows systolic BP, diastolic BP and gravidity status of the study groups. Mean systolic BP (mm of Hg) were 110.43±8.52 and 155.86±16.91 in Group-I and Group-II respectively. Mean diastolic BP (mm of Hg) were 70.29±8.82 and 101.57±8.20 in Group-I and Group-II respectively. In Group-I number of primigravida were 15(30%) and multigravida were 35(70 %.). In Group-II numbers of primigravida were 22(44%) and multigravidas were 28(56%).

Table II: Blood Pressure and Gravidity status of the study groups

Parameters	Group-I (control) n=50	Group-II (case) n=50
Systolic BP (mmHg) Mean± SD	110.43±8.52	155.30±15.59
Diastolic BP (mmHg) Mean± SD	70.29± 8.82	101.30±8.31
Primi	15(30%)	22 (44%)
Multi	35 (70%)	28(56%)

Table III is showing comparison of serum TC, TG, HDL-C and LDL-C between study groups. Serum TC (mg/dl) was 181.24 ±23.00and 194.00 ±29.79 in Group-I and Group-II respectively. There was significant difference (p=0.018) of serum TC between the studygroups. Serum TG (mg/dl) was 183.60±27.11 and 221.78±58.84 in Group-I and Group-II respectively. There was significant difference (P<0.001) of serum TG between the study groups. Serum HDL-C (mg/dl) was 41.20± 3.75 and 33.40± 5.53 in Group-I and Group-II respectively. There was significant difference (P<0.001) of serum HDL-C between the study groups. Serum LDL-C (mg/dl) was 105.26±16.91, and 117.26± 25.40 in Group I and Group II respectively. There was significant difference (p =0.008) of serum LDL-C between the study groups.

Table-III: Lipidemic status of the study groups

Parameters	Group-I (control) n=50	GroupII (case) n=50	t-valu	p-valu
TC (mg/dl) Mean±SD	181.24± 23.00	194.00±29.79	-2.397	0.018
TG (mg/dl) Mean±SD	183.60±27.11	221.78±58.84	-4.167	<0.001
HDL-C(mg/dl) Mean±SD	41.20 ±3.75	33.40± 5.53	8.254	<0.001
LDL-C (mg/dl) Mean±SD	105.26+18.10	117.26±25.40	-2.721	0.008

Discussion

The etiology of preeclampsia is still one of the major unsolved miseries in obstetrics. Till now it is one of the leading causes of maternal and fetal mortality both in developed and developing countries [21]. Despite advances in prenatal care, frequency of preeclampsia has not changed. Research addressing this disorder has been extensive during the past decade, but has not resulted in substantial improvement in methods of prediction or prevention of the disease. A major impediment in the development of such methods is our poor understanding of the various pathological mechanisms that lead to preeclampsia.[1]

The pathogenesis of preeclampsia continues to be a challenge [22]. Although numerous basic, clinical and epidemiologic studies have been conducted over the last half century; its causes are still elusive [18]. Several lines of evidence suggest that preeclampsia is a multi-etiologic syndrome with heterogeneous biologic heterogeneous biologic pathways. This fact has been cited to explain the variability in its clinical presentation and relatively common in consistency of patho-physiologic studies [22]. One hundred pregnant women in third trimester were selected from Sylhet MAG Osmani Medical College

Hospital. Fifty normotensive pregnant women were selected as control (Group I) and fifty preeclapmtic women were selected as case (Group II). This study design was similar to the study done by Cekmen et al[10].

Mean maternal age (years) of group I (control) and group II (case) were 26.08±5.51 and 27.46±6.03 respectively. Mean gestational age (week) of control and cases were 34.56±2.79 and 35.36±3.11 respectively. Maternal age and gestational age of the study groups were matched, so that chance of variation of study parameters due to age variation could be eliminated. The age distribution of our study subjects were consistent with the study done by Cekmen et al. who had shown plasma lipoprotein concentrations in pregnancy induced hypertension.[10] In that study preeclamptic women and nomotensive women had maternal age (years) 27.56±1.05 vs. 26.48±0.92 (p=NS) and gestational age (weeks) 36.4±1.2 vs. 37.7±1.01 (p= NS).

There were significant difference of serum TC, TG, HDL-C and LDL-C between group-I and group-II. These findings were similar to the findings of Uzun et al.[15] These differences of lipid status between the study groups may be indicative of probable association of abnormal lipid profile with development of preeclampsia. This study shows that mean serum TG was markedly raised in preeclapmsia than normotensive pregnancy. Mean serum HDL-C of cases were below normal level. Mean serum TC and LDL-C were in normal levels in both cases and controls.

These findings were consistent with the studies done by Belo et al[23]. This acute atherosis bears a striking resemblance to atherosclerotic lesion of coronary arteries both showing fibrinoid necrosis of the vessel wall, disruption of the endothelium, aggregates of platelets, and accumulation of lipid-laden macrophages (foam cells).This is considered to be a true atherosclerosis like change.[6] It has been postulated that defective placentation resulting from lipid or non-lipid related causes leading to placental hypoxemia might initiate a cascade of events including excessive lipid peroxidation in placental tissue[24]. The preeclamptic dyslipidemia is not a consequence of the disease because it is present long before the disorder becomes clinically overts.[25]

The association between dyslipidemia and risk of preeclampsia is biologically plausible and is compatible with what is known about the patho-physiology of preeclampsia. At least three hypothesized mechanisms for the dyslipidemia and preeclampsia association have been described in the literature. First, investigators have noted that elevated serum lipid and lipoproteins may induce endothelial dysfunction secondary to oxidative stress. They also noted that dyslipidemia may impair trophoblast invasion, and thus contributing to a cascade of patho-physiologic event that lead to the development of preeclapmsia. Triglyceride accumulation in endothelial cells is associated with decreased release of prostacyclin. Second mechanism is the pathologic process of preeclampsia via dysregulation of lipoprotein lipase resulting in a dyslipidemic lipid profile. Third possible mechanism may be via the metabolic syndrome[19]. We recommend lipid profile investigation in early pregnancy. So that early detection and treatment of dyslipidemia may reduce maternal and perinatal mortality and morbidity.

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ORIGINAL ARTICLE

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Comparison of Lipid Profile in Different Grades of Ultrasound Proven Non-Alcoholic Fatty Liver Disease

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Abstract

The cross-sectional study was conducted among 90 ultrasound proven different grades non-alcoholic fatty liver diseases (NAFLD) of which 39 males and 51 female to compare serum lipid abnormalities. The demographic and lipid profile such as total cholesterol, serum triglycerides, serum HDL and serum LDL were recorded. The mean age of the patients was 49.77 ± 11.34 years, Grade I was 52.2%, Grade II was 40.0% and Grade III was 7.8%. Serum total cholesterol (200.11 ± 30.92 mg/dl, 222.36 ± 27.01 mg/dl, 270.57 ± 42.21 mg/dl; p=0.001), triglyceride (194.26 ± 71.47 mg/dl; 313.89 ± 85.65 mg/dl and 407.57±98.53 mg/dl; p<0.001) and LDL (129.70±27.54 mg/dl, 137.44±21.19 mg/dl and 158.86 ± 28.35 mg/dl; p=0.016) were significantly higher in increasing grades of NAFLD. However, HDL level was significantly lower in increasing grades of NAFLD (34.64 ± 7.87 mg/dl, 28.61±6.79 mg/dl and 26.71 ± 5.71 mg/dl; p<0.001). In conclusion increasing grades of NAFLD are significantly associated with increasing levels of serum total cholesterol triglyceride and LDL and decreasing HDL. Non-alcoholic fatty liver disease (NAFLD), Ultrasonography, Lipid profile, HDL cholesterol, LDL cholesterol, serum triglycerides, total serum cholesterol.

[OMTAJ 2017; 16 (2)]

Introduction

Fatty liver is an acquired reversible disorder of metabolism resulting in an accumulation of triglycerides within the hepatocytes. Probably the most common cause of fatty liver is obesity. Excessive alcohol intake produces a fatty liver by stimulating the fatty liver lipolysis as does starvation. Other causes of fatty liver includes poorly controlled hyperlipidemia, diabetes, excess endogenous or exogenous corticosteroids, pregnancy, total parenteral hyper-alimentation, severe hepatitis, glycogen storage disease, jejuno-ilieal bypass procedures for obesity, cystic fibrosis, congenital generalized lipodystrophy, several chemotherapeutic agents including methotrexate and toxins such as carbon tetra chloride and yellow phosphorus.

Correction of the primary abnormality is usually reverse the process although it is now recognized that the fatty infiltration of the liver is the precursor for significant chronic disease in a percentage of patient.[1] Earlier reports indicated that majority of cases of NAFLD are relatively mild and have a benign course. However, now it has been documented that number of these cases can progress to fibrosis, cirrhosis, liver failure and hepatocellular carcinoma and thus contributes to liver related mortality and morbidity. [2,3]

Most patients with NAFLD have no symptoms or signs of liver disease at the time of diagnosis, although many patients report fatigue or malaise and a sensation of fullness or discomfort on the right side of the upper abdomen. Hepatomegaly is the only physical finding in most patients.[4] Liver biopsy is a sensitive method for diagnosis of NAFLD but it is painful and invasive procedure with rare, but potentially life threatening complications like bleeding[5]. To evaluate and confirm the usefulness of ultrasonography for diagnosis of NAFLD, the present study aims to diagnose NAFLD non-invasively by ultrasound and to compare ultrasonographically diagnosed NAFLD with serum lipid profile.

Materials and Methods

This cross sectional study comprised 90 patients attending The Department of Radiology and Imaging, Sylhet MAG Osmani Medical College Hospital between February 2017 and July 2017. All patients had age more than 18 years, ultrasound proven fatty liver cases without hepatitis, history of no alcohol intake and not on any lipid lowering medicine were included in the study. Consent from the subjects was taken to participate after explaining the objective of the study.

All the 90 subjects included in the present study were

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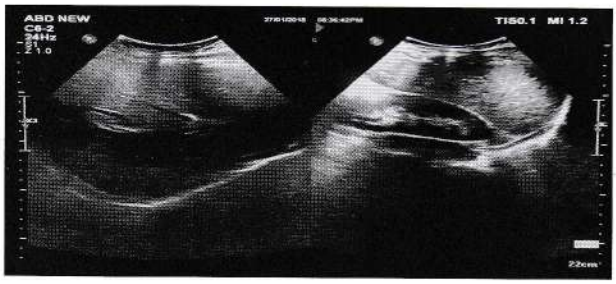
subjectedto a detailed history taking and systematic examination. Ultrasonographic (US) examination of all the patients was done for diagnosing and classifying grades of fatty liver grades. Subjects were considered as cases if they have fatty liver according to the standard criteria accepted by the American Gastroenterology Association i.e., an increase in hepatic echogenicity as a reference, the presence of enhancement and lack of differentiation in the periportal intensity and the vascular wall due to great hyperechogenicity in the parenchyma.

The sonographic examinations were carried out on LOGIC P5 Ultrasound with 3.75 MHz curvilinear probe. Grading of non-alcoholic fatty liver on ultrasonography is as follows: **Grade I:** Slightly increase in the echotexture. Liver presents as bright compared to the cortex of the kidney (Figure 1). **Grade II:** Moderately diffuse increased echogenicity of liver with slight decreased visualization of the intrahepatic vessels. (Figure II). **Grade III:** Significant increase in the echotexture with poor/ no visualization of intrahepatic vessels and diaphragm along with poor penetration of the posterior portion of the right hepatic lobe (Figure III).[5] Enzymatic methods were used for determination of serum cholesterol using Bio-Diagnostic Kit and triglyceride by Human triglyceride kit. Estimation of HDL- cholesterol was done by precipitation method. HDL precipitant and subsequent determination of cholesterol by enzymatic method.[6] LDL- cholesterol was calculated according to the formula given by Friedwald et al.[7]

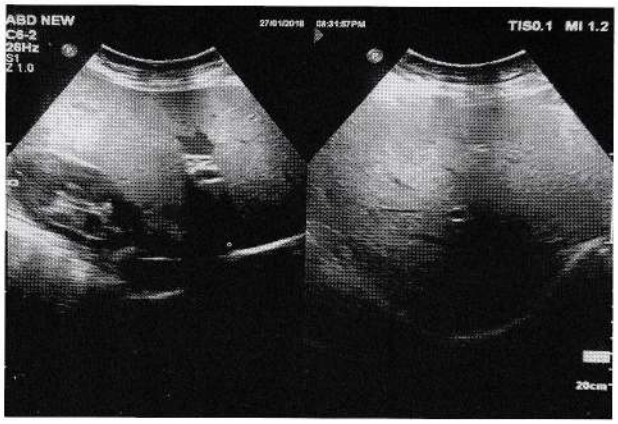
Data were collected and analyzed using SPSS (Staistical Package for Social Science) version 22.0. The categorical variables were expressed and frequency and percentage; while numerical variable were expressed as mean and standard deviation comparison was done using Analysis of variance test (ANOVA) and P value <0.05 was considered statistically significant. Grading of non-alcoholic fatty liver on ultrasonograohy

Fig I : Grade I Minimal diffuse increase in the fine echoes. Liver appears bright compared to the cortex of the kidney.



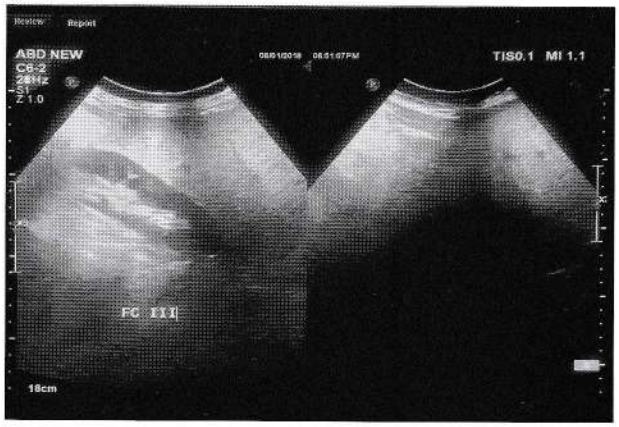
Normal visualization of diaphragm and intahepatic vessel borders.

Fig II : Grade II Moderate diffuse increase in the fine echoes.



Slightly impaired visualization of the intrahepatic vessels and diaphragm.

Fig III : Grade III Marked increase in the fine echoes.



Poor or no visualisation of intrahepatic vessels and diaphragm and poor penetration of the posterior, segment of the right lobe of the liver .

Results

The age of the patients ranged from 30 years to 72 years with the mean age of 49.77 ± 11.34 years (Table-I); 46 (51.2%) patients were in the age group of 40 to 59 years, 22 (22.5%) patients were in the age of 30 to 39 years; 19 (21.1%) patients were in the age of 30 to 39 years and 3 (3.3%) patients were in the age group of 70 to 79 years. There were 39 (43.3%) males and 51 (56.7%) females with ratio of male to female of 1:1.31(Table I). Majority of the patients were in Grade I (52.2%) followed by Grade II (40.0%), and Grade III (7.8%) (Table I).

Table I: Basic characteristics of the patients (n=90)

Basic characteristics	Frequency	Percentage
Age		
Mean	49.77+11.34	
30 -39 years	22	24.4
40 -49 years	23	25.6
50 -59 years	23	25.6
60 -69 years	19	21.1
70 -79 years	3	3.3
Sex		
Male	39	43.3
Female	51	56.7
Grading of Fatty Liver		
Grade -I	47	52.2
Grade -II	36	40.0
Grade -III	7	7.8

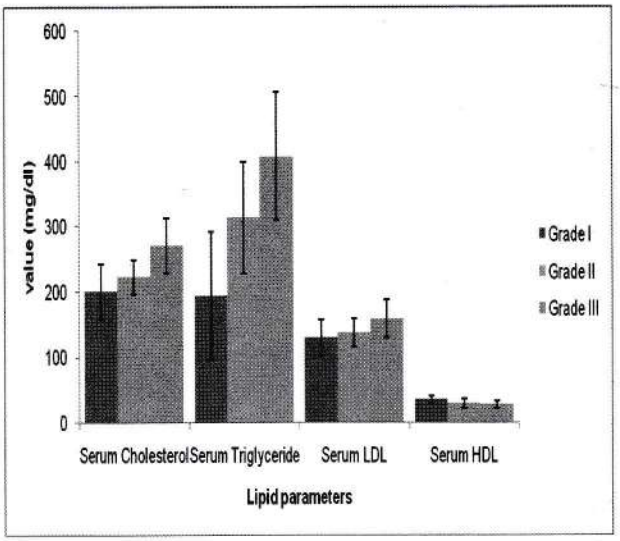


Figure IV: Comparison different grade of NAFLD and Serum Lipid Profile

In the present study total cholesterol level was significantly higher in increasing grades of NAFLD (200.11 ± 30.92 mg/dl, 222.36 ± 27.01 mg/dl; 270.57 ± 42.21 mg/dl; p=0.001). Similarly, triglyceride level (194.26 ± 71.47 mg/dl; 313.89 ± 85.65 mg/dl and 407.57±98.53 mg/dl; p<0.001) and LDL level (129.70±27.54 mg/dl, 137.44±21.19 mg/dl and 158.86 ± 28.35 mg/dl; p=0.016) were significantly higher increasing grades of NAFLD. However, HDL level was significantly lower in increasing grades of (34.64 ± 7.87 mg/dl, 28.61±6.79 mg/dl and 26.71 ± 5.71 mg/dl; p<0.001) (Figure 4).

Discussion

In this study the age of the patients ranged from 30 years to 72 years with the mean age of 49.77 ± 11.34 years. This result was supported by Mahaling et al.[8] that the mean age of 49.14+9.65 years. The result was consistent with the study of Rao et al.[6] This results almost similar with the Indian studies[9,10] as well as most of the western studies also[11,12].

This study also revealed that 51.1% patients were in the age group of 40 to 59 years, 22.5% patients were in the age of 30 to 39 years, 21.1% patients were in the age of 30 to 39 years and 3.3% patients were in the age group of 70 to 79 years . The findings are almst similar to Mahaling et al.[8] & Santoshini et al.[13] In this study 43.3% patients were males and 56.7% were females with ratio of male to female of 1:1.3. This result was almost similar to the study of Rao et al.[6] that 37.3% patients were males and 62.67% were females among their NAFLD cases. This may be due to that in our setting the alcohol pattern are more prevalent among males than females. In the present study majority of the patients were in Grade I (52.2%) followed by Grade II (40.0%), and Grade III (7.8%). This result is almost similar to Mahaling et al[8]. &. Santoshini et al.[13]

In the present study total cholesterol level was significantly higher in increasing grades of NAFLD (200.11 ± 30.92 mg/dl, 222.36 ± 27.01 mg/dl, 270.57 ± 42.21 mg/dl; p=0.001). Similarly, triglyceride level (194.26 ± 71.47 mg/dl; 313.89 ± 85.65 mg/dl and 407.57±98.53 mg/dl; p<0.001) and LDL level (129.70±27.54 mg/dl, 137.44±21.19 mg/dl and 158.86 ± 28.35 mg/dl; p=0.016) were significantly higher increasing grades of NAFLD. However, HDL level was significantly lower in increasing grades of NAFLD (26.71 ± 5.71 mg/dl) patients as compared to Grade I (34.64 ± 7.87 mg/dl, 28.61±6.79 mg/dl and 26.71 ± 5.71 mg/dl; p<0.001). Mahaling et al.[8] reported that that increasing grades of NAFLD were significantly associated with increasing levels of serum total cholesterol and LDL and decreasing HDL. However no significant association was found between serum triglyceride levels (P value-0.05) and increasing grades of sonographically diagnosed NAFLD. Sen et al[14].found that total cholesterol level was significantly higher among fatty liver Grade III (300.57±167.98).Similarly, triglyceride level was also higher among the fatty liver Grade III (431.61±48.76) patients as compared to the grades and the differences were statistically significant. However, LDL was almost similar among all the grades of the patients.

Differences in body-fat distribution or antioxidant

systems, possibly in the context of a genetic predisposition, may be among the explanations. A net retention of lipids within hepatocytes, mostly in the form of triglycerides, is a prerequisite for the development of nonalcoholic fatty liver disease. The primary metabolic abnormalities leading to lipid accumulation is not well understood, but they could consist of alterations in the pathways of uptake, synthesis, degradation, or secretion in hepatic lipid metabolism resulting from insulin resistance. Insulin resistance is the most reproducible factor in the development of nonalcoholic fatty liver disease.[15]

A limitation of this study is that the diagnosis of NAFLD was based on ultrasonography and was not confirmed by liver biopsy as well as lack of controls to investigate the risk of NAFLD. Ultrasonography is by far the commonest method of diagnosing NAFLD in clinical practice.

Conclusion

It may be concluded that increasing grades of NAFLD on USG are significantly associated with increasing levels of serum total cholesterol triglyceride and LDL and decreasing HDL. However a case-control study is recommended to find better understanding of lipid levels among NAFLD subjects.

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ORIGINAL ARTICLE

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Factors affecting the Patient Satisfaction at Outpatient Department in a Tertiary Level Hospital

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Abstract

Patient's satisfaction is a significant issue for outpatient department (OPD). The purpose of the study was to explore the factors affecting the satisfaction of patients attending OPD at tertiary level hospital using a semi-structured questionnaire with 325 respondents through a cross-sectional study. Of them, 26.5% were male and 73.5% were female; 8.8% (191) include the age group of 16-30 years followed by 31-45 (25.8%), 46-60 (12.3%). Housewives attended mostly (45.8%), followed by students (26.2%). Secondary levels of education were complete by 25.2% followed by 24% higher secondary, 21.8% primary level and 7.7% were illiterate. Almost half (48.9%) of the respondents would motivate others to take treatment in the same hospital and would motivate others to rely upon for treatment. Service providers were easily and comfortably met by 93% of the respondents and 54.8% of them opined that the service providers were co-operative and could communicate easily. The hospital was in right track in delivering service to the clients regarding the quality of the service as opined by 55.4% of the respondents and 78.8% evaluated the service was good. Waiting place and lobby was comfortable according to 56.7% of the respondents. There was a significant association between level of education and satisfaction of the doctors consultation time ($p<0.001$); there is also significant association between confidence of the respondent upon the service provided and willingness to refer others to the hospital ($p<0.001$). This study showed that by clinician's communicating, attitude determines patient's satisfaction although socio-demographic, and institutional factors play significant role.

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Introduction

Patient satisfaction is a topic that is important both to medical (health) care providers, the patients (consumers) themselves and other third-party stakeholders in the medical care industry. For health care providers ensuring that consumes are satisfied is a continuous effort. It is therefore critical to them that the true state of patient satisfaction is known. Satisfaction can be describe as a patient's reaction to several aspects of their service experience. Patients thereby evaluate the health-care services as well as the providers from their own subjective point of view.[1]

There are several motivations for surveying patient satisfaction. It may influence health-care utilization, can be a predictor of subsequent health-related behavior and whether patients are willing or not to recommend their health-care provider to others.[2] Patient satisfaction is a useful measure in assessing patterns of communication. Even though patients may not be able to judge specific technical aspects, they provide the best source of accurate information regarding clarity of explanations, helpfulness of information patients are receiving, barriers to obtaining care or the physician's interpersonal behavior.[3]

In 2011, in a survey at 32 different large tertiary hospitals in the USA to identify the relationship of nursing care, physician care and physical environment to the overall patient satisfaction and the results showed that all attributes were statistically significant and positively related to overall satisfaction; however, nursing care was the most critical to increase overall patient satisfaction. The researchers also found that the courtesy and respect of healthcare providers impact more on patient satisfaction while communication and explanation are the second most important aspect,[4] although survey conducted at 13 acute care hospitals in Ireland revealed that effective communication and clear explanation had the strongest impact in improving the overall patient satisfaction among other attributes of care.[5]

While three other studies found that interpersonal communication skills of physicians in terms of their attitude, explanation of conditions, level of care, emotional support, respect for patient preferences and involving patients in decision making were more influential factors than clinical competence and hospital tangibles on patient satisfaction.[6-7] A survey conducted in a tertiary care academic hospital in the USA showed that only 33% of physicians were rated as excellent for their communication behavior which suggests that there

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is room for improvement in physician communication behavior in the hospital to improve quality of care.[8] In addition, the main outcome of a study using the data of 202 participants from general acute care hospitals in the USA, concluded that most determinants of patient satisfaction was related to communication, empathy and caring from hospital personnel.[9]

Material and Methods

This was a descriptive type of cross sectional study conducted to find out the factor affecting the satisfaction of patients attending OPD at tertiary level hospital in Bangladesh with a sample size of 325 using a pretested semi-structured questionnaire from January 2017 to July 2017. Purposive type of non-probability sampling technique used and the data was collect by face to face interview method. Ethical issues were strictly follow throughout the study and guideline from BMRC was follow. After collection, the data was check for any error or omission and cleaned; analyzed using SPSS version 21, presented with tables and chart.

Result

Out of 325 respondents male were 86 (26.5%) and female was 239 (73.5%). Among the respondents 212 (65.2%) were found married to be followed by unmarried 105 (32.3%). More than half (60%) were came from urban area. Secondary level of education were completed by 25.2% of the respondents followed by 24% completed higher secondary, 21.8% primary level, 13.5% completed graduation, 2.55% masters, 4.6% had informal education and 7.7% of the respondents were illiterate. Among the respondents spouse 36.9% were illiterate followed by 17.8%, 12.6%, 6.8%, 5.8% and 2.2% completed primary, secondary, higher secondary, graduation and masters respectively.

Almost half (48.9%) of the respondents would motivate others to take treatment in the same hospital, and similar (48.9%) of the respondents would motivate others to rely upon the same hospital for treatment. About 93% of the respondents commented that the met their service provider easily and comfortably. More than half (54.8%) of the respondents opined that the service providers were co-operative and could communicate easily. The hospital is in right track in delivering service opined by (55.4%) of clients. Regarding the quality of the service, 78.8% of the respondents evaluated the service was good. About the waiting place, 56.7% of the respondents expressed their satisfaction and opined waiting place and lobby was comfortable; only 11.7% opined was waiting place was not comfortable.

Table I: Distribution of the Respondent's by Age Group (n=325)

Age Group	Frequency	Percent (%)
16-30	191	58.8
31-45	84	25.8
46-60	40	12.3
61-75	7	2.2
76 & Above	3	0.9
Mean ± SD	32.18±13.355	

Table II: Distribution of the Respondent's by Occupation (n=325)

Nature of Job of the Respondents	Frequency	Percent (%)
Student	85	26.2
Teacher	10	3.1
Service Holder	32	9.8
Business Man	27	8.3
Labor	17	5.2
Housewife (For Female)	151	45.8
Jobless	3	0.9
Nature of Job of S pouse		
Teacher	5	1.5
Service	49	15.1
Business	85	26.2
Labor	25	7.7
Housewife (For Female)	49	15.1
Jobless	112	34.4

Table III: Distribution of the Respondent's by Monthly Family Income (n=325)

Monthly Family I ncome (BDT)	Frequency	Percent (%)
1000-5000	28	8.6
5001-10000	39	12.0
10001-15000	49	15.1
15001-20000	62	19.1
20001-Above	147	45.2

Table IV: Distribution of the Respondent according to Level of Patient Satisfaction with Medical Consultations (n=325)

Level of Satisfaction	Frequency	Percent (%)
Dissatisfied	85	26.1
Satisfied	240	73.9
Total	325	100

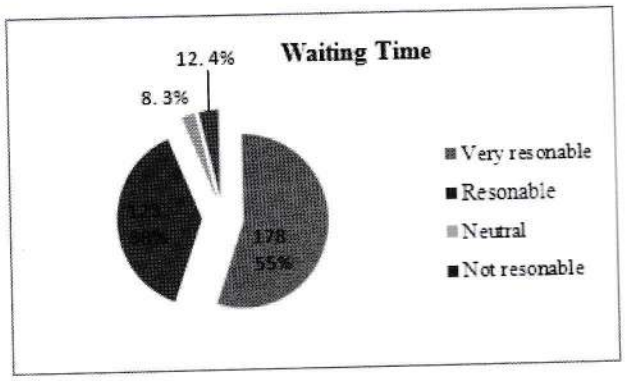

Figure I: Distribution of Respondents according to the Opinion regarding Waiting Time

Table V: Distribution of the Respondents by Association between Level of Confidence and Willingness to Motivate others to Take Treatment in the same Hospital

Level of Confidence	Motivate others to Take Treatment in this Hospital					p-value
	Never	May not be	No Comments	Can Say	Must Say	
Very Confident	1	1	1	30	67	0.001
Confident	0	7	7	105	87	
Neutral	1	0	0	5	4	
Less Confidence	1	1	0	3	0	
No Confidence	3	0	0	0	1	

Table VI: Distribution of the Respondents by Association between Level of Education and Level of Satisfaction of Doctor's Consultation Time

Level of Education	Level of Satisfaction				p-value
	Highly Satisfied	Relatively Satisfied	No Comments	Relatively Dissatisfied	
Illiterate	10	12	3	0	0.001
Informal	11	4	0	0	
Primary	45	24	0	2	
Secondary	49	32	0	1	
Higher Secondary	50	26	1	1	
Graduation	20	23	0	1	
Masters	3	6	0	0	

Discussion

The purpose of this study was to explore the factors affecting the satisfaction of patients attending OPD at tertiary level hospital in Bangladesh with a sample size of 325. Study showed that 73.5% of the respondents were female and rest of them were male among them 58.8% of the respondents were in age group 16-30 years followed by 25.8%, 12.3% and 2.2% were in age group 31-45, 46-60 and 61-75 years respectively.

A similar findings were observed in a cross-sectional analytical study in the year 2015 conducted in a primary health care centre in rural Bangladesh carried out among the patients attending the outpatient department (OPD) of Upazilla Health Complex, Dhamrai, Bangladesh.[10] In the current study, 45.8% of the respondents were housewives and 26.2% were students, among them 34.4% of the spouses were jobless, 26.2% were businessmen and 15.1% were servicemen and housewives as well. Majority of the respondents (48.9%) would motivated others to take treatment in this hospital. A similar study conducted at Dhamrai in 2016 showed that 96.6% of the patients were satisfied with the attitude of doctors, and very few respondents were dissatisfied.[11] Another study conducted in Srinagar, India also reported that more than 90% patients were satisfied with hospital services which was similar to our study finding.[12]

Study showed that about 93% of the respondents met their service provider easily, 4.9% opined it was difficult. During the meeting time of the doctor, about 91% of the respondents were positive. More than half (55.4%) of the respondents opined that the hospital was in right track and only 4.6% opined it was in difficult condition. According to 78.8% of the respondents, the service was good and only 0.9% opined badly. A survey conducted in Dhaka City at June 2007 involving inpatients in public and private hospitals showed that the unavailability of doctors and nurses, as well as their negative attitudes and behaviors, are major hindrances to the utilization of public hospitals. The situation is further compound by lack of drugs, and long travel and prolong waiting times.[13]

Majority of the respondents (73.9%) were satisfied on consultation time of doctors, only 26.1% were not satisfied. A cross sectional study aimed at attitude of patients, assessing their satisfaction level towards ease of getting care, facilities offered at the hospital, attitude of the staff at the hospital and overall status of the hospital revealed that attitude of doctors, nurses and other personnel of hospital which would match patient expectation and lead to satisfaction.[14] Among all respondents, 56.7% opined that waiting place and lobby were comfortable. Majority of them (93.5%) evaluated doctor's service was good. There was a significant association between level of confidence on treatment provided ($p<0.001$). Level of education and level of satisfaction of doctor's consultation time also found to be significantly associated ($p<0.001$). Modern health care organizations have identified the patient as an ultimate consumer of hospital services and understand the importance of patient satisfaction, establishing this as the yardstick.[15]

In a study of patient's exploring satisfaction in the outpatient department, found long waiting time is one of the factors, which lead to dissatisfaction. Waiting time, regardless of the length of the actual wait is an important area to address for enhancing overall satisfaction ratings.[16]

Conclusion

Patient satisfaction is multifaceted and a very challenging outcome to define. Patient expectations of care and attitudes greatly contribute to satisfaction. This study showed that by service providers communicating capability, attitude determines patient's satisfaction although socio-demographic, and institutional factors play significant role. One stop service may be necessary to cut down waiting time before consulting the doctor and improvement of behavior from service providers can further ensure the quality of service.

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ORIGINAL ARTICLE

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Vitamin D and C-peptide status in healthy Bangladesh adult.

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Abstract

Vitamin D is known for its calcium regulatory function, but widespread distribution of vitamin-D receptor (VDR) draws attention for its extra-osseous diverse functional role. VDR is present in pancreatic ?-cells and is related to calcium activated insulin secretion. C-peptide is a 31 amino acid polypeptide molecule that connects 'A' and 'B' chains of proinsulin and co-secreted with insulin in equimolar concentration. After secretion rapid extensive hepatic extraction of insulin and constant renal clearance of C-peptide unaffected by hepatic inactivation makes C-peptide concentration as reflection of endogenous insulin secretory status. In this study 80 non-diabetic healthy people were studied for vitamin D and C-peptide status in Sylhet region of Bangladesh. Fasting serum 25(OH)D and C-peptide concentration were estimated. HOMA-IR calculated for evaluation of insulin resistance. There was no significant difference of C-peptide and HOMA-IR between 34 subjects with family history of DM and 36 subjects without family history of DM. Though all study subjects were sufficient vitamin D status, yet there was significant difference of 25 (OH)D between 37 females (48.3±14.9 ng/ml) and 43 males (56.6 ±11.6 ng/ml). The study subjects were not obese, but there was significant positive correlation of BMI with C-peptide and HOMA-IR and negative correlation (insignificant) with vitamin D. There was also negative correlation of vitamin D with C-peptide (insignificant). It may be concluded that vitamin D may play role in insulin secretion and study to explore association is needed with different risk population like DM or Prediabetes.

[OMTAJ 2017; 16 (2)]

Introduction

Vitamin D is present in two forms D_2 and D_3. Vitamin D_3 is synthesized in the skin by the action of sunlight, UV-B on 7-dehydrocholesterol. Vitamin D_3 synthesized in the skin and the main dietary forms, vitamin D (ergocalciferol, found in plants, yeasts and fungi) and D (cholecalciferol, animal origin) first have to be converted in the liver and then in the kidney. As vitamin D is present in only a limited number of foods, supplements are necessary for people that don't get sufficient sun exposure, such as young children, housewives, office workers and elderly.

Vitamin D is activated via two steps, in each one hydroxyl (OH) group is added. In the first step-which occurs in the liver-one hydroxyl group is added to vitamin D_3 (and D_2) at the 25-position to form calcidiol (25-hydroxyvitaminD), the major circulating form of vitamin D. In the second step-which takes place in the kidney-another hydroxyl group is added to form 1,25-dihydroxyvitamin D (calcitriol), the active form that is responsible for the physiological effects of vitamin D. The classic role of vitamin D is to regulate calcium and phosphorus metabolism. To perform its biological roles, calcitriol binds to a specific receptor called the vitamin D receptor (VDR), which is located in the nuclei of cells of target tissue that include bone, kidney, and intestine-tissues involved in the maintenance of calcium homeostasis-as well as immune, endocrine, hematopoietic, skin, and tumor cells.[1,2]

Normal blood level of 25(OH)D is >30 ng/mL, level <20 ng/mL is deficient and level 20-30 ng/dL is considered as insufficient[3]. Vitamin D receptors are present in tissues that aren't directly involved in calcium metabolism suggests that vitamin D has other functions not related to calcium homeostasis. In addition to regulating DNA, calcitriol is known to have so called non-genomic actions. In intestinal cells, calcitriol acts via nuclear VDR, resulting gene activation, formation of mRNA and consequent synthesis of calbindin proteins responsible for dietary calcium absorption. In some cells, calcitriol acts via cell-surface receptors, which results in the extremely rapid opening of intracellular calcium channels and subsequent activation of an intracellular signaling cascade. This effect is thought to inhibit cell proliferation and promote cell differentiation.[4]

Vitamin D is related to regulation of calcium homeostasis and calcium is associated with secretion of insulin from pancreatic B-cells. Glucose and other

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stimuli form stimulus-secretion coupling involving 2nd messenger calcium. Vitamin D also play role in insulin sensitivity. It has been found that circulating 25(OH)D is inversely associated with IR[4-5]. C-peptide is the connecting peptide, a short 31-amino-acid polypeptide that connects insulin's A-chain to its B-chain in the proinsulin molecule. Due to favorable C-peptide kinetics,1) equimolar secretion with insulin, 2) negligible hepatic extraction, 3) constant renal clearance, 4) proportional changes in secretion rate and its peripheral concentration under varying physiological conditions, its concentration more accurately reflect changes in insulin secretion than insulin concentration which is affected by large and variable hepatic extraction[6].

C-peptide (0.5-2.0 ng/ml) increases in IR. Hypovitaminosis D has been found to be associated with increased incidence of components of metabolic syndrome including Diabetes Mellitus.[2] Due to alarming increased incidence of DM worldwide including Bangladesh, and association of vitamin D and calcium with secretory status of insulin, ensuring normal vitamin D status may have preventive measure of DM. Lack of consistency in vitamin D intervention outcome on insulin secretion and sensitivity, needs more observational studies. In this perspective this study was done to see status of C-peptide and vitamin D in nondiabetic healthy people of Sylhet region, Bangladesh.

Materials and methods

It was an observational study done during January to December 2016 in the department of Biochemistry, Sylhet MAG Osmani Medical College, Bangladesh. Eighty (80) healthy non diabetic study subjects of 20-60 years ages were selected from general population. FBS was estimated with enzymatic colorimetric method, C-peptide and 25(OH)D were estimated by ELISA. HOMA (homeostatic model assessment) method of assessing β-cell function and IR (insulin resistance) are calculated from basal FPG and C-peptide concentration using the HOMA calculator software (http://www.dtu.ox.ac.uk/homa)[7-8] This software was used to generate the IR index (HOMA2IR), insulin sensitivity (HOMA%S), and β-cell function index (HOMA%B). Independent Student's t-test and Pearson 's correlation test were performed. P-value<0.05 was considered statistically significant.

Results

Mean age of study subject was 41.4 ± 3.9. Mean serum C-peptide level was 1.18 ±0.56 ng/ml and Vitamin D level was 52.8 ±13.8 ng/ml [Table: 1]. There were 43 male and 37 female subject in the study and vitamin D level in female (48.3 ±14.9) was significantly lower than male (56.6 ±11.6) [Table-III]. Significant positive correlation of BMI with C-peptide and HOMA-IR found [Table - IV].

Table I: Anthropometric and clinical variables of study subjects

Parameters	Mean±SD
Age (years)	41.4 ±3.9
Height (cm)	158.9 ±8.4
Weight (kg)	57.26 ±8.02
BMI (kg/M^2)	22.66 ±2.78
Gender (Male/Female)	43/37
C-peptide (ng/ml)	1.18 ±0.56
FBG (mmol/L)	4.8 ±0.8
25(OH)D (ng/ml)	52.8 ±13.8
HOMA-IR	0.85 ±0.42
HOMA B%	95.11 ±35.48
HOMA S%	142.59 ±57.69

Table II: Family history of DM of study subjects

Parameters	+ve family history (n=34)	-vefamily history (n=36)	p-value
FBS	4.9 ±1.0	4.7 ±0.6	0.43
C-peptide	1.3 ±0.7	1.1 ±0.4	0.07
HOMA-IR	0.95 ±0.06	0.77 ±0.31	0.07

Table III: C-Peptide and Vitamin D status between male and females

Parameters	Male(n=43)	Female (n=37)	p-value
25(OH)D	56.6 ±11.6	48.3 ±14.9	<0.01*
C-peptide	1.13 ±0.53	1.24 ±0.58	0.36

*Student's t-test, p value <0.05 was considered significant

Table IV: Correlation of BMI, C-peptide, HOMA-IR and Vit-D

Parameters		r-value	p-value
BMI	C-peptide	0.263	0.01 *
	HOMA - IR	0.284	0.01 *
	25(OH)D	-0.035	0.7
Vitamin D	C- peptide	-0.157	0.164

Pearson's correlation, p value <0.05 was considered significant

Discussion

Vitamin D is known for its established role on calcium metabolism. As vitamin D receptor (VDR) is widely distributed in various tissues, it has been now attracted research for its extracalcemic role. VDR is present in pancreatic β-cells and it has been proposed to play role on insulin secretion by modulating intracellular calcium uptake. Insulin and C-peptide are co-secreted in equimolar concentration. Insulin is rapidly degraded in liver but C-peptide does not undergo hepatic extraction. For this reason, estimation of serum C-peptide reflects insulin status.

HOMA-IR was assessed as index of assessment of insulin resistance. In this study 80 non diabetic healthy adult subjects of both sex were selected to assess the vitamin 25(OH)D (25-hydroxy cholecalciferol) and C-peptide status in healthy population of Sylhet region of Bangladesh. Baseline characteristics show normal BMI, 25(OH)D and C-peptide in study subjects. There were 43 males and 37 females. Positive family history of DM was found in 34 subjects. There was no significant

difference of C-peptide or HOMA-IR between subjects with or without family history of DM.

There was significantly reduced vitamin D in females compared to males, though within normal range of serum concentration. No significant difference of Serum C-peptide was observed though it was slightly raised in females with lower vitamin D, reflecting a trend of IR in hypovitaminosis D. Pearson's correlation analysis showed significant positive correlation of BMI with C-peptide and HOMA-IR and insignificant negative correlation with vitamin D. On the other hand vitamin D and C-peptide was inversely correlated though not statistically significant. Optimal vitamin D homeostasis may be essential for both insulin secretion and action, two fundamental features in the pathogenesis of insulin resistance and diabetes. African-Americans experience a disproportionately high prevalence of vitamin D deficiency and increased risk for diabetes.

In the study by Chandler et al (2015)[9] of overweight and obese African-Americans, it was hypothesized that vitamin D supplementation would increase C-peptide, a marker of insulin secretion. For each additional 1000 IU/d of vitamin D_3 taken, non-fasting C-peptide was significantly increased by 0.42 ng/mL ($p<0.001$). The effect of change in plasma 25(OH)D with change in C-peptide was examined. For each 1ng/ml increase in 25(OH)D concentration between baseline and 3 months, there was a significant 0.02ng/mL increase in C-peptide ($p=0.03$). Micka Ann (2009)[10] found low vitamin D status (24 ng/ml) among 147 Bangladeshi women of reproductive age. In her study she proposed that VDR is expressed in active B cells, T cells, and macrophages, which suggests that vitamin D is involved in immune system regulation on some level.

Epidemiological evidence in support of this theory, it has been observed that individuals with autoimmune diseases (such as multiple sclerosis, diabetes, Crohn's disease, inflammatory bowel disease, and ulcerative colitis) and certain infectious diseases, such as tuberculosis, tend to be deficient in vitamin D. It has also been proposed that poor vitamin D status increases cancer risk, as it is thought that the vitamin D response elements located on over 200 human genes may regulate cell proliferation, differentiation, and apoptosis, making vitamin D a key protective factor against cancer. In the present study, level of vitamin D and C-peptide was normal, though significantly reduced vitamin D was found in females, probably due to their less sun exposure.

C-peptide was normal in both males and females. Though there was a trend of negative association of vitamin D and C-peptide, low vitamin D status and its role of insulin secretion was not supported in our study. It may be concluded that though there was no significant correlation of vitamin D with C-peptide and thus IR, yet there was a trend of negative correlation. Further study is needed with deficiency prone target people of vitamin D to explore its association with IR and development of DM.

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ORIGINAL ARTICLE

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Pattern of Ischaemic Heart Disease in Coronary Care Unit of Sylhet MAG Osmani Medical College Hospital.

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Abstract

Patients presenting with cardiac emergencies to hospitals are admitted to the coronary care unit (CCU). In Bangladesh, there has been an increase in patients with ischaemic heart diseases (IHD). To assess the pattern of ischaemic heart diseases in patients admitted in coronary care unit of a teaching hospital. This cross sectional study was undertaken in the Department of Cardiology, Sylhet MAG Osmani Medical College Hospital during the period from January 2012 to December 2014. A total 23147 patients were admitted in CCU and among them 17620 patients were IHD cases. The prevalence of IHD was 76.1% among the CCU admission. Most of the patients were age above 40 years (89.1%), 71.8% patients were male and 28.2% were female with a ratio of male to female of 2.54:1. Pattern of IHD admission were ST Elevation acute myocardial infarction (STEMI) (54.4%), Non ST elevation acute coronary syndrome (Non ST-ACS) (30.6%) and chronic stable angina (15.0%). This study has found that almost three-quarters of cardiac disease were due to IHD and their patterns are ST elevation MI, Non ST-ACS and stable angina in decreasing order of frequency. Efforts should be directed towards risk factors to combat and reduce ischaemic heart disease.

[OMTAJ 2017; 16 (2)]

Introduction

Coronary artery disease (CAD) is a major cause of mortality, and is a global health problem reaching epidemic proportions in both developed as well as developing countries.[1] It is responsible for about 30% of deaths worldwide.[2] Estimates from the Global burden of Disease Study suggests that by the year 2020 this part of the world will have more individuals with atherosclerotic cardiovascular disease than any other region.[3] The South Asian countries of India, Pakistan, Bangladesh, Srilanka, and Nepal contribute the highest proportion of the burden of cardiovascular diseases (CVDs) compared to any other region globally.[3,4]

Bangladesh has been experiencing epidemiological transition from communicable disease to non-communicable disease (NCD). The overall mortality rate has decreased significantly over the last couple of decades. But deaths due to chronic diseases, specially the 'fatal four' i.e. cardiovascular disease (CVD), cancer, chronic respiratory disease and diabetes, are increasing in an alarming rate.[5] Among CVDs, IHD is the leading cause of death in Bangladesh.[6]

There is an increase in the emergency hospital admissions due to IHD in different parts of the world[7,9]. Also; there is a rise in the burden of non-communicable diseases in Bangladesh which is similar to other developing countries in the world. Both these factors had lead to an increase in the number of patients admitted to the coronary care units (CCU). The CCU is one of the most important advancement in the care of patients with acute coronary syndrome (ACS) and other cardiac emergencies.

The key feature of these units is their ability to provide 24 hours nonstop services round the clock with experienced staff and advanced facilities. As CCUs became widespread, the mortality rates decreased from 30% to 5% approximately. Apart from ACS, cardiac diseases with hemodynamic instability and conduction disorders are also treated in these units.[10] Coronary care units themselves are undergoing transition, wherein they are changing from being intensive coronary care units to being coronary care units.[11]

There is lack of data about patients presenting with ischemic heart diseases in CCU of Sylhet MAG Osmani Medical College Hospital, which is a large teaching hospital in Bangladesh. So we intend to study the pattern of ischaemic heart diseases in patients admitted in the CCU of our hospital.

Materials and Methods

This was a cross sectional study conducted among the patients admitted at CCU of Sylhet MAG Osmani

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Medical College Hospital during the period of January 2012 to December 2014. A total of 23147 patients got admitted during this period and 17620 patients were diagnosed as IHD. The inclusion criteria were all the patients admitted at CCU of Sylhet MAG Osmani Medical College Hospital, any age and both sex. Patients were diagnosed according to latest definition of ischaemic heart diseases. Ischaemic heart diseases were classified as ST segment elevated MI, Non ST acute coronary syndrome and chronic stable angina. Data were collected using structured pretested format. The collected data were analyzed by Statistical Package for Social Science (SPSS) for windows version 21.0. Descriptive analysis was made to describe the pattern of the diseases.

Results

A total 23147 patients were admitted in coronary care unit of SOMCH and 17620 patients were ischaemic heat disease (IHD). So, the prevalence of IHD was 76.1% among the coronary care unit admission (Table I). Out of total IHD admitted patients 1911 (10.9%) were below 40 years of age, 8075 (45.8%) were the age group of 40-60 years and 7634 (43.3%) were the age group of above 60 years (Table II).

Among them 12646 (71.8%) were male and 4974 (28.2%) were female with a ratio of male to female of 2.54:1 (Figure 1). Pattern of IHD admission were ST Elevation acute myocardial infarction (54.4%, n=9582), Chronic stable angina (15.0%, n=2637) and Non ST elevation acute coronary syndrome (30.6%, n=5401) (Table III).

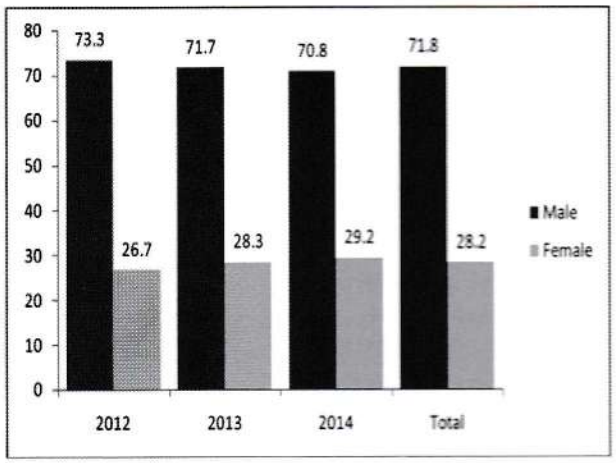

Figure I. Sex distribution of the IHD patients (n=17620).

Table I. The annual distribution of admissions and IHD

Years	Total Admission	Total IHD	Prevalence
2012	5605	4634	82.7
2013	8344	6326	75.8
2014	9198	6660	72.4
Total	23147	1762	76.1%

Table II. Age distribution of IHD patients (n=17620)

Years	<40 years	40-60 Years	>60 Years
2012	454 (9.8%)	2143 (46.2%)	2037 (44.0%)
2013	688 (10.9%)	2858 (45.2%)	2780 (43.9%)
2014	769 (11.5%)	3074 (46.2%)	2817 (42.3%)
Total	1911 (10.9%)	8075 (45.8%)	7634 (43.3%)

Table III. Pattern of IHD patients (n=17620)

Years	ST elevation MI	Chronic stable angina	Non ST elevation ACS
2012	2456 (53.0%)	819 (22.5%)	1359 (29.3%)
2013	3505 (55.4%)	875 (13.8%)	1946 (30.8%)
2014	3621 (54.4)	943 (14.2%)	2096 (31.5%)
Total	9582 (54.4%)	2637 (15.0%)	5401 (30.5%)

Figure in the parenthesis indicates corresponding percentage.

Discussion

Our study is one of the largest comprehensive CCU evaluation studies, in which 23147 patients were assessed over an extended period of three years. Katz et al.[2] examined 29,275 patients admitted to the CCU of a tertiary care medical institution. Casella et al.[13] evaluated, 6986 patients over a 14-day period of patients admitted

to Italian CCUs. There are few reports in our country regarding this issue; the pattern of cardiac disease in CCU of Dhaka Medical College Hospital was reported among 2169 patients,[14] and 2415 patients.[15] In this study the prevalence of IHD was 76.1% among the CCU admission. This result was consistent with the study of Chowdhury et al. [14]

They reported that 78% of cardiac patients were IHD. This result was also correlated with the study of Dogan et al. [10] They reported 65.0% of CCU admission was ACS While Chowdhury et al.[15] reported lower frequency of IHD (45%) among their CCU patients in another report.

In this study 10.9% patients were below 40 years of age, 45.8% were the age group of 40-60 years and 43.3% were the age group of above 60 years. Chowdhury et al[15]. reported 9% patients were below 30 years of age, 24% were the age group of 31- 44 years 67% were the age group of above years. The difference may be due to inclusion of all patients admitted in CCU in their study.

This study revealed that 71.8% patients were male and 28.2% were female with a ratio of male to female of 2.54:1. Similar pattern of sex distribution was reported in most the studies.[16] Chowdhury et al.[15] reported 56% patients were male and 44% were female in a study in Bangladesh. This may be due the fact that fewer females visit health care facilities for treatment due to lack of educational awareness and for socio-economic reasons.

Pattern of IHD admission were ST Elevation acute myocardial infarction (54.4%), chronic stable angina (15.0%) and Non ST elevation acute coronary syndrome (30.6%). This result was correlated with the study of Dogan et al.[10]

They reported that 43.4% patient s of IHD were STEMI, 21.6% were NST ACS. Strength of the study was involvement of large sample with long study period. But there were some limitations too. First of all the risk factors were not detected out in this study and secondly the outcome of IHD was not noted in this study.

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ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 16 Number 2

Association Between Thyroid Autoimmunity and Graves' Ophthalmopathy of Newly Detected Patient With Graves' Disease.

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Abstract

Graves' ophthalmopathy (GO) is one of the important pathognomic features of Graves' disease (GD). This study was carried out to observe any association between thyroid autoimmunity and Graves' ophthalmopathy of newly detected patient with Graves' disease. This cross sectional study comprised of 100 newly detected Graves' disease patient in the department of endocrinology, BSMMU. Detailed history, clinical examination as well as investigation [TSH, FT3, FT4, Anti-thyroid antibodies, Thyroid scan and radioactive iodine uptake (RAIU)] were done on individual basis. Data were collected in prescribed proforma after consent of the patients and processed using SPSS program (version-22.0). 76% of subjects had positive antibody and 50% of participants had Graves' ophthalmopathy. Among ophthalmopathy, 80% had positive antibodies. Anti-TPO antibody correlated with ophthalmopathy.

[OMTAJ 2017; 16 (2)]

Introduction

Graves' disease is one of the most prevalent autoimmune endocrine disorders[1]. and accounts for 60-80% cases of thyrotoxicosis.[2] Central element of autoimmunity directed against the TSH-receptor[3] and the vast majority of patients with Graves' disease have detectable TSH-receptor autoantibodies in serum.[4,5] Autoantibodies that bind to the thyrotropin receptor on thyroid follicular cells and stimulate excess production of thyroid hormone.[6]

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Antibodies reacting to components of eye muscle and fibroblasts are present in sera of patients with Graves' ophthalmopathy.[7] The presence of anti-thyrotropin-receptor antibodies in virtually all patients with Graves' ophthalmopathy suggests that immunoreactivity against the thyrotropin receptor underlies both Graves' ophthalmopathy and hyperthyroidism.[8]

Patients with autoimmune thyroid disease (AITD) have immune reactivity both antibodies and cell-mediated immunity, directed to the TSH receptor, thyroid peroxidase (TPO) and thyroglobulin (TG).[9] Up to 90% of patients with Graves' disease have antibodies directed to the "microsomal antigen" in the thyroid, known to be thyroid peroxidase.[10,11] Lower proportions, approximately 50%, have antibodies directed against TG.[12]

Immunity to TSH-R is believed to lead to production of numbers cytokines in the orbital tissue, which actually mediate the inflammatory process in GO.[13] Crisp et al observed immunoreactivity TSH-R in samples of normal and orbital fat and differentiation of preadipocytes into adipocytes was induced by TSH stimulation.[14,15] In addition to the relation to Graves' ophthalmopathy, TSHR signalling may be important in adipose tissue development.[16] Haraguchi et al. 1999 report that TSH causes proliferation and inhibits differentiation of rat preadipocytes, again supporting the idea that TSH-R may be an important regulator of this process in animals and possibly in man, at least in adipocytes in the orbit. Immunity to TSH-R is believed to lead to production of numbers cytokines in the orbital tissue, which actually mediate the inflammatory process in GO.[13]

Materials and Methods

This cross sectional study comprised of 100 newly diagnosed participants with Graves' disease attending in the department of endocrinology, BSMMU. Subjects were selected on the basis of history as well as clinical and biochemical findings. After full explanation about the purpose of the study, written informed consent was taken from all the eligible participants. Disease specific history was taken from each subject and relevant examinations were done. Investigations [TSH, FT3,

FT4, anti-thyroid antibodies, thyroid scan, radioactive iodine uptake] were done on individual basis. Each individual was interviewed by using structured questionnaires. Data were recorded in a prescribed proforma and processed by SPSS program (version 22).

Results

Present research studied autoimmunity and ophthalmopathy of 100 newly detected patient with Grave s disease and consecutively recruited from the department of endocrinology, BSMMU. Out of 50 patients having ophthalmopathy, 40 had positive antithyroid antibodies. On the other hand 36 out of 50 having no ophthalmopathy despite positive antibody status.

Table-I describes the clinical activity score (CAS) observed in patient with ophthalmopathy. Mean (± SEM) was found to be 1.26 ±0.136 of the 50 subjects having ophthalmopathy. 4(8%) shows active stage (score >3) and rest 46 (92%) had CAS inactive stage.

Table I: Clinical activity score (CAS) of GO in newly diagnosed patient with Graves' Disease (n=50)

Clinical Activity Score (CAS)	Values
Mean score (Mean ± SEM)	1.26 ±0.136
Score ≥ 3 (active)	04(8%)
Score <3 (inactive)	46(92%)

Table II: shows the correlation between antibodies and GO. Anti- TPO and Anti-TG Ab titre strongly correlate each other (r=0.347, P= <0.001). GO shows significant correlation with Anti TPO titre (r=0.195, P= <0.001).

Variable(s)	r	p
Ophthalmopathy vs. anti-TPO titre	0.195	0.051
Anti-TG vs. anti-TPO titre	0.347	<0.001

Table-III shows the predictive capacity of important variables over GO. It was found that low TSH was an independent predictors for GO (P=0.023).

Table III: Multiple regressions for ophthalmopathy in newly diagnosed Graves' disease

Variable(s)	B	SE	β	t	p
Constant	.496	.285		1.741	0.085
Anti -TPO titre	0.000	0.000	0.133	1.319	0.190
Goiter	0.119	0.105	0.117	1.136	0.259
TSH	-0.957	0.414	0.238	2.310	0.023

Discussion

GD is considered as an autoimmune thyroid disease involving autoimmunity against many antigenic components. As part of this autoimmunity, there is eye involvement causing ophthalmopathy, an embarrassing manifestation for the disease.[14,15] Kits for assay of all these antigenic components and autoimmune markers against them are not available widely. Among measurement of anti- TPO and anti-TG Ab are widely exercised and of this two, anti -TPO is relatively more important for autoimmunity for the disease. In present study 76% had positive antibody either single or both antibodies. Other investigators have also observed positive antibody among 50-80% patients with GD.[17,18]

As mentioned above, ophthalmopathy is a relatively specific and important manifestation for GD.[19,20] Present study observed ophthalmopathy in 50% of subjects of which 80% of subjects had positive antithyroid antibodies indicating a strong link and significant correlation of thyroid autoimmunity and Graves' ophthalmopathy. Ophthalmopathy is also considered in light of CAS for the management purpose.[21] Evaluation of CAS for the fifty subjects with ophthalmopathy in the present study observed that about 90% of the subjects had inactive CAS that does not required any active management. Therefore, it is pertinent to assume that if management can be initiated in the early part of the diagnosis there might be a possibility of escaping the hazards and sufferings, observed in Graves' ophthalmopathy. In this point of view GD should be tried for early diagnosis and management intervention.

The present study observed a significant correlation of GD with anti-TPO antibody titre. It appears that the magnitude and intensity of the autoimmunity may be important factors for triggering ophthalmopathy which also reflected by the findings of near significant independent predictability of antibody titre and relatively lower TSH over ophthalmopathy.

Conclusion

A good number of subjects had positive antibody and Graves ophthalmopathy. Among ophthalmopathy, 80% had positive antibodies. Anti-TPO antibody correlated with ophthalmopathy.

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Review ARTICLE

The Osmani Medical Teachers Association Journal Volume 16 Number 2

Management of Urinary Bladder Cancer - A Recent Review

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Abstract

The main treatment of urinary bladder cancer is radiotherapy & surgery. Radiation therapy is highly effective in treating urinary bladder tumor with preservation of normal anatomical and functional activities. The cure rate is comparable to surgery. Surgery is mutilating and often refused by the patient. The purpose of this brief review is to know about the recent development in the field of management of urinary bladder cancer. Urinary bladder cancer, management. Recent insight

[OMTAJ 2017; 16 (2)]

Introduction

Treatment selection is based on the extent or stage, histology, size and multiplicity of tumors and the age, general medical condition of the patient. For certain patients, one modality is sufficient. For others, a combined-modality approach is required. For superficial tumors, cystoscopic resection with or without intravescical therapy is preferred . Once invasion into the muscle is documented, the standard treatment is surgical resection of the bladder, i. e. radical cystectomy or radical radiotherapy both is comparable. After cystectomy, and depending in whether disease is documented outside the bladder, systemic therapy, i.e. chemotherapy and adjuvant radiotherapy may be advised. Demonstrating the superiority of one modality over other requires large number of patients and long follow up, to be clinically meaningful1-3.

Description

Management of superficial and T1 Disease: Superficial tumors are biopsied and removed by transurethral resection (TURBT) or diathermy at the time of cystoscopy. Random biopsies of the bladder are carried out to exclude carcinoma in situ. In the majority of patients, these tumors tend to recur rather than invade (up to 60% recurrence rate). For this reason, cystoscopic follow up needs to be life long.[3,4,5]

If recurrence are multiple or high grade, intravescical chemotherapy or BCG should be used to reduce the recurrence rate to 40%. Intravescical BCG may reduce the recurrence rate for carcinoma in situ (CIS) from 80% to 40% and may also delay the rates of progression. Cystectomy or radiotherapy is indicated if these measures fail. Superficial tumors do respond completely too radical radiotherapy in over 75% of cases [3,6,7] . Management of invasive bladder cancer (T1 and T3) Surgery and radiotherapy both are the standard treatment modalities for invasive bladder cancer.

Management of T2 Disease

Endoscopic resection (TURBT) is inadequate to control these tumors alone. Additional radical treatment with either cysto-prosto-urethrectomy (removal of the bladder and prostate with diversion of ureter) or radical radiotherapy is required. Local practice will determine the treatment option. Most of the Europe and America have favoured radical cystectomy as the treatment of choice.

In the UK radical radiotherapy with salvage cystectomy for these patients with persistent or recurrent more commonly adopted. This policy has the advantage that, the patient has a better chance of tumor control with the bladder intact. If radiotherapy fails, there is a 30% chance of successful salvage by cystectomy. By contrast, if primary cystectomy fails, radical cystectomy is rarely successful for recurrent disease. Each policy carries a similar 5-years survival of about 40-50% Adjuvant chemotherapy following radical radiotherapy or cystectomy to improve survival is yet to be evaluated by randomized controlled trial [3,4,6,7] .

Management of T3 Disease

If investigations have demonstrated macroscopic extension of disease out side the bladder, cure rates fall to around 20% at 5 years. Such patients are more commonly treated with radical radiotherapy than with

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surgery. Pre-operative radiotherapy followed by cysto-urethrectomy is an alternative approach; however no survival advantage has been demonstrated. Combined modality treatment with concurrent chemotherapy (such as cisplatin) and radiotherapy remains under evaluation.

Management of T4 Disease:

A distinction must be made between T_4 mean tumor penetrating into the prostate or vagina. T_4 tumors include both aggressive deeply invasive tumors infiltrating the prostate and less aggressive superficial tumors extending into the prostatic urethra and or ducts. The later has a much better prognosis than the former. T_4 tumors should be treated radically , either surgically or by radiation therapy. T_4 tumors are fixed to neighbouring structures, are inoperable and should be treated with palliative radiotherapy [3,5,7,8]

The criteria for radical radiotherapy includes : age less than 80 years; adequate general medical condition; no inflammatory bowel disease or adhesions; good bladder function; transitional cell carcinoma; (Adenocarcinoma and squamous cell carcinoma are less radio sensitive and they are better treated by cystectomy); single tumor, less than 7 cm in maximum diameter; recurrent T_1 G-III, T_2 - T4a; no metastasis [7-9]

Dose and energy for radical radiotherapy

55Gy in 20 daily fractions over 4 weeks (9-16 MV photons) or 64Gy in 32 daily fractions over 6.5 weeks (9-16MV photons). Dose and energy for palliative radiotherapy: 30Gy in 10 daily fractions over2 weeks (9-10MV) [4].

Chemotherapy

Response rate greater than 50% have been reported, using cisplatin based regimens such as CMV (cyclophosphamide, methotrexate and vinblastin) or MVAC (methotrexate, vinblastin, adriamycin, cisplatin) for metastatic disease. Other newer drugs used are, paclitaxel, gemcitabine, Ifosphamide etc. Intravescical agents used are, BCG vaccine and mitomycin-C [3,8,9,10,11].

Results of treatment

The 5 years survival for radical treatment is 40-60% for T1-T2, disease and 5-30% for T3 and T4 disease [3,7,8,9,12,13] .

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Manuscripts are examined by editorial staff and usually sent to reviewers. Rejected manuscripts will only be returned if accompanied by stamped and self-addressed envelope.

Letters about potentially acceptable manuscripts will be sent to the corresponding author after the review process is complete.

1 Recommendation for the conduct, Reporting, Editing and Publication of Scholarly work in Medical Journals (ICMJE Recommendations). International Committee of Medical Journal Editors. Available at www.icmje.orglicmje-recommendations

2 Additional information regarding manuscript reparation and relevant editorial policy is available in the editorial office