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# Misuse of Antibiotic Accelerating Antibiotic Resistance

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**Introduction:**
Antibiotics are medicines used to prevent and treat bacterial infections. Antibiotic resistance occurs when bacteria change in response to the use of these medicines. Bacteria, not humans or animals, become antibiotic-resistant. These bacteria may infect humans and animals, and the infections they cause are harder to treat than those caused by non-resistant bacteria. Antibiotic resistance leads to higher medical costs, prolonged hospital stays, and increased mortality. The world urgently needs to change the way it prescribes and uses antibiotics. Even if new medicines are developed, without behavior change, antibiotic resistance will remain a major threat.

**Scope of the problem:**
Antibiotic misuse, sometimes called antibiotic abuse or antibiotic overuse, refers to the misuse or overuse of antibiotics with potentially serious effects on health. It is a contributing factor to the development of antibiotic resistance including the creation of multi-drug resistance bacteria, informally called 'superbugs'. Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhoea, and foodborne diseases – are becoming harder, and sometimes impossible, to treat as antibiotics become less effective. Where antibiotics can be bought for human or animal use without a prescription, the emergence and spread of resistance is made worse. Similarly, in countries without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-used by the public. Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.

**Prevention and control:**
Antibiotic resistance is accelerated by the misuse and overuse of antibiotics, as well as poor infection prevention and control. Steps can be taken at all levels of society to reduce the impact and limit the spread of resistance.

**Individuals:**
To prevent and control the spread of antibiotic resistance, individuals can:

- Only use antibiotics when prescribed by a certified health professional.
- Never demand antibiotics if your health worker says you don't need them.
- Always follow your health worker's advice when using antibiotics.
- Never share or use leftover antibiotics.
- Prevent infections by regularly washing hands, preparing food hygienically, avoiding close contact with sick people, practicing safer sex, and keeping vaccinations up to date.
- Prepare food hygienically, following the WHO Five Keys to Safer Food (keep clean, separate raw and cooked, cook thoroughly, keep food at safe temperatures, use safe water and raw materials) and choose foods that have been produced without the use of antibiotics for growth promotion or disease prevention in healthy animals.

**Policy makers**
To prevent and control the spread of antibiotic resistance, policy makers can:

- Ensure a robust national action plan to tackle antibiotic resistance is in place.
- Improve surveillance of antibiotic-resistant infections.
- Strengthen policies, programmes, and implementation of infection prevention and control measures.
- Regulate and promote the appropriate use and disposal of quality medicines.
- Make information available on the impact of antibiotic resistance.

**Health professionals**
To prevent and control the spread of antibiotic resistance, health professionals can:

- Prevent infections by ensuring your hands, instruments, and environment is clean.

- Only prescribe and dispense antibiotics when they are needed, according to current guidelines.
- Report antibiotic-resistant infections to surveillance teams.
- Talk to your patients about how to take antibiotics correctly, antibiotic resistance and the dangers of misuse.
- Talk to your patients about preventing infections (for example, vaccination, hand washing, safer sex, and covering nose and mouth when sneezing).

**Healthcare industry**

To prevent and control the spread of antibiotic resistance, the health industry can:

- Invest in research and development of new antibiotics, vaccines, diagnostics and other tools.

**Agriculture sector**

To prevent and control the spread of antibiotic resistance, the agriculture sector can:

- Only give antibiotics to animals under veterinary supervision.
- Not use antibiotics for growth promotion or to prevent diseases in healthy animals.
- Vaccinate animals to reduce the need for antibiotics and use alternatives to antibiotics when available.
- Promote and apply good practices at all steps of production and processing of foods from animal and plant sources.
- Improve biosecurity on farms and prevent infections through improved hygiene and animal welfare.

**WHO response**

Tackling antibiotic resistance is a high priority for WHO. A global action plan on antimicrobial resistance, including antibiotic resistance, was endorsed at the World Health Assembly in May 2015. The global action plan aims to ensure prevention and treatment of infectious diseases with safe and effective medicines.

The "Global action plan on antimicrobial resistance" has 5 strategic objectives:

- To improve awareness and understanding of antimicrobial resistance.
- To strengthen surveillance and research.
- To reduce the incidence of infection.
- To optimize the use of antimicrobial medicines.
- To ensure sustainable investment in countering antimicrobial resistance.

A political declaration endorsed by Heads of State at the United Nations General Assembly in New York in September 2016 signaled the world's commitment to taking a broad, coordinated approach to address the root causes of antimicrobial resistance across multiple sectors, especially human health, animal health and agriculture. WHO is supporting Member States to develop national action plans on antimicrobial resistance, based on the global action plan.

**Key facts:**

- Antibiotic resistance is one of the biggest threats to global health, food security, and development today.
- Antibiotic resistance can affect anyone, of any age, in any country.
- Antibiotic resistance occurs naturally, but misuse of antibiotics in humans and animals is accelerating the process.
- A growing number of infections – such as pneumonia, tuberculosis, gonorrhoea, and salmonellosis – are becoming harder to treat as the antibiotics used to treat them become less effective.
- Antibiotic resistance leads to longer hospital stays, higher medical costs and increased mortality.

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** Source- WHO-2019*

# Effects of Paddy Dusts on FVC, $FEV_1$ and $FEV_1$/FVC ratio in Male Rice Mill Workers without Protector

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**Abstract:**

**Context:** Among the global risk factors of morbidity and mortality the occupational lung diseases are becoming a great concern. Exposure to paddy dusts in the rice mills causing the workers to be associated with a long history of proliferative and fibrotic diseases in the lungs and also adverse effects on skin, nose and eyes. The aim of this study was to assess the effects of paddy dusts on FVC, $FEV_1$ and $FEV_1$ / FVC ratio of paddy dust exposed rice mill male workers specifically male workers. **Methods:** This cross sectional analytical study was conducted in the department of Physiology, Rangpur Medical College (RpMC), Rangpur from July, 2017 to June, 2018. In this study lung function was being assessed by measuring different parameters of lung volume such as FVC, $FEV_1$, $FEV_1$/FVC ratio. Reduction of these parameters from their normal range was taken into account for impairment of lung function. The study group enrolled 30 healthy male rice mill workers without protector exposed to paddy dust during working in rice mills and the control consisted of age, sex, height, weight and BMI matched 30 healthy males from surrounding community who were not exposed to paddy dust. FVC, $FEV_1$ and $FEV_1$/FVC ratio of all the subjects were measured by digital spirometer. Statistical analysis was done by independent sample 't' test which was performed by computer based software SPSS-24.0 version for windows. **Results:** The mean predicted values of FVC, $FEV_1$ and $FEV_1$/FVC ratio between the male rice mill workers without protector and control group were not significant. The mean measured value and percentage of predicted value of FVC and $FEV_1$ were significantly ($p< 0.05$) lower in the male rice mill workers without protector than the male control group but there were no statistically significant ($p> 0.05$) differences in mean measured value and percentage of predicted value of $FEV_1$/FVC ratio. **Conclusion:** Evaluation of these parameters are helpful in assessing lung function impairment in paddy dust exposed rice mill workers with implicating the importance of usage of protectors during working in the rice mills to prevent the hampering of lung function among the rice mill workers.

**Indexing words:** Paddy dust, Forced vital capacity (FVC), $FEV_1$ (Forced expiratory volume in 1 second), $FEV_1$/FVC ratio

## Introduction:

Definite type of occupational hazards are certainly related to occupational health, which studies on all factors relating to work, working methods, condition of work and the working environment.[1] Occupational respiratory disease can be defined as an acute or chronic disorder that arises from the inhalation of airborne agents in the work place mainly organic dust.[2] The dust exposed in rice mills is a complex organic dust with varied composition including particles of husk, cuticular hair, pollen, bacteria and mucous spore.[3] Paddy dust is known to have a high silica content. The kind of exposure like paddy dust (containing biogenic silica) can cause both restrictive and obstructive type of lung diseases including such responses as extrinsic allergic alveolitis, toxic syndrome, farmer's lung, chronic bronchitis, asthma and interstitial lung diseases.[4] Decrease in various lung function parameters in paddy dust exposed workers may be due to exposure to industrial dust, poor ventilation, non use of face masks and lack of proper exhaust facility.[1] The occupational diseases depend on

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concentration, size, solubility, weight and shape of the dust particle along with the duration of exposure apart from variation in personal immunity. The Swedish National Board of occupational safety and health has prescribed the dust exposure limit of 10 mg/$m^3$ and 5 mg/$m^3$ for normal and organic dust respectively.[5] Several reports have suggested unprotected dust in agricultural work stations may lead to pulmonary fibrosis exhibiting a significant drop in $FEV_1$ and FVC in the workers exposed to paddy dusts.[6]

In occupational respiratory diseases, spirometry is one of the important diagnostic tool. Periodic testing by spirometer plays a significant role in detecting pulmonary diseases in its earlier stages when corrective measures are more likely to be beneficial.[7] To the best of researcher's knowledge there has not been any recent study to identify and assess the health risk of occupational health hazards and safety measures of the rice mill workers against paddy dust exposures in Bangladesh.

Thus the aim of this study was to identify and assess the occupational health hazards among paddy dust exposed workers by measuring this spirometric lung function parameters.

**Methods:**

This cross sectional analytical study was conducted in the department of Physiology in Rangpur Medical College from July 2017 to June 2018. Protocol of this study was approved by Ethical review committee of Rangpur Medical College. For this study 30 healthy male rice mill workers aged between 20-45 years without protector (group-A) were selected from different rice mills of different districts in Rangpur division. Age, sex and BMI matched 30 healthy subjects (group-B) from surrounding community not exposed to paddy dust were selected as control. Fasting serum glucose level, serum creatinine, serum alanine amino transferase levels were estimated in both the groups of the present study for exclusion of DM, kidney disease and liver disease. All the values of these parameters were within the normal range in both groups.

All the subjects were non obese and free from smoking, any type of chest deformities, asthma, COPD, DM, HTN, kidney diseases and any type of systemic illness. Before performing the tests, all the subjects were briefed about the nature, purpose and benefits of the study. Informed written consent of the study subjects were taken in easily understandable Bengali phrases. Detailed family and medical history were taken. All the information was recorded in a pretested data collection form. FVC, $FEV_1$ were measured and $FEV_1$/FVC ratio was automatically calculated by Autospiro (Digital Spirometer). After inputting of age, height, weight of each subject into the spirometer, the predicted value of FVC, $FEV_1$, $FEV_1$ /FVC ratio were automatically calculated by the digital spirometer. Then for measured value several forced expiratory maneuver (with two minutes interval in between each) performed by the subjects and from the values three maximum were recorded. Among these three the maximum one was selected automatically and printed out for data computation. Percentage of predicted value for each parameter was also calculated automatically by the digital spirometer. The readings were taken in standing position. Data analysis was done by using a computer based software SPSS, 24.0 versions for window. Statistical analysis was done by unpaired 't' test. p value <0.05 was accepted as level of significance.

**Results:**

Mean age, height, weight and body mass index were almost similar in male control and rice mill workers without protector and there were statistically no significant differences (p>0.05) between the groups.

**Table 1:** Mean (±SD) values of general characteristics of study subjects (n=60)

| Parameters | Group A (n=30) | Group B (n=30) |
|---|---|---|
| Age(years) | 37.27±2.490 | 36.83±2.350 |
| Height(m) | 1.67±0.0324 | 1.65±0.052 |
| Weight(kg) | 63.167±4.218 | 62.233±3.883 |
| BMI(kg/$m^2$) | 22.567±1.240 | 22.443±1.196 |

In this study there was no significant difference of mean predicted values of FVC and $FEV_1$ between group A and B. The mean measured value and percentage of predicted value of FVC and $FEV_1$ were significantly lower (p< 0.05) in group A than in group B. There were no statistically significant differences in mean predicted value, measured value and percentage of predicted value of $FEV_1$/FVC ratio between group A (male rice mill workers without protector) and group B ( male control)).

Table 2: Showing statistical analysis of mean values of FVC, $FEV_1$ and $FEV_1$% of study subjects:

| Lung function parameters | Measurements | Mean(±SD) | | 't' value | p value |
|---|---|---|---|---|---|
| | | Group A | Group B | | |
| **FVC** | Predicted value(L) | 3.73(±0.399) | 4.39(±0.428) | 6.174 | $0.545^{NS}$ |
| | Measured value(L) | 2.68(±0.227) | 4.34(±0.447) | 18.16 | $0.013^{S}$ |
| | Percentage of predicted value (%) | 66.76(±4.59) | 99.10(±3.10) | 31.96 | $0.009^{S}$ |
| **$FEV_1$** | Predicted value(L) | 3.415(±0.162) | 3.628(±0.19) | 4.661 | $0.551^{NS}$ |
| | Measured value(L) | 3.145(±0.123) | 3.513(±0.38) | 4.703 | $0.002^{S}$ |
| | Percentage of predicted value (%) | 66.20(±6.166) | 99.31(±2.89) | 26.108 | $0.002^{S}$ |
| **$FEV_1$/FVC** | Predicted value(L) | 85.00(±1.37) | 86.61(±1.77) | 3.910 | $0.113^{NS}$ |
| | Measured value(L) | 85.14(±8.79) | 85.06(±2.30) | -0.062 | $0.950^{NS}$ |
| | Percentage of predicted value (%) | 99.36(±10.47) | 98.34(±1.67) | -0.680 | $0.498^{NS}$ |

**Discussion:**

In the present study, mean measured values of FVC, $FEV_1$ and $FEV_1$/FVC ratio in healthy control group were within normal range and also similar reported by other investigators from different countries.[4,8] There were no statistically significant differences of mean predicted values of FVC, $FEV_1$ and $FEV_1$/FVC ratio between the groups. However no published data of these study parameters in paddy dust exposed workers are available for comparison from our country. The observations in this study indicated that although obstructive pulmonary impairment was more frequent, both types of changes were present in rice mill workers. Due to paddy dust exposure fall in FVC indicated restrictive lung changes and fall in $FEV_1$ indicated obstructive lung changes.[9] Both these decreases were statistically significant than the control subjects. Mean measured and percentage of predicted values of FVC of male rice mill workers without protector were significantly lower than the control males which findings were similar to the studies by other investigators also.[3,4,6,9,10-12] Some previous studies also showed significant decrease in mean measured and percentage of predicted values of $FEV_1$ in male rice mill workers without protector in comparison to the control as collaborated by this study.[3,4,6,9,11-13] No significant ($p>0.05$) change in $FEV_1$/FVC ratio between both the groups were found in this study which is further supported by similar findings observed by Itagi et al[9], Musa et al[10] and Wickramage et al[12]. The decrease in FVC might be due to much more changes to the bronchi and elastic components of lungs resulting in restrictive type of lung impairment. Decrease in $FEV_1$ showed that exposure to dust caused early obstructive pulmonary impairment which further increased with increase in numbers of years of exposure.[14] Though various suggestions made by different investigators as mentioned earlier as possible causes of lung functions impairment but it is difficult to comment on exact mechanisms in this type of study. From the discussions of researchers it covers a few way in this regard of mechanism; macrophages and mucocilliary system were responsible for the clearance of dust particles from the lungs. Inhalation of paddy dusts over long time might lower the ability of macrophages to eliminate particles and impaired the activity of cilia lining the bronchi with decreased rate of airway clearance. This might result in penetration of the dust particles into the interstitium. As a result of subsequent inflammatory responses, hypertrophy and hyperplasia of mucous glands occurred which were causing progressive impairment of lung functions with increased work of breathing resulting in lower values of FVC, $FEV_1$.[15] Another mechanism responsible for this inflammatory reaction was mentioned by the researchers supposed to be the chronic allergic effects of paddy dust which produced sufficient IgE in the body. IgE bound with the mast cell and basophil causing release of agents including SRSA, protease, histamine, neutrophil and eosinophil chemotactic factor at alveolar or bronchiolar site. Such type of immunologically induced inflammation due to inhalational exposure to a large variety of antigens caused increasing lung parenchymal and airway

resistance secondary to tissue damages and inflammation mediated fibrotic changes.[15] In this study it is suggested that repeated microinsults to the lungs on each exposure to the toxic component of paddy dusts would have damaging effects, thus a long time exposure to paddy dusts cause progressive impairment of lung functions and adversely affects the parameters such as FVC, $FEV_1$. There is no effects on $FEV_1$/FVC ratio because may be due to proportionately decrease in $FEV_1$ and FVC in male experimental group without protector in comparison to the control subjects.

**Conclusion:**

From this study, it can be concluded that rice mill workers without protector exposed to paddy dust usually suffer from impaired lung function. So it is suggested that the rice mill workers and the rice milling authority should implement appropriate measures like regular use of respirator and other protective measures like face masks, aprons, goggles, hand gloves and making the use of these protectors mandatory during working, maintenance of proper ventilation, raising awareness about the occupational health hazards among the workers for prevention of developing impaired lung functions.

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# Effects of Tobacco Consumption on Serum Creatinine & eGFR levels in Smokers

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**Abstract:**
**Background:** The recent decades have been a massive global increase in tobacco use. Tobacco use is a major preventable cause of premature death and diseases. Immediate availability and the low price give rise to high consumption of tobacco smoking and causes alteration of renal functions. The study was aimed at to observe the effects of tobacco consumption on renal functions in smokers. **Methods:** This cross sectional analytical study was conducted from July 2016 to June 2017 in the Department of Physiology, Rangpur Medical College, Rangpur. A total number of 60 subjects of both sexes were selected, among them 30 were apparently healthy non-smoker subjects as control group (group A) and 30 were apparently healthy smoker subjects (group B). The subjects were selected from different area of Rangpur city. The effects of cigarette smoking on renal functions were studied by measuring the levels of serum creatinine and eGFR. For statistical analysis independent sample "t" test was performed by computer based software SPSS-17.0 version for windows. **Results:** Serum creatinine levels were significantly higher ($p<0.001$) & eGFR levels were significantly lower ($p<0.001$) in smoker subjects as compared with the healthy control subjects. **Conclusion:** The increased serum creatinine & decreased eGFR levels in smoker subjects were evidence of development of renal function impaired due to tobacco smoking and this might offer a new approach to renal function impairment prevention in population with tobaccco smoking.

**Indexing words**: Tobacco smoker, Creatinine, eGFR

**Introduction:**
Tobacco is a product prepared from the plant by curing them[1]. Tobacco contains the alkaloid nicotine, which is an extremely addictive drug[1,2]. In addition to nicotine, tobacco contains thousands of other chemicals such as cresol, pyrene, DDT, carbon monoxide, ammonia, hydrogen cyanide, acetone, methanol, formaldehyde, arsenic, cadmium etc[3,4]. Dried tobacco leaves are mainly used for smoking in cigarettes, cigars, pipe tobacco, and flavored shisha tobacco. They can be also consumed as snuff, chewing tobacco and dipping tobacco[1].There are two kinds of commonly used tobacco products in Bangladesh i.e. smoking and smokeless tobacco products[4].

In Bangladesh 43.3% of adults (41.3 million) use tobacco either in smoking and/or smokeless form. More than five million people die globally each year due to tobacco related illness, the figure expected to increase to 8.3 million by 2030[5,6].

Now a day the adverse effects of smoking on renal function have gained more attention, because it is associated with excessive morbidity and mortality. In addition to its known cardiovascular consequences of cigarette smoking are also considered to be the common particular risk factor for the renal function disorders[7]. Some researchers observed cigarette smoking identified as an important risk factor cause renal dysfunction, not only in subjects with pre-existent primary renal disease, hypertension and diabetes mellitus but also in healthy subjects[8].

Tobacco smoke contains over 4,000 particles and gases, some of which are nephrotoxic. Particles include heavy metals known to cause tubular injury such as cadmium and lead, which may reach serum concentrations above 40% in smokers[9]. Cigarette smokers are exposed to significant amounts of cadmium (Cd) and lead (Pb), which also accumulate in kidney tissue more than in any other organ[10]. Nicotine causes mesangial cell proliferation and this change is observed in kidneys of active smokers[11].

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In smokers alteration of the relevant biochemical parameters may be indicators of onset of renal failure. The kidney functions are affected adversely in smoker non-tobacco chewer group, indicated by the elevation of serum creatinine and decrease of eGFR[13].

According to the official Agricultural Statistics (2010) three varieties of tobacco- Jati, Motihari and Virginia – are grown in different districts of Bangladesh. Rangpur still remains highest with 40,345 acres during 2008-2009[12].

The purpose of this study was to asses the effect of tobacco on some renal parameters of smoker subjects of northern region because the rate of tobacco use is more among the people of this region. As far as our knowledge, this kind of study was not previously done in our country. This study would increase awareness about the adverse effects of unjudicial tobacco use on renal system.

**Methods:**

The cross-sectional analytical study was conducted in the Department of Physiology, Rangpur Medical College, Rangpur from July 2016 to June 2017. The Rangpur Medical College Ethical Committee and Thesis Protocol Review Committee approved the study protocol. Total number of 60 apparently healthy subjects of both sexes with age 30-45 years was selected for this study by purposive sampling method. They were divided into: Group A – comprises 30 apparently healthy non- smokers and Group B - 30 apparently healthy smokers. The subjects included in each group matched in their age and socio-economic condition. The duration of smoking is more than three years. Height and weight of the subjects were measured. As tobacco chewing may produce similar effects on renal function, so tobacco chewer persons were excluded from both groups. All the subjects were free from history of liver, heart, lung and other chronic systemic diseases, obesity & diabetes mellitus, hypertension. Pregnant and lactating mother was also excluded from the study.

After selection of subjects, the objectives and the procedure of the study were explained in detail to them and their informed written consent were taken. A standard questionnaire was filled after taking history and through clinical examinations. At the first day all study procedures were maintained and advised the subjects to be in overnight (8-10 hrs) fasting state. They were asked to attend next day at 8.00 A.M. at the Department of Physiology, Rangpur Medical College, Rangpur. Fasting venous blood sample was collected following standard procedure. Serum creatinine was estimated at the Department of Biochemistry, Rangpur Medical College, Rangpur.

eGFR (estimated glomerular filtration rate) was calculated by Cockcroft-Gault formula by using serum creatinine level, age, sex and body weight of the patients[14].

For statistical analysis independent sample "t" test was performed by computer based software SPSS-17.0 version for windows.

**Results:**

Table 1 shows that the mean serum creatinine levels was significantly higher ($p<0.01$) and eGFR levels was significantly lower ($p<0.01$) in smoker non- tobacco chewer subjects than those of healthy control subjects.

**Table 1:** Mean ± SD of serum Creatinine and eGFR levels in two groups (n=60)

| Variables | Group A (non-smokers) Mean ± SD Range (L- H) | Group B (Smokers) Mean ± SD Range (L- H) | p value |
|---|---|---|---|
| Serum Creatinine mg/dl | 0.8967 ± 0.13515 (0.70–1.10) | 1.4000 ± 0.15536 (1.10–1.70) | 0.000*** |
| eGFR ml/min/1.73m$^2$ of body surface area | 96.4440 ± 19.40323 (66.30–139.68) | 68.0887 ± 8.78026 (53.94–87.50) | 0.000*** |

A= Apparently healthy subjects of non-smokers (Control)
B= Apparently healthy subjects of smokers (Experimental)
n= Number `of subjects
$p<0.05$ was considered as significant
# Normal range of serum creatinine level is 0.6 – 1.3 mg/dl[15]
**#** Normal range of eGFR level is ≥ 90 ml/min per m$^2$ body surface area[16]

**Discussion:**

In this cross sectional study, serum creatinine levels were significantly higher ($p<0.01$) and eGFR levels were significantly lower ($p<0.01$) in smoker non tobacco chewer subjects than those of healthy control subjects which is comparable to others.[7,17]

Literature review suggested several mechanisms for these changes of serum creatinine and eGFR levels in smoker non-tobacco chewer subjects. Higher levels of serum creatinine and lower levels of eGFR in smoker non-tobacco chewer subjects might be due to tobacco contains nicotine and also some toxic components which are nephrotoxic cause alteration of the kidney functions. The effects of heavy metals in tobacco like Cadmium (Cd) and Lead (Pb) cause glomerular dysfunction lead to renal damage. Tobacco smoking induces renal damage through enhancing the synthesis of free radicals lead to alter the glomerular functions and increase the serum creatinine and decrease eGFR levels. In addition, smoking causes generation of high amounts of carboxyhemoglobin and decrease oxygen delivery to tissue lead to hypoxia causes ischemia in renal glomeruli and basement membrane which causes impairment of renal functions. Nicotine increases mesangial cell proliferation through activation of nicotinic receptors. Tobacco smokes responsible for impairment of renal function which indicated by increase serum creatinine and decrease eGFR levels.[7]

Smoking increases the risk of atherosclerosis in the arteries of lower extremity and increased stiffness of central vessels causes increased energy transmission to low resistance arterioles in the kidneys, which is a key factor in the pathogenesis of glomerular and tubular damage.[17]

From the results of the present study, higher serum creatinine and lower eGFR levels in smoker non tobacco chewer subjects might be due to tobacco smoking for a prolong period of time which induced sustained rise of blood nicotine, carboxyhemoglobin levels and also free radicals cause impaired renal functions in tobacco smokers.

**Conclusion**

In this present study, it has been concluded that higher serum creatinine and lower eGFR levels in smoker non-tobacco chewer subjects might be due to renal functions impairment in tobacco smoking for a prolong period of time which induced sustained rise of blood nicotine level. But exact mechanism of high levels of serum creatinine and lower levels of eGFR in this group of people could not be demonstrated from this type of study. So, estimation of serum nicotine level, in same study population with large sample size which may help us to avoid bias. Reduction in tobacco smokes improves renal function impairment & reduces mortality and morbidity in smokers.

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# Outcomes of Transcanalicular Laser-assisted Dacryocystorhinostomy in Patients with Chronic Dacryocystitis

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**Abstract:**

**Objective:** The main objective of this prospective, non-comparative case series study of 71 consecutive procedures was to analyze the success rate, procedure time and other complications of transcanalicular diode laser-assisted dacryocystorhinostomy (laser DCR) in patients with chronic dacryocystitis. **Methods:** This study comprised of 71 eyes of 52 patients with chronic dacyocystitis came to ophthalmology department of Rangpur Medical College Hospital for surgery. Osteotomy was done by applying 980 nm diode laser with power of 10 watts via an optic fibre through upper and lower canaliculi. Operating area of all patients was anesthetized by surface and local anesthetic agents. Success of the procedure was measured by patency of lacrimal drainage system on irrigation. **Results:** 71 successive transcanalicular laser DCR without silicon tube intubation in 52 patients were performed. The lacrimal system was functional in 58 (81.3%) cases, and failed in 15 (18.3%) cases. The average procedure time was 11 min (range 9-21 min). **Conclusions:** Transcanalicular laser DCR appears to be an effective, minimally invasive quick and safe procedure yielding a satisfactory success rate.

**Indexing wards:** Transcanalicular dacryocystorhinostomy, Diode laser

**Introduction:**

Nasolacrimal duct obstruction (NLDO) is the most common cause of chronic dacryocystitis. In treatment of the patients with chronic dacryocystitis, external dacryocystorhinostomy (DCR) is the "gold standard"[1, 2, 3] for its highest success rate. Toti in 1904 first described DCR as an external approach to the sac through a skin incision in the medial canthus, resecting the adjacent lacrimal sac and nasal mucosa with their intervening bones. Alternative techniquesto external DCR, such as balloon catheter dilatation, endonasal DCR, laser-assisted endolaserDCR have been applied to increase the rate of success.[4,5]

The next step in the development of less traumatic DCR is the transcanalicular approach. In this approach, first described in 1963 by Jack, a probe is inserted through the lacrimal puncta via the canaliculus into the lacrimal sac following the anatomical pathway of tear outflow.[22]

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Osteotomy is performed by laser energy [6] through an optic fiber, which is inserted into the punctum and is moved towards the nasal wall.[7,21] Different wavelengths of lasers have been used to perform osteotomy as for DCR procedure. As part of a transnasal approach: Holmium: Yttrium-Aluminum Garnet (Ho:YAG) laser, potassium-tytanyl-phosphate (KTP) laser, Neodymium:YAG (Nd:YAG) laser, Erbium:YAG (Er:YAG) laser, and diode laser are used. Recent popularity of laser surgical technique over mechanical DCR techniques include: Incision free procedure that avoids visible scaring, requires shorter operating time, precise cutting and removal of tissue by ablation, minimal trauma to adjacent tissue, produces less bleeding, possibility to perform the procedure endoscopically.

The present study prospectively evaluated the surgical success and safety in patients with nasolacrimal duct obstruction treated with multidiodetranscanalicular laser in a series of 71 successive procedures.

**Methods:**

A prospectivenoncomperative case series study was taken for 71 eyes of 52 patients with chronic dacryocystitis that were admitted to ophthalmology department of Rangpur medical college hospital for operation from April 2018 to

April 2019. The study was carried out in accordance with the tenets of the Declaration of Helsinki and informed consent was obtained from all patients. All patients underwent Transcanalicular laser dacryocystorhinostomy.

After complete ophthalmic examination, nasolacrimal duct obstruction was confirmed preoperatively with lacrimalirrigation and in each case. Blood tests were obtained from all patients to analyze systemicdiseases. The patients were selected according to the following criteria: (i) no history of nasolacrimal duct surgery; (ii) no canalicular obstruction; (iii) no history of traumatic injury to the ocular or nasal region; (iv) no concomitant nasal pathology, such as septum deviation, concha bullosa, nasal polyposis, andatrophicrhinitis; (v)absence of active in fective dacryocystitis;(vi) absence of dryeyeandlowerlidlaxity. Additional intranasal abnormalities and paediatric cases were excluded from the study.

All operations were performed under local anesthesia. Before the surgery, topical anesthetic drops (oxybuprocaine hydrochloride 0.4%) were put on the conjunctiva and cornea. Then intranasal, infraorbital, and lateral nasal side anesthesia were applied with a solution mixture of epinephrine hydrochloride and lidocaine. After dilating the lacrimal puncta, the fiber was inserted through the canaliculus to the wall of the sac. The feeling of a hard stop is essential during the insertion process. With the endoscopic visualization of the nasal cavity, the redlight reflex of the fiber is clearly seen on the nasalwall of the middle turbinate plane. In this way, the target tissue was determined by the laser light guide.

Diode laser (INTER medic multidiode S15 OFT$^{TM}$) parameters were settled at 10W in 500ms pulse mode potency, taking care not to prolong each impact to avoid over heating the structures. After reaching then as alcavity, the osteotomy was expanded sufficiently with the fiber manipulation. A Crawford-type aspirator was used to displace the middle turbinate medially to protect the septum and middle turbinate and to maintain adequate exposure to the surgical site. Laser application was continued until the width of the new ostium be comes greater than 5mm diameter. The size of osteotomy was controlled by the use of the nasal endoscope. At the end of the surgery, laser probe was removed and lacrimal irrigation with saline solution was administered.

Postoperative treatment included antibiotic and steroid eye drops, nasal steroid spray were to be used four times a day for 2 weeks. Oral antibiotic was to be used if necessary. Follow-up examinations were scheduled for the first day, first week and three months after operation. Patency of nasolacrimal duct was determined as absence of tearing or successful irrigation of the lacrimal




**Figure 1:** Diode laser (INTERmedicmultidiode S15 OFT$^{TM}$) machine



**Figure 2:** An endoscopic tower with a rigid endoscope



**Figure 3:** semi-rigid fibro optic laser probe introduced through lower canaliculi

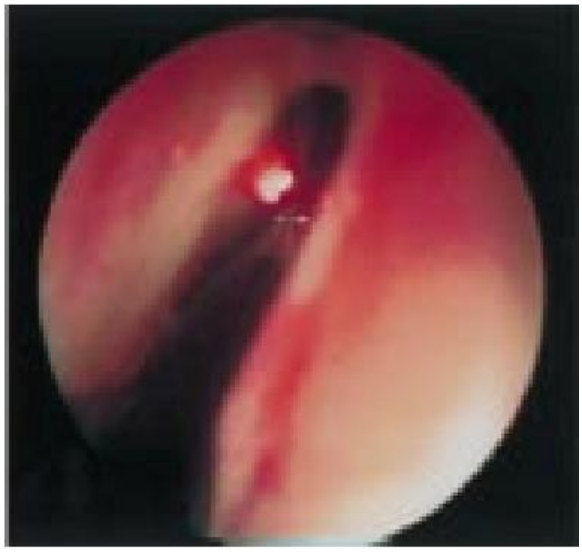


**Figure 4:** Endoscopic view of red light reflex of laser seen on nasal wall of middle turbinate where ostium was created

**Results:**

We performed 71 successive tran scanalicularendolaser DCR of 52 patients from April, 2018 to April, 2019. Male was 16 (30.8%) and females was 36 (69.2%), bilateral involvement was found in 13 (25%) and average age 52 years (range 21- 65 years). The average procedure time was 11 minutes (range 9 to 21 minutes). Final success rate was (58/71) 81.7%.

We noticed swelling of ipsilateral lower eyelid in 29 cases, and bruising in six cases. The swelling usually resolved within 2-3 days and bruising disappeared after 1-2 weeks. Three cases developed common canalicular thermal injury due to strayed laser emissions while undergoing intervention. The results of these cases were obtained as unsuccessful cases. By endoscopic examination, formation of postoperative granulomas occurred in two cases. These granulomas were removed, but there was mucosal scaring around the osteotomized area and the results were evaluated s failure cases.

**Discussion:**

Transcanalicular laser DCR is a minimally invasive surgical procedure, which has the great advantage of accessing the operating field through anatomic pathways.Thesuccess rates of laser DCR are generally lower than those of external DCR, which is considered to be the "gold standard"[1-3]. Success rates of external DCR usually range between 85-99%, and are usually greater than 90%[8,9]. However, the advantages of laser DCR over external DCR are lack of scar development, fewer morbidities, diminished perioperative and postoperative bleeding, intact pump mechanism because of unaffected medial canthal tendon and a less invasive procedure. The technique can be easily applied under local anaesthesia. In our study, since we have applied this technique only recently, we did not include paediatric cases in the study because of their narrower intranasal operative field.

In different studies, success rates of transcanalicular laser DCR have varied between 59-92%, mostly< 85%.[10-17]The success rate in our study is 81.7%. We attribute this, because of creating proper sized ostial openings, selective patients and surgery done by two experienced surgeons in external DCR technique. Restenosis at the site of osteotomy is one of the leading causes of long-term failure in DCR.[19,20] An osteotomy of more than 10 mm in diameter can be routinely achieved by the classic approach, and a slightly smaller osteotomy of 7-9 mm is achieved with the transnasal approach.[18] The osteotomy size in our series was on an average 5 mm. We believe this is sufficient when using our technique, as there is minimal trauma to the surrounding mucosa and connective tissue, resulting in less postoperative scarring.

There are certain disadvantages of this procedure: Some concern handling of the laser and the costs of it. Other disadvantages are synechia and granulation tissue formation, common canalicular stenosis and low success rate in paediatric patients. Otherwise, transcanalicular laser DCR is the alternative modalities to external DCR or endonasal DCR. The absence of skin scars, shorter duration of the operation, shorter learning-curve, lack of orbital perforation risks, need for fewer number of instruments, reproducibility of the techniques, better perioperative and postoperative hemostasis, ease of application by the ophthalmologists, earlier rehabilitation, lower morbidity rates and easy applicability under local anaesthesia have made these techniques attractive alternatives. However, we believe that success rates will increase in parallel with advancements in instrumentation increased surgical experience and insertion of bicanalicular silicon tube intubation.

**Conclusions:**

The transcanalicular laser DCR without bicanalicular intubation is a minimally invasive, short procedure yielding good results and comparable to other conventional procedures. Further studies are required to clarify the results of transcanalicular laser DCR in patients with chronic dacryocystitis.

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# Frequency of Transfusion Transmitted Infections in Blood Donors of Prime Medical College Hospital, Rangpur, Bangladesh

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**Abstract:**
Blood transfusion is a distinct mode of transmission of infections to the recipients. Hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus (HIV), malaria and syphilis can be easily transmitted to the recipients during blood transfusion. Transfusion transmitted infections (TTIs) create major burden on health care system. Blood donor selection is very much important because infected individuals serve as an asymptomatic reservoir and a potential source of transmission of some diseases. A retrospective study was carried out over a period of three and a quarter years' i.e. from 02/05/2016 to 03/08/2019 in the northern area of Bangladesh. The study was performed to determine the prevalence of transmission of HBV, HCV, HIV, malaria and syphilis during blood transfusion in order to provide information for relevant national health policies. Out of 8356 sample of blood donors, recorded mean prevalence for HBsAg, HCV, HIV, malaria and syphilis was 0.957%, 0.047%, 0%, 0% and 0.287% respectively. This study reflect that blood transfusion is one of the major risk factors of spread the TTIs which showed the importance of the mandatory screening of these infection markers during donation of blood.

**Indexing words:** TTIs, HBV, HCV, HIV, Malaria, Syphilis, Blood donors.

## Introduction:

Heaptitis B virus (HBV), Hepatitis C virus (HCV), Human immune deficiency virus (HIV) and syphilis are the most important agents in transfusion transmitted infections (TTIs) and these diseases are a great health care problem in the world. In Bangladesh, especially in the Hill tracts, malaria is additional health burden. The incidence rate throughout the world are not easy to determine given the asymptomatic and latent nature of the diseases before the clinical presentation[1]. Every blood transfusion therefore carries a potential risk for transmissible diseases[1,2]. According to the WHO estimate, the lack of effective screening of blood donors results in up to 16 million new infections with hepatitis B, 5 million new infections with hepatitis C and 160,000 new cases of HIV infections every years[3].

Blood transfusion is a therapeutic procedure, as there is no genuine substitution. But contaminated blood transfusion can transmit infectious diseases and can be fatal instead of saving life. Safe blood transmission services are very much important for high quality health care system[4] and require organized structure, well-educated staff and uninterrupted electricity supply.

Evaluation of datas on these prevalence of TTIs among blood donors permits an assessment of the accurate estimate of risk of TTIs which helps in the creation of long-term strategies to improve public health and to prevent spreading of the disease in the population[1]. The purpose of present study was to provide the detail epidemiological analysis of TTIs in blood donors of northern part of Bangladesh.

## Methods:

The present retrospective study was carried out at blood bank of Prime Medical College Hospital, Rangpur after due ethical clearance from the institutional ethical committee. The data of present study corresponds to period of May of 2016 to July of 2019 and includes in house voluntary and replacement donors. The donors were first required to fill up a registration form which includes all the information like personal details, occupation and medical history.

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Hemoglobin estimation was performed and donors with haemoglobin less than 13g/dl were excluded. The donors were then screened by medical officer according to blood donor selection criteria. Only the first time donors were included in this study. Individuals with good health and physically fit were selected as blood donors. The age range of the donor was 18 to 55 years. The donors were then asked to sign the donor questionnaire and consent form. Any sunject who have previous history of HBV, HCV and HIV infections were excluded from the study. Blood sample was collected and tested in the blood bank of Prime Medical College Hospital. HBsAg, anti-HCV, anti-HIV and Venereal Disease Research Laboratory test (VDRL) for syphilis were detected using BEST2000 ELISA (Biokit, Spain), according to manufacturer's instructions. All seropositive samples were re-tested for the confirmation with the same serological test kit for confirmation.

**Observations and results:**

The study was based on records of blood bank. Total number of donor is 8356.

**HBV infection:** HBsAg positive rate for blood donors was found to be 0.957% (80 out of 8356 donors)

**HCV infection:** HCV prevalence was found to be 0.047% (4 out of 8356 donors)

**HIV infection:** HIV prevalence was found to be 0.000% (0 out of 8356 donors)

**Malaria infection:** Malaria prevalence was found to be 0.000% (0 out of 8356 donors)

**Syphilis infection:** VDRL was found to be reactive in 0.287% donors (24 out of 8356 donors).

**Table 1:** Percentage of doners infected by different infections (n=8356)

| Infections | No of doners infected | percentage |
|---|---|---|
| HBV infection | 80 | 0.957% |
| HCV infection | 4 | 0.047% |
| HIV infection | 0 | 0 |
| Malaria infection | 0 | 0 |
| Syphilis infection | 24 | 0.287% |

**Discussion:**

Hepatitis B and hepatitis C are the two of the common causes of chronic liver diseases. In this regard, hepatitis B is leading which is followed by hepatitis C disease. Chronic liver diseases result in a fatal disease called cirrhosis of liver [5,6,7]. HIV causes acquired immune deficiency syndrome (AIDS). In this disease condition the defensive immune system of the body is depressed. As a result, the patient becomes prone to develop various other infectious diseases[8]. In Bangladesh, malaria is endemic in 13 of 64 districts. About 14 million people in this country are at risk of the disease[9]. Syphilis may involve the central nervous system and may cause permanent disabilities. It is one of the common sexually transmitted diseases[10]. Limited surveillance data is present for HIV and syphilis in Bangladesh. In this country, the prevalence of AIDS remains low, certainly lower than the neighbouring countries[6]. Therefore, Bangladesh still has opportunity to take proper steps to prevent its spread.

Some authors state that blood donors may not be considered the representative of general population as the prevalence rate may underestimate or overestimate due to their different characteristics[11,12].

Hepatitis B and hepatitis C viruses are mostly transmitted as blood borne diseases. Needle sharing to prepare or inject drugs is responsible for easy transmission. In our country, now a days, disposable syringes are widely used. Moreover, blood transfusion is performed after proper screening tests. Therefore, in this present study, the number of positive HBV and HCV cases is not so alarming.

In Brazil, screening tests among blood donors was mandatory in 1993. That is one of the significant factors of low magnitude of hepatitis in all studied population in Brazil[13].

In the present study, prevalence of hepatitis B is more than hepatitis C infection. Not a single donor was found infected by HIV and malarial parasite. But the screening tests revealed 0.28% positive donors for syphilis. HIV is mainly spread by having sex or sharing needles. In Bangladesh, still the religious values are better than many other countries. That is why no positive HIV cases were found in this study. Malaria is not endemic in the northern part of Bangladesh. This fact is reflected in this study also.

**Conclusion:**

Safe blood, free from transfusion transmitted infections is our desired goal. In our country,

frequent screening before blood transfusion is widely practiced. Needle sharing is no longer continued here. Religious practices in Bangladesh are still remarkable. Therefore, the present situation, specially for HBV and HCV is not so alarming. But similar studies should be conducted in different places in our country to know the overall real condition of TTIs, so that more effective measure can be taken accordingly. Results of this study reflect that more effective procedure should be adopted in the screening tests to prevent the transmission of transfusion mediated infections more effectively.

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# Microscopic Estimation of the Volumes of Components of Umbilical Cord in Pregnancy Complicated with Hypertension

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**Abstract:**
**Context:** Clinically the adverse effects of hypertensive pregnancy are well established. Hypertensive pregnancies changes histological structures of umbilical cord which produce fetal and maternal complications. The present histological study was done to find out the area occupied by Wharton's jelly and total vessels area of umbilical cord in pregnancies complicated with hypertension. **Method:** This crosssectional, analytical study was done in the Department of Anatomy, Rangpur Medical College Rangpur from July 2014 to June 2015. The study was carried out on 60 (sixty) human umbilical cord, 30 from normotensive mothers (control group) and 30 from hypertensive mothers (hypertensive group). The umbilical cords were selected from Obstetric ward of Gynecology and Obstetrics Department, Rangpur Medical College Hospital, Rangpur after taking written permission. Area occupied by Wharton's jelly and total vessels area were measured microscopically by point counting method on prepared histological slides. **Result:** The mean (±SD) of proportional volume of area occupied by Wharton's jelly in placental side of umbilical cord was 82.00±1.46% and 68.55±7.49% and the mean (±SD) of proportional volume of Wharton's jelly area in fetal side of umbilical cord was 81.54±.78% and 71.28±6.01% in both control and hypertensive group respectively. The mean (±SD) of proportional volume of total vessels area in placental side of umbilical cord was 18.06±1.48% and 31.59±8.63% and the proportional volume of the mean (±SD) of total vessels area in fetal side of umbilical cord was 18.19±.70% and 28.64±5.98% in control and hypertensive group respectively. Whereas the jelly area was significantly decreased in hypertensive umbilical cord in both sides of the cord, the vessel area was significantly increased in hypertensive cord in both sides of the cord. **Conclusions:** Hypertension causes significant structural changes in umbilical cord that affects fetal and maternal wellbeing. So this study would be helpful for those who are concerned for mother and child health.

**Indexing words:** Umbilical cord, Hypertension, Volume component.

## Introduction:

The umbilical cord is a combination of blood vessels in which the tunica adventitial coat is formed by Wharton's jelly[1]. It is the nexus between the fetus and the placenta, thus umbilical vessels configuration may be an indicator of fetal status[2] and considered in understanding feto-maternal functional relationship and related clinical conditions[3].

Mucous connective tissue of Wharton jelly, present in the umbilical cord consists of a specialized, almost gelatin like extracellular matrix. It is largely made up of mucopolysaccharides (hyaluronic acid and chondroitin sulphate) and some fibroblast and macrophages[4]. It also contains cells with similar characteristics of smooth muscle ones and that allows its contractile functions[5, 6]. Wharton's jelly occupies large intercellular spaces located between thin, wispy collagen fibers. It is an important constituent of cord as it is the metabolically active tissue involved in exchange between amniotic fluid and umbilical vessels and is vital to the outcome of pregnancy. As a mucous tissue it protects and insulates umbilical

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blood vessels. Wharton's jelly, when exposed to temperature changes, collapses structures within the umbilical cord and thus provides a physiological clamping of the cord (an average of) 5 minutes after birth[7]. A reduction in the area of Wharton jelly resulting in a thin cord may cause restricted growth and low birth weight of the fetus[8].

Systemic diseases affecting mother can impose serious impacts on Wharton's jelly content thus affecting the cord architecture and finally the outcome of pregnancy. Hypertensive disorder of pregnancy is a leading cause of maternal and neonatal mortality and morbidity worldwide, particularly in developing countries, occurring in around 8% of pregnancies. These disorders causes intrauterine growth retardation due to utero-placental insufficiency and complications related to prematurity[9].

Microscopically the two umbilical arteries carry deoxygenated blood from fetus to mother, have a media composed of two muscle layers, an inner longitudinal and an outer circular. The internal elastic lamina is indistinct and missing in some places. A true adventitia is lacking in the segment within the umbilical cord[10]. One umbilical vein that passes through umbilical cord, carry oxygenated blood from placenta to fetus. Microscopically, umbilical vein larger in diameter, thin wall with single layer of disorganized circular smooth muscle and an internal elastic lamina[11].
Although the umbilical cord is one of the most vital components of the fetal anatomy, it is still one of the least studied fetal structures. Given that the umbilical cord is vulnerable to a number of abnormalities that may occur during pregnancy, labor, or delivery, it is important to investigate the underlying mechanisms of the development of cord morphology and possible pathologies associated with it, because this may provide insight regarding fetal growth within the intrauterine environment and its impact on later life[12].

**Methods:**

This cross- sectional analytical study was carried out on 60 (sixty) human umbilical cords. Out of the 60 umbilical cords, 30 were collected from normotensive mothers of uncomplicated pregnancies (control group) and 30 from mothers with hypertensive disorders of pregnancy (hypertensive group). Ethical clearance was taken from the Ethical Board of Rangpur Medical College. The umbilical cords were collected from Gynecology and Obstetrics Department, Rangpur Medical College Hospital, Rangpur after taking written permission. Umbilical cords of both normal vaginal and caesarian delivery were included. All samples were collected from singleton live pregnancy. Gestational period was between 35-42 weeks and maternal age within 20-45 years. An inclusion criterion for control group was **u**mbilical cord derived from mothers having blood pressure less than 140/90 mmHg. Inclusion criteria for hypertensive disorders group was umbilical cord derived from mothers having blood pressure 140/90 mmHg and above.

Common exclusion criteria were umbilical cord delivered from mothers with Rh negative blood group, VDRL positive, HBsAg positive, presence of any other known systemic pathology (diabetes mellitus, CLD, CVD, CKD and hematological disorders) and any congenital anomalies of the baby.

The samples were collected immediately after delivery and were examined for completeness in recent state. After then umbilical cord was cut 2 cm from the site of insertion. Then the umbilical cords and placenta were placed in 10% formalin filled plastic jar with cover for at least 7 days. Each jar was duly tagged with an identification number along with maternal name and BP. All the umbilical cords were collected and measured in similar manner.

For histological study, two tissue blocks were taken; one from placental end of cord, another from fetal end of cord. Slides were prepared following routine histological technique.

**Estimation of proportional volume of Wharton's jelly and Total vessels area**

The volume proportions of Whartons Jelly and blood vessels were determined by 'the point counting technique' for gross specimen described by Aherne and Dunnil (1966), proposed by Chalkley (1943-44)[13]. The principle depends on the fact that in a composite organ, the volumes of the components are equivalent numerically to the relative areas occupied by these components on cut surfaces. If a grid of regularly spaced points are placed over the cut surfaces, the number of points over these components will be proportional to their area, and hence, to their volume.
The proportion of volume of Wharton's jelly and total vessels area in the umbilical cord were determined with the replica of point counting Zeiss I integrating eyepiece prepared in a

transparent plastic sheet and was placed into the eyepiece. The integrating eyepiece contains a point network of 25 points, spaced at 70 µm, arranged within a circle which delimits the counting field.

The counting was done under light microscope (Olympus BX41, made in Japan) at low magnification (×10 objective ×10 eyepieces), in slides stained with routine H&E stain. The position of each point of grid, falling on any component of the Wharton's jelly and vessels areas was recorded for each field (Figure 1). Then the eyepiece was rotated and keeping the field constant and again the position of each point was recorded. Thus 50 points were recorded for each field. In this manner all the available fields were counted in both slides prepared from each cord. Total points were summated that hitting either Wharton's jelly area or vessels area and percentage of those was calculated. These percentages indicate the proportional volume of each component. The total number of points hitting each components of umbilical cord was summed up and expressed as a percentage. These percentage represents the proportional volume of the different components occupying the umbilical cord namely Wharton's jelly, umbilical arteries and vein.

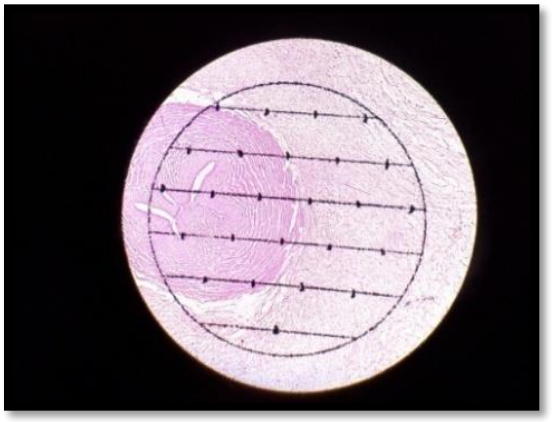


**Figure 1** Photomicrograph showing method of measurement of Wharton's jelly area and total vessels area by point counting method by a replica of Zeiss I integrating eyepiece.

**Result:**

Table 1 shows the mean (±SD) of proportional volumes of Wharton's jelly area in placental and fetal side of cord in control and hypertensive group.

It was observed that the mean (±SD) of proportional volume of area occupied by Wharton's jelly in placental side was 82.00±1.46% and 68.55±7.49% and 81.54±.78% and 71.28±6.01% in fetal side of the cord in control and hypertensive group respectively. The Wharton's jelly area were significantly lower in hypertensive group than in control group (p=.000) in both sides of the cord.

It could be revealed from the table that the area occupied by Wharton's jelly in both placental and fetal side was similar in control group but was somewhat reduced in placental side in hypertensive group than the fetal side (p>.05).

**Table 1:** Area occupied by Wharton jelly in placental side and fetal side of umbilical cord in control and hypertensive group (n=30in eachgroup)

| Variables | Groups | | p value |
|---|---|---|---|
| | Control | Hypertensive | |
| Wharton jelly area | 79.89 – 87.8 | 49.11 – 80.58 | .000(S |
| Placental side (%) | 82.00 ±1.46 | 68.55 ±7.49 | |
| Wharton jelly area | 79.37 – 83.5 | 58.62 – 82.24 | .000(S) |
| Fetal side (%) | 81.54 ±.78 | 71.28±6.01 | |

Results are shown as range and mean±SDs
p values reached from unpaired students t test
S: significant at 95% confidence level

Negative correlation was found between gestational age and Wharton's jelly in both fetal and placental side and reached a significant level in placental side only ($r^2$=.131, p=.049) in hypertensive group (Figure 2).

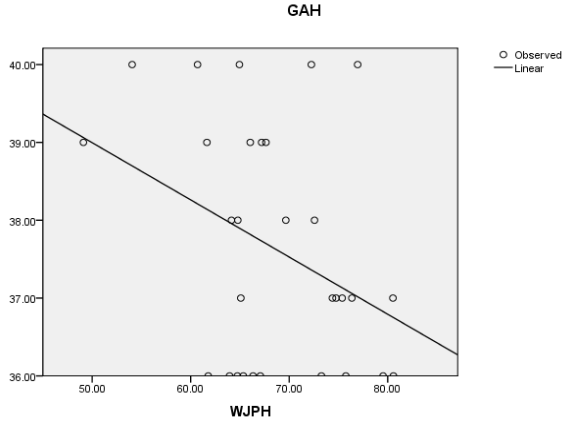



**Figure 2** Negative correlation between gestational age (GAH) and Wharton's jelly (WJPH) in placental side of hypertensive group ($r^2$ =.131, p =.049)

Regarding the proportional volume of vessel area, Table 2 shows the mean (±SD) of proportional volume of total vessels area in placental side of umbilical cord was 18.06±1.48% and 31.59±8.63% and in fetal side of umbilical cord was 18.19±.70% and 28.64±5.98% in control and hypertensive group respectively. The total vessel area was significantly higher in hypertensive group than in control group (p=.000).

Again it was observed from Table 2 that the mean of proportional volume of vessel area in placental side was more prominent in hypertensive group (p>.05) but in control group the mean value was similar.

**Table 2:** Area occupied by blood vessels in placental side and fetal side of umbilical cord in control and hypertensive group (n=30in eachgroup)

| Variables | Groups | | p value |
|---|---|---|---|
| | Control | Hypertensive | |
| Vessel area | 12.19 – 20.1 | 19.41 – 57.23 | .000 (S) |
| Placental side (%) | 18.06 ±1.47 | 31.59 ±8.63 | |
| Vessel area | 13.5 – 20.63 | 14.75 – 41.37 | .000 (S) |
| Fetal side (%) | 18.64 ± .70 | 28.64 ±5.98 | |

Results are shown as range and mean±SDs
p values reached from unpaired students t test
S: significant at 95% confidence level

**Discussion:**

It could be remembered that whereas the mean proportional volume of Wharton's jelly area in placental and fetal side (82.0±1. 46% vs 81.54±.779%) were similar in control group the mean value was somewhat lower in the placental side than fetal side (68.55±7.49%vs 71.28 ± 6.0%) in hypertensive group. But in both side of the cord, Wharton's jelly area was reduced significantly in hypertensive group than in control group. It was also found that there was significant negative correlation Wharton's jelly area and gestational age in hypertensive group (Figure 2).

Wharton's jelly consists of a fundamental amorphous substance containing glycosaminoglycans, proteoglycans and, predominantly, hyaluronic acid. It also contains cells with similar characteristics of smooth muscle ones and that, allows its contractile function. These cells constitute an interconnected network of collagen that form canaliculi and perivascular spaces permitting adequate blood flow to the fetus in cases of umbilical cord compression during pregnancy or delivery[14]. Wharton's jelly surrounds the umbilical vessels which constitutes the major part of human umbilical cord and provides a thick protective mantle around vessels[11].

Damasceno and de Lima[15] stated that the changes in the quantity or quality of Wharton's jelly affects the diameter of the umbilical cord and the hemodynamics of its vessels, leading to impaired fetal blood flow and consequently low weight gain and fetal demise. This constriction in the umbilical cord was due to the absence of Wharton's jelly that may be the cause of fetal death.

Barbieri et al[16] studied on a direct relationship between gestational age and the area of Wharton's jelly in the umbilical cord. There is an increase in the area of WJ as a function of gestational age until around 32 weeks, after which these measurements remain practically stable until the end of pregnancy. Findings of their study showed a positive and linear relationship between estimated fetal weight and the area of WJ, but only until the 26th week of gestational age, since then onwards there is almost no change in the area of WJ compared to estimated fetal weight.

Ilie et al[17] studied on Wharton's jelly, both qualitative and quantitative, found positive correlation with hypertension and intrauterine fetal growth restriction and establish pathogenic mechanisms for some groups of stillbirths.

Srivastava et al[7] studied on 60 umbilical cords. They found diameter of Wharton's jelly was smaller in hypertensive group than control group. They stated that if hypertension could be timely detected and properly managed, the complication of pregnancy and their adverse consequences can be avoided.

Reduction in the Wharton's jelly may be associated with single umbilical artery which may increase the rate of perinatal morbidity and mortality[18].

Milnerowicz et al[19] found thin cord with thinnest vessels and smaller content of Wharton's jelly in pregnancy induced hypertension results in IUGR.

Again, in the present study the proportional volume of vessel area was increased significantly in hypertensive than control group in

both placental (31.59±8.63% vs 18.06±1.47%) and fetal sides (28.64±5.98% vs18.19±.70%) of the cord. So it could be suggested that vessel area in the umbilical cord on both sides was increased in the expense of the amount of Wharton's jelly in the hypertensive group.

Again in the present study, the proportional volume of the vessel area in placental side of umbilical cord was similar to fetal side18.06±1.47% vs18.19±.70% in control group but vessel area was increased a little in placental side 31.59±8.63% vs 28.64±5.98% in hypertensive group.

The work of present study was done according to Bangal et al[20] but they found decrease in cord diameter but increase in total cord area in placental side in both control and PIH group. But in the present study the increase in vessel area and decrease in Wharton's jelly area was pronounced on both side of cord in hypertensive group than in control.

Inan et al[21] studied on comparative morphological difference between umbilical cords from chronic hypertensive and preeclamptic pregnancies. They stated that thickness of the umbilical cord vessels remained nearly constant, whereas both the total area and lumen area were reduced. These changes correlate with the histopathological findings, suggesting mainly vasocostrictive effect as a result of reduced uteroplacental perfusion followed by fetal hypoxia and intrauterine growth retardation in hypertensive pregnancy.

**Conclusion:**

Present study indicates that decrease Wharton's jelly area causes lean umbilical cord in hypertensive pregnant women and thickening of vascular wall causes obstructing feto-placental circulation leading to anoxia and fetal death. If Hypertension could be timely detected and properly managed, the complications of pregnancy and their adverse consequences can be avoided.

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# Comparative Study between Oral Valacyclovir and Oral Acyclovir in the Treatment of Herpes Zoster

**Sharmin Kabir[1], Ishrat Bhuiyan[2], Md. Shahadat Hossain[3], Mahfuza Aktar[4], Md. Manjurul Karim[5]**

**Abstract:**

**Background:** Valacyclovir is an oral prodrug of acyclovir. It has a bioavailability 35 times greater than that of oral acyclovir. Moreover the convenient dose schedule as well as quicker cesation of post herpetic neuralgia makes valacyclovir more effacious than acyclovir in treating herpes zoster. So, the present study was planned to compare the efficacy and safety of oral valacyclovir over oral acyclovir in the treatment of herpes zoster. **Methods:** This was a clinical trial conducted in the outpatient department of Dermatology and Venereology at Shaheed Suhrawardy Medical College and Hospital, Dhaka between the period of April 2016 to September 2016. Sixty patients were selected according to the inclusion and exclusion criteria. All the patients were randomized into two groups. Group A as Valacyclovir (n=30) and group B as Acyclovir (n=30). Complete history was taken from the patient. Thorough clinical examination was done. Relevant investigations report was collected. All the informations were recorded in the fixed questionnaire. Collected data was classified, edited, coded and entered into the computer for statistical analysis by using SPSS-19. **Result:** Mean age was found 38.93±8.29 years in group A and 41.36±8.36 years in group B. 17 (56.7%) patients were male in group A and 16 (53.3%) in group B. Majority (56.7%) patients were thoracic in group A and group B respectively. In group A erythema, maculopapular rash, vesicle, bullae and crusting were present 29 (96.7%) cases, 28 (93.3%) cases, 22 (73.3%) cases, 22 (73.3%) cases and 14 (46.7%) cases respectively. In group B erythema, maculopapular rash, vesicle, bullae and crusting were present in 30 (100.0%) cases, 30 (100.0%) cases, 29 (96.7%) cases, 25(83.3%) cases and 17 (56.7%) cases respectively. Incidence of postherpetic neuralgia was found in 21 (70.0%) cases in group A and in 25 (83.3%) cases in group B. After 7 days treatment with valacyclovir in group A and acyclovir in group B, it was observed that symptoms and signs were reduced in both groups but more effectively in group A though the differences between the groups were statistically non-significant. However, it was observed that the patients of both groups showed similar remission pattern on 15$^{th}$ and 29$^{th}$ day. In baseline, mean pain scoring were 6.26±2.22 and 6.53±1.81 minutes in group A and group B respectively. At 3$^{rd}$ days, mean pain scoring was found 5.47±1.85 minutes in group A and 5.93±1.72 minutes in group B. At 8$^{th}$ days, mean pain scoring was found 4.23±1.50 minutes in group A and 5.13±1.45 minutes in group B. At 15$^{th}$ days, mean pain scoring was found 2.00±1.22 minutes in group A and 3.25±1.07 minutes in group B. At 22$^{th}$ days, mean pain scoring was found 0.76±0.74 minutes in group A and 1.75±0.95 minutes in group B. At 29$^{th}$ days, mean pain scoring was found 0.00±0.00 minutes in group A and 1.17±0.57 minutes in group B. The mean score at 8$^{th}$, 15$^{th}$, 22$^{th}$ days were statistically significant ($p<0.05$) between two groups. **Conclusion:** It can be concluded that administration of valacyclovir three times daily was an effective and safe treatment for acute herpes zoster. Treatment with valacyclovir has the benefits of rapid resolution of skin lesions, zoster associated pain, post herpetic neuralgia compared to acyclovir and valacyclovir has the convenience three times daily dosing, thereby ensuring better patient compliance, which makes this regimen an excellent choice for treatment of herpes zoster.

**Indexing words:** Herpes Zoster, Valacyclovir, Acyclovir

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## Introduction:

Herpes Zoster remains an important medical problem throughout the world. It results due to reactivation of an earlier latent infection with the varicella zoster virus in dorsal root ganglia.[1,2] As reactivation of the virus is linked to diminished virus specific immunity it develops mainly in the elderly and immunocompromised patient.[3]

During the prodome of herpes zoster patient reports headache, photophobia and malaise, may be associated with fever. The disease begins with localized abnormal skin sensations ranging from itching, tingling to severe pain, which preceded the skin lesions by one to five days.[1] An erythematous maculopapular rash unilaterally distributed progresses to cluster of clear vesicles which continue to form 3 to 5 days and evolve through stages of pustulation, ulceration and crusting.[2] Healing occurs over a period of 2 to 4 weeks and often results in scarring and permanent changes in pigmentation. The cutaneous eruption is unilateral and does not cross the midline; lesions overlap adjacent dermatomes in 20% cases.[4]
Pain is the most common complaint for which patients with herpes zoster seek medical care.[5,6] Pain persisting after rash healing occurs in more than 50% of untreated patient and is the major complication of older patients.[7,8] The pain is often accompanied by abnormal sensations such as allodynia, tingling or numbness and decreases gradually over several months in most patient. Although some patients have pain persisting beyond 6 months.[8-10]

Post herpetic neuralgia (defined as pain that persists more than 30 days after the onset of rash or after cutaneous healing) is the most feared complication.[11] Both the incidence and the duration of postherpetic neuralgia are directly correlate with the patient's age.[12,14-16] The reported incidence of post herpetic neuralgia ranges from 8 to 70% and increased with age. In one study, the overall prevelance of post herpetic neuralgia was 8% after 30 days and 4.5% after 60 days.

In a number of previous studies treatment with valacyclovir 1000 mg three times daily for 7 days showed a significant advantage over treatment with acyclovir in reducing the duration of post herpetic neuralgia. Valacyclovir, the I-valyl ester of acyclovir is rapidly converted to acyclovir after oral administration and results that acyclovir bioavailability 3 to 5 times greater than that of oral acyclovir in human.[15,16] Biotransformation of valacyclovir to acyclovir is virtually complete after oral administration with each gram of valacyclovir yeilding approximately 700 mg of acyclovir and 300 mg of the essential amino acid valine. On the basis of this and preclinical studies, it was anticipated that the established safety profile of acyclovir would be retained with valacyclovir.[16]
The aim of the present study therefore was an attempt to evaluate the efficacy and safety of oral valacyclovir over acyclovir in the treatment of herpes zoster in different population of Bangladesh.

**Method:**
A randomized clinical trial was conducted among 60 patients of herpes zoster who attending in the outpatient department of Dermatology & Venereology at Shaheed Suhrawardy Medical College & Hospital, Dhaka during April 2016 to September 2016. Protocol of this study was approved by Ethical review committee of Shaheed Suhrawardy Medical College. Informed written consent was taken from each patient. All herpes zoster patients were recruited as per inclusion criteria who was randomly divided into two groups, 30 patients were treated with oral valacyclovir (group A) and the rest 30 patients with herpes zoster were treated with oral acyclovir (group B). Group A were treated with oral valacyclovir 1000 mg 3 times daily for 7 days and group B were treated with oral acyclovir 800 mg 5 times daily for 7 days and patients were followed up on day 3$^{rd}$ ,8$^{th}$, 15$^{th}$, 22$^{th}$, 29$^{th}$ and assessed for the efficacy and safety by observing the clinical improvement and these data were recorded. The medicines were purchased by the patients himself or herself. Statistical analysis was carried out by using the Statistical Package for Social Sciences version 19.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous data. The quantitative observations were indicated by frequencies and percentages. Chi –Square test was used to analyze the categorical variables, shown with cross tabulation. Unpaired t-test was used for continuous variables. p values <0.05 was considered as statistically significant.

**Results:**
Mean age was found 38.93±8.29 years in group A and 41.36±8.36 years in group B. Seventeen (56.7%) patients were male in group A and 16(53.3%) in group B. Majority (56.7%) patients were thoracic in group A and group B respectively. The difference were not statistically significant (p>0.05) between these two groups (Table 1).

**Table 1:** Demographic characteristics of the study patients

| Demographic characteristics | Group A (n=30) | Group B (n=30) | p value |
|---|---|---|---|
| **Mean age (years)** | 38.93±8.29 | 41.36±8.36 | [a]0.263[ns] |
| **Sex:** | | | |
| Male | 17 (56.7%) | 16 (53.3%) | [b]0.795[ns] |
| Female | 13 (43.3%) | 14 (46.7%) | |
| **Types of herpes zoster:** | | | |
| Thoracic | 17 (56.7%) | 17 (56.7%) | |
| Cervical | 8 (26.7%) | 9 (30.0%) | [b]0.787[ns] |
| Lumbosacral | 4 (13.3%) | 2 (6.7%) | |
| Trigeminal | 1 (3.3%) | 2 (6.7%) | |

ns= not significant
[a]p value reached from unpaired t-test
[b]p value reached from chi square test
Group A= Valacyclovir
Group B= Acyclovir

Patients were selected randomly as group A and B randomly in alternate manner. After selection, In group A, erythema was present in 29(96.7%) cases, maculapapular rash present in 28(93.3%) cases, vesicle was present in 22 (73.3%) cases, bulla present in 22 (73.3%) cases and crusting was present in 14(46.7%) cases.
In group B, erythema was present in 30(100.0%) cases, maculopapular rash was present in 30(100.0%) cases, vesicle was present in 29(96.7%) cases, bulla was present in 25(83.3%) cases and crusting was present in 17(56.7%) cases (Table 2).

**Table 2:** Clinical findings of integumentary system of the study patients

| Clinical findings of integumentary system | Group A (n=30) | Group B (n=30) |
|---|---|---|
| Erythema | 29(96.7%) | 30(100.0%) |
| Maculopapular rash | 28(93.3%) | 30(100.0%) |
| Vesicle | 22(73.3%) | 29 (96.7%) |
| Bulla | 22(73.3%) | 25 (83.3%) |
| Crusting | 14(46.7%) | 17 (56.7%) |

After 7 days treatment with valacyclovir in group A and acyclovir in group B, it was observed that symptoms and signs were reduced in both groups but more effectively in group A though the differences between the groups were statistically non-significant (Table 3). However, from Table 4 and 5, it was observed that the patients of both groups showed similar remission pattern on 15th and 29th day.

**Table 3:** Distribution of patients according to observation and scoring at follow up on the 8th day, i.e. 7 days after initiating treatment

| Observation and scoring at follow up | Group-A Valacyclovir | Group-B Acyclovir | p value |
|---|---|---|---|
| No new lesion | 28 (93.3) | 26(86.7) | 0.671[b] |
| Reduction of erythema | 26(86.7) | 23(76.7) | 0.317[a] |
| Reduction in size of involved area | 29(96.7) | 24(80.0) | 0.103[b] |
| Reduction in pain severity score | 17(56.7) | 12(40.0) | 0.493[a] |

[a]Chi-square test was done to measure the level of significance
[b]Fisher's Exact test was done to measure the level of significance
# Figure within parenthesis indicates in percentage

**Table 4:** Distribution of patients according to observation &scoring at follow up. This assessment was done on the 15th day, i.e. 14 days after initiating treatment

| Observation and scoring at follow up | Group-A Valacyclovir | Group-B Acyclovir | p value |
|---|---|---|---|
| No new lesion formation | 30(100.0) | 30(100.0) | - |
| Reduction in erythema | 30(100.0) | 30(100.0) | - |
| Reduction in size of involved area | 30(100.0) | 29(96.7) | 0.999[b] |
| Reduction in pain severity score | 24(80.0) | 20(66.7) | 0.493[a] |

[a]Chi-square test was done to measure the level of significance
[b]Fisher's Exact test was done to measure the level of significance
# Figure within parenthesis indicates in percentage

**Table 5:** Distribution of patients according to observation &scoring at follow up. This assessment was done on the 29th day, i.e. 28 days after initiating treatment.

| Observation and scoring at follow up | Group-A Valacyclovir | Group-B Acyclovir | p value |
|---|---|---|---|
| No new lesion formation | 30(100.0) | 30(100.0) | - |
| Reduction in erythema | 30(100.0) | 30(100.0) | - |
| Reduction in size of involved area | 30(100.0) | 30(100.0) | - |
| Reduction in pain severity score | 30(100.0) | 30(100.0) | - |

Figure within parenthesis indicates in percentage

The presence of post herpetic neuralgia was more common in the acyclovir group than the valacyclovir group (83.3% vs 70.0%) but no significant difference (p=0.222) was found (Table 6).

**Table 6: Incidence of post herpetic neuralgia of the study patients**

| | Group A (n=30) | Group B (n=30) | p value |
|---|---|---|---|
| 29th day | 21 (70.0%) | 25 (83.3%) | 0.222ns |

ns= not significant
p value reached from chi square test

In baseline, mean pain score were 6.26±2.22 and 6.53±1.81 minutes in group A and group B respectively. At 3rd days, mean pain score was found 5.47±1.85 minutes in group A and 5.93±1.72 minutes in group B. At 8th days, mean pain score was found 4.23±1.50 minutes in group A and 5.13±1.45 minutes in group B. At 15th days, mean pain scoring was found 2.00±1.22 minutes in group A and 3.25±1.07 minutes in group B. At 22th days, mean pain score was found 0.76±0.74 minutes in group A and 1.75±0.95 minutes in group B. At 29th days, mean pain score was found 0.00±0.00 minutes in group A and 1.17±0.57 minutes in group B. The mean score at 8th, at 15th, at 22th days were statistically significantly lower (p<0.05) in group A than group B (Table 7).

**Table 7: Pain score in different follow up day**

| Pain score | Group A (n=30) | Group B (n=30) | p value |
|---|---|---|---|
| Baseline | 6.26±2.22 | 6.53±1.81 | 0.608ns |
| At 3rd day | 5.47±1.85 | 5.93±1.72 | 0.323ns |
| At 8th day | 4.23±1.50 | 5.13±1.45 | 0.022s |
| At 15th day | 2.00±1.22 | 3.25±1.07 | 0.001s |
| At 22nd day | 0.76±0.74 | 1.75±0.95 | 0.001s |
| At 29th day | 0.00±0.00 | 1.17±0.57 | - |

s= significant, ns= not significant
p value reached from unpaired t-test

**Discussion:**

The study described the controlled investigation to date of antiviral agents for the treatment of herpes zoster. In this comparative study, it was demonstrated that treatment with valacylovir three times daily was effective in treating patients with herpes zoster.

The present study shows that among the total 60 patients, 33 (55%) were males and 27(45%) were females. Overall women may have a slightly greater risk of developing zoster when compared to men[17] but in this study males were more affected than females though the difference was not statistically significant (p=0.795).

The present study shows that mean age was found 38.93±8.29 years in group A and 41.36±8.36 years in group B. Usually the chance of developing herpes zoster increases with age as it is proved in previous studies.[18] As the subjects were selected randomly here the differences between the age group was not statistically significant (p=0.263).

In this series it was observed that thoracic involvement of herpes zoster was most common and 17(56.7%) patients in each group were found. Similar result observed in Soul-Lawton et al[19].

Skin lesions improved faster in patients on Valacyclovir compared to Acyclovir. An earlier study also noticed the faster resolution of skin lesion in Valacyclovir group but their findings were not statistically significant. Pain is the most common debilitating feature of herpes zoster.[19] The majority of patients experience pain immediately before and during the acute rash phase. However a more important clinical concern is to prevent or reduce the possibility of persistent pain.

The present study shows that the presence of post herpetic neuralgia was more common in the acyclovir group than the Valacyclovir group

(83.3% vs 70.0%) but difference was statistically not significant (p=0.222). However a large multicentre study found that the treatment with valacyclovir for 7 days significantly reduced the incidence of the post herpetic neuralgia compared to acyclovir.[18]

In baseline, mean pain score were 6.26±2.22 and 6.53±1.81 minutes in group A and group B respectively. At 3rd days, mean pain score was found 5.47±1.85 minutes in group A and 5.93±1.72 minutes in group B. At 8th days, mean pain score was found 4.23±1.50 minutes in group A and 5.13±1.45 minutes in group B. At 15th days, mean pain score was found 2.00±1.22 minutes in group A and 3.25±1.07 minutes in group B. At 22th days, mean pain score was found 0.76±0.74 minutes in group A and 1.75±0.95 minutes in group B. At 29th days, mean pain score was found 0.00±0.00 minutes in group A and 1.17±0.57 minutes in group B. The mean score at 8th, at 15th, at 22th days were statistically significant ($p<0.05$) between two groups. Valacyclovir recipients had a mean duration of 40 days of pain after lesion resolution compared to 60 days of pain after lesion resolution for acyclovir recipients. In terms of zoster related discomfort it is estimated that valacyclovir provides a 25% benefit over Acyclovir.[19] This study also shows that skin lesion and zoster associated pain improved significantly faster in the Valacyclovir group than Acyclovir.[18,19]

Safety profile of Acyclovir has been carefully established during >18 years of clinical use. In the present study there was no clinically significant difference in nature, frequency of severity, adverse events between the two treatment groups, as reported in earliest studies.[18,19]

**Conclusion:**

In conclusion, our study demonstrated that administration of Valacyclovir three times daily was an effective and safe treatment for acute herpes zoster. Treatment with Valacyclovir has the benefits of rapid resolution of skin lesions, zoster associated pain, post herpetic neuralgia compared to Acyclovir. Also Valacyclovir has the convenience three times daily dosing, thereby ensuring better patient compliance, which makes this regimen an excellent choice for treatment of herpes zoster.

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# Efficacy of Misoprostol only and Mifepristone with Misoprostol in Non-viable First Trimester Termination of Pregnancy

**Tasnim Sarwar[1], Tamanna Hamid[2]**

**Abstract:**
**Objective:** To compare the effectiveness, success rate and induction to abortion interval between administration of misoprostol only and mifepristone with misoprostol in first trimester abortions (6-12 weeks). **Methods*:*** This randomized clinical trial was conducted on 100 women with non-viable first trimester pregnancy need termination; divided two groups each consisting of 50 women. Group-I received only misoprostol; 600 mcg initial vaginal insertion followed by 200 mcg sublingually every 8 hour until abortion was completed. Women in Group-II received mifepristone 200 mg orally and after 12 hours tab misoprostol 400 mcg sublingually. **Results:** The success rate in Group-I was 90 %, whereas in Group-II it was 98 %. The mean of induction-abortion interval in Group-I was 28.13±3.1 hours where as in Group-II which was significantly less 17.28±2.04 hours ($p$<0.001). There was significant difference in the mean blood loss also, 95.12±7.12 ml in Group-I and 74.52±4.12 ml in Group-II. Also in Group-II lesser misoprostol dose was required. **Conclusion:** Pretreatment with mifepristone significantly reduces the need for curettage, the induction-abortion interval and the misoprostol dose along with minimal blood loss.

**Indexing words:** Misoprostol, Mifepristone, First trimester, Abortion, Induction-abortion interval (IAI)

## Introduction:

The word abortion derives from Latin aboriri that means 'to miscarry.' Abortion is defined as the spontaneous or induced termination of pregnancy before fetal viability. The National Centre for Health Statistics, Centre for Disease Control and Prevention, and World Health Organization (WHO) defines abortion as pregnancy termination before 20 weeks of gestation or a fetus weighing <500 grams[1]. Most common cause of first trimester abortions is incomplete abortion, blighted ovum, and missed abortion.

Medical methods of abortion have been proved to be safe and effective[2]. The most effective regimens rely on the antiprogestin, mifepristone, which binds to progesterone receptors resulting in necrosis and detachment of placenta. It also softens the cervix and causes mild uterine contractions. It sensitizes the uterus to the action of prostaglandin which is given 1–2 days later, like synthetic prostaglandin E1 analogue, misoprostol, which binds to myometrial cells causing strong myometrial contractions and causes cervical softening and dilatation. This leads to expulsion of fetus from the uterus[3].

The effects of medical methods of abortion are similar to those associated with spontaneous abortion and include uterine cramping and prolonged menstrual-like bleeding. Bleeding occurs 9 days on an average but can last up to 45 days in rare cases[4].

The present study was undertaken to compare the effectiveness of simultaneous administration of mifepristone and misoprostol versus misoprostol alone in first trimester abortion.

## Methods:

This was a randomized clinical trial carried out at the Department of Obstetrics and Gynaecology, Combined Military Hospital, Rangpur, during the period between January 2019 and June 2019. Ethic approval was obtained from Ethical Committee of Combined Military Hospital, Rangpur Cantonment. All patients with first trimester abortion prepared for medical termination. Information about the study was available to patient during consenting. The author had discussed the procedures with patients and they accepted and consented. Detailed history was taken, clinical examination including gynecological examination and

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ultrasonography was performed. 100 patients with first trimester abortion including incomplete abortion, missed abortion, blighted ovum were divided into two groups:

**Group-I:** 50 patient with first trimester abortion received only misoprostol; 600 mcg initial vaginal insertion followed by 200 mcg sublingually every 8 hours until abortion was completed.

**Group-II:** 50 patient with first trimester abortion received mifepristone 200 mg orally and after 12 hours tab misoprostol 400 mcg sublingually.

Inclusion criteria were: (1) women aged more than 18 Years (2) singleton pregnancy (3) women with incomplete abortion or blighted ovum or missed abortion (4) willing to follow the study protocol and provide informed consent and (5) willing to undergo required follow-up and surgical management when indicated. The exclusion criteria were women with (1) H/o previous three or more cesarian section (2) multiple pregnancy (3) contraindications to mifepristone and misoprostol like chronic or acute adrenal, hepatic or renal failure (4) cardiovascular disease, (5) poorly controlled seizure disorder (6) on anticoagulant therapy, known clotting defect (7) hemoglobin less than 8 gm/dl and (8) known or suspected pelvic infection. Women who fulfilled the criteria for the trial were interviewed and given an explanation of the trial. An informed written consent was obtained. A pelvic ultrasound examination was performed to confirm the abortion and to exclude multiple pregnancies. The side effects including nausea, vomiting, diarrhea and fever were recorded. The blood pressure, pulse, temperature and frequency of uterine contractions are monitored. After abortion, the products of gestation (fetus and placenta) were examined to see whether the abortion was complete. After fetal expulsion if placenta is not expelled then surgical evacuation under general anesthesia was performed. Rh antibody was given to Rh negative mothers. The amount of blood loss during abortion was assessed clinically and recorded. The number of doses of misoprostol required were calculated and recorded. Collection of patients data and statistical analysis were done by SPSS version 22.

**Results:**

There were no statistically significant differences between the two groups in age (Group I: mean 23.1± 4.16 years, range 17-36 years, median 24 years; Group II: mean 24.46±5.87 years, range 18-40 years, median 25 years; p=0.104), parity, H/O previous cesarian section and gestational age (Group I: mean 8.12±1.09 weeks; Group II: mean 8.22±1.18 weeks). Successful abortion was significantly higher in Group II compare to Group I. Total blood loss, induction-abortion interval and duration of bleeding significantly lower in Group II compare to Group I. Nausea, vomiting, diarrhoea were not significantly different in two groups.

**Table 1:** Comparison of patients characteristics between two groups (n=100)

| Variables | Group I (n=50) | Group II (n=50) | p-value |
|---|---|---|---|
| Age (years) | 23.14±4.1 | 24.46±5.8 | 0.104 |
| ZParity- Primi | 15(30.0%) | 15(30.0%) | 1.000 |
| Multi | 35(70.0%) | 35(70.0%) | |
| H/O previous cesarean section | 10(20.0%) | 10(20.0%) | 1.000 |
| Gestational weeks | 8.12±1.09 | 8.22±1.18 | 0.661 |
| Successful abortion | 45(90.0%) | 49(98.0%) | 0.0194* |
| Curettage needed | 5(10.0%) | 1(2.0%) | 0.242 |
| Induction abortion interval | 28.13±3.14 | 17.28±2.04 | <0.001* |
| Total blood loss | 95.12±7.12 | 74.52±4.12 | <0.001* |
| Duration of bleeding | 1.34±0.21 | 1.12±0.11 | <0.001* |
| Nausea | 0(0.0%) | 1(2.0%) | 0.371 |
| Vomiting | 2(4.0%) | 1(2.0%) | 0.559 |
| Fever | 0(0.0%) | 0(0.0%) | - |
| Diarrhoea | 4(8.0%) | 1(2.0%) | 0.178 |
| Blood transfusion | 0(0.0%) | 0(0.0%) | - |
| Analgesia | 0(0.0%) | 0(0.0%) | - |

**Group-I:** First trimester abortion received only Misoprostol; 600 mcg initial vaginal insertions followed by 200 mcg sublingually every 8 hour until abortion was completed.

**Group-II:** First trimester abortion received Mifepristone 200 mg orally and after 12 hours Tab. Misoprostol, 400 mcg sublingually.

**Discussion:**

Medical method for termination of non-viable pregnancy is becoming popular now a days to avoid the risk of anesthesia, surgical injuries of cervix, uterus, other organs as well as the cases of uterine perforation (0.12-1.98%), blood transfusion (0.5%), necessity of repeating

surgical intervention (1%) and ongoing pregnancy due to failure of surgical intervention (0.2%)[5-8]. Medical methods of abortion have been proved safe and effective.

This trial compared the difference in IAI, dose of misoprostol required and amount of blood loss in first trimester abortions with misoprostol only and mifepristone plus misoprostol. There was no difference in the prevalence of gastrointestinal side effects between the two groups. Nearly all the women in our study aborted before 24 hours like other similar studies conducted by Elami et al[9], Dickinson et al[10] and Borgatta and Kapp[11]. Borgatta and Kapp[11] reported a success rate of 95% within 24 hour. In our study, the success rate was 90% in Group-I and 98% in Group-II (Table 1). The mean induction abortion interval in Group-I was 28.13±3.1 hour where as in Group-II which was significantly less 17.28±2.04 hour ($p$<0.001*). Modak et al[12] in a comparative study of sublingual and vaginal misoprostol in second trimester abortions reported a complete abortion at 24 hour of 79.41% (in sublingual group) and mean IAI of 12.28 h. Ngoc et al.[13] in their double blind study reported the mean IAI was statistically shorter for mifepristone plus misoprostol group compared to misoprostol only group (8.1 hour and 10.6 hour, respectively, with a $p$≤0.01). Dabash et al[14] in their study reported mean IAI of 10.4 ± 6.8 hour in mifepristone group and 20.6 ± 9.7 hour in misoprostol only group. Reduction in induction to abortion interval is likely to improve the acceptability of women[13]. Wildschut et al[15] in their review article on medical methods for mid- trimester termination of pregnancy suggested that mifepristone plus misoprostol is the most efficient regimen and 3-hourly intervals of misoprostol administration are more effective than 6-hourly intervals. Mifepristone enhances the action of misoprostol there by reducing the induction to abortion interval and dose of misoprostol .The mean dose of misoprostol required in Group-II was significantly lower compared to Group-I like in other similar studies[13].

We also observed that in Group-II the mean blood loss (74.52±4.12 ml) was less, probably due to shorter IAI. Hou et al[16] in their study reported a total abortion rate of 95–100% within 24 hour, mean IAI was shorter in parous women (6.3 ± 3.7 hour) and the mean blood loss 2 hour after expulsion of products of conception was 98.3 ± 76.2 ml. Nagaria et al[17] reported a success rate of 100%, and the mean IAI was significantly shorter and the mean dose of misoprostol required was less in the mifepristone pretreated group. Also the mean blood loss was slightly higher in the misoprostol only group. Garg et al[18] reported a success rate of 96% in the buccal group in the second trimester abortion.

## Conclusion:

Outcome of the study is pretreatment with mifepristone significantly increases the success rate, reduces the induction abortion interval, dose of misoprostol required and blood loss compared to using only misoprostol, thus increasing the patient compliance and thereby reducing the rate of surgical intervention, morbidity and mortality.

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# Evaluation of Postoperative Complications of Total Thyroidectomy

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**Abstract:**

**Context:** Total thyroidectomy is choice for the treatment of differentiated thyroid carcinoma DTC). In order to lower the morbidity rates, total thyroidectomy is also suggested in recent years for benign diseases. The major complications associated with thyroidectomy include injury to the recurrent laryngeal nerve, damage to the parathyroid glands and hypocalcemia, which have the potential to be lifelong & costly issues for a patient. So the aim of study was to find out the early and intermediate post-operative complications of total thyroidectomy. **Methods:** This is a longitudinal study carried on 30 patients who underwent total thyroidectomy in the Department of Surgery and ENT of Rrangpur Medical College hospital. Detailed analysis of the patients who had underwent total thyroidectomy were done regarding investigations, diagnosis and indication for surgery, occurrence of individual complications, patient outcome, duration of stay and follow up. All the information was recorded in pre tested questionnaire. **Results:** Among 30 patients, within 40-60 years, 15(50%) patients were belonged. Twenty eight (93.3%) patients were females; two patients (6.7%) were male. Out of 30 patients, 18 patients (60%) developed complications & among them 5 patients (16.7%) developed multiple complications & all 3 cases of papillary carcinoma developed one or more complications. In case of multinodular goiter complications rate was 60%. Voice change (40%) & temporary hypocalcaemia (36.7%) were the most common complications developed after the procedure. Other complications were superior laryngeal nerve palsy (23.3%), temporary recurrent laryngeal nerve palsy (13.3%), neck hematoma (3.3%), respiratory obstruction (3.3%), temporary hypocalcaemia plus recurrent RLN palsy (6.7%), temporary hypocalcaemia plus SLN palsy (6.7%), airway obstruction with hematoma (3.3%). **Conclusion:** In comparison with other studies, complication rates were higher in our study. But different complication rates were found in different studies and small scale studies showed higher complications rate than larger scale study. Also, as lack of advanced facilities, some of complications were assessed by subjective assessment & it might be a cause of over expressed results.

**Indexing words:** Total Thyroidectomy, Multinodular Goiter, Differentiated Thyroid Cancer, Recurrent Laryngeal Nerve Injury.

## Introduction:

Neoplastic, inflammatory and endocrine abnormalities of the thyroid gland are extremely common, affecting approximately 11% of the general population.[1] Total thyroidectomy is generally reserved for patients with thyroid malignancy, toxic thyroid disease (thyrotoxicosis or toxic multinodular goiter), or clinically significant goiter. The major postoperative complications include hemorrhage, wound infection, hypocalcemia, respiratory obstruction, thyroid storm, hypoparathyroidism and laryngeal nerve injuries.[2]

Now, there is a change in a surgical practice from subtotal thyroidectomy to total thyroidectomy for benign thyroid diseases.[3] Though near total thyroidectomy has been advocated by some surgeons, it has been proposed by majority that total thyroidectomy is the treatment of choice in patients with differentiated thyroid cancer (DTC).[4,5]

Compared to thyroid surgery for benign thyroid disease, complication rates after thyroid surgery for malignant thyroid disease have been reported higher in some studies, while some series have reported no significant difference.[6]

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Complications such as bleeding, hypocalcaemia and Recurrent Laryngeal Nerve Injury (RLNI) represent nearly half of all the complications after thyroid surgery.[7]

The right sided nerve is at higher risk of injury due to its anatomical variation compared to the left side. In addition to the hoarseness that occurs with unilateral RLNI, bilateral RNLI leads to dyspnea and often life threatening glottal obstruction.[8,9] Mechanism of injury to the nerve includes complete or partial dissection, traction, contusion, crushing, thermal damage, missed placed ligature or compromised blood supply.[10]

Voice disorders after thyroid surgery are generally transient but sometimes permanent. These usually occur as a result of a nerve lesion (recurrent or external laryngeal nerve).[11,12,13] The causes of voice disorders without RLNI are multiple, including external laryngeal nerve injury; cricothyroid muscle injury; large laryngotracheal skeleton dissection, specially when the infrahyoid muscles are sectioned; and orotracheal intubation.[14]

Hypocalcaemia after total thyroidectomy is a potential early complication. The majority of cases are secondary to temporary hypoparathyroidism, with recovery in three weeks to six months. However upto33% of patients experience permanent hypoparathyroidism.[15]Transient hypocalcaemia ranges from 0.3% to 49%, and that of permanent hypocalcaemia ranges from 0% to 33%.[16]

Airway complication is a common postoperative complication encountered after thyroidectomy. Tracheomalacia is the most common airway complication. Others are laryngeal edema. RLN palsy and hematoma.[17] The incidence of post surgical neck hematoma ranges from 0.3% to 1.7%.[18,19]

Total thyroidectomy has been accepted as current surgical therapy for benign and malignant thyroid disorders. So it is essential to assess the safety of total thyroidectomy.

**Methods:**

This is a longitudinal study carried out on 30 patients in the Department of Surgery & ENT, Rangpur Medical College Hospital, Rangpur, Bangladesh from 13th June, 2018 to 13th December, 2018 a period of 6 (six) months.

All patients were selected purposively according to inclusion and exclusion criteria who underwent total thyroidectomy procedure for different thyroid pathologies.

Apart from routine investigations, the commonly performed special investigations done before total thyroidectomy were - thyroid function test (100%), indirect laryngoscopy (100%), FNAC of thyroid swelling (96.7%), USG of the Neck (53.3%) and Thyroid autoantibodies (6.7%). All of the patients were euthyroid before surgery and all patients had normal Vocal Cords.

Patients with RLN palsy diagnosed preoperatively by IDL examination, patients with hypoparathyroidism, patients with h/o previous thyroid surgery and patients with undifferentiated thyroid cancer are excluded.

Each of the complications was tried to assess by both subjective and objective assessment.

After being discharged, every patient was followed up weekly upto one month over phone and at their follow up visits.

The researchers were duly careful about ethical issue related to a scientific study. Detailed information regarding preoperative evaluations, operation notes, occurrence of postoperative complications were obtained in each cases. Collected data was classified, edited, coded & entered into the computer.

Data were analyzed with using computer software SPSS (Statistical Package for Social Sciences) version-20.

**Results:**

In the study, 50% patients were belonged within 40-60 age group (Table 1).

**Table 1:** Age distribution of patients (n=30)

| Age group (in year) | No of Patients | Percentage |
|---|---|---|
| <20 | 04 | 13.3% |
| 20 - 40 | 10 | 33.3% |
| 40 - 60 | 15 | 50% |
| >60 | 01 | 3.3% |
| **Total** | **30** | **100%** |

Out of 30 cases, 28 (93.3%) patients were female and only 2 (6.7%) cases were male (Table 2).

**Table 2:** Sex distribution of patients (n=30)

| Sex of the patients | No of Patients | Percentage | p-value |
|---|---|---|---|
| Female | 28 | 93.3% | |
| Male | 02 | 6.7% | .035 |
| **Total** | **30** | **100%** | |

Out of 30 patients 25 patients (83.3%) presented with multinodular goiter (Table 3).

**Table 3:** Types of thyroid disease for which total thyroidectomy was carried out (n=30)

| Types of thyroid disease | No of patient | Percentage | p-value |
|---|---|---|---|
| Multi nodular goiter | 25 | 83.3% | |
| Papillary carcinoma of thyroid | 03 | 10% | |
| Solitary thyroid nodule (benign according to FNAC) | 02 | 6.7% | .041 |
| **Total** | **30** | **100%** | |

Voice change (40%) and temporary hypocalcaemia (36.7%) were the most common complications developed after the procedure (Table 4).

**Table 4:** Types of complications developed after total thyroidectomy procedure (n=30).

| Name of complication | No of patient | Percentage | p-value |
|---|---|---|---|
| Voice change | 12 | 40% | |
| Temporary hypocalcaemia | 11 | 36.7% | |
| Superior laryngeal nerve palsy (SLNP) | 07 | 23.3% | |
| Temporary RLN palsy | 04 | 13.3% | |
| Neck hematoma/ Hemorrhage | 01 | 3.3% | |
| Respiratory obstruction | 01 | 3.3% | 0.76 |
| Temporary hypocalcaemia + RLN palsy | 02 | 6.7% | |
| Temporary hypocalcaemia + SLN palsy | 02 | 6.7% | |
| Airway obstruction + Hematoma | 01 | 3.3% | |

Out of 30 patients, 18 patients (60%) developed complications and among them 5 patients (16.1%) developed multiple complications and all 3 cases of papillary carcinoma develop one or more complications (Table 5).

**Table 5:** Disease complication correlation (n=30)

| Disease of thyroid gland | Total number of patients | Number of patient developed complications | Nature of complication | |
|---|---|---|---|---|
| | | | Single | Multiple |
| Multinodular goiter | 25(83.3%) | 15(60%) | 11(44%) | 4(16%) |
| Papillary carcinoma of thyroid | 03(10%) | 03(100%) | 02(66.7%) | 01(33.3%) |
| Solitary thyroid nodule | 02(6.7%) | - | - | - |
| **Total** | **30(100%)** | **18(60%)** | **13(43.3%)** | **05(16.7%)** |

Though 4 (13.3%) developed unilateral RLN palsy, no one developed bilateral RLN palsy. Among the 7 patients (23.3%) of superior laryngeal nerve (SLN) palsy, 5 cases were due to surgery for multinodular goiter and 2 cases due to surgery for papillary carcinoma. Among the 11 cases of temporary hypocalcaemia, 8 patients due to surgery for multinodular goiter and 3 patients due to surgery for papillary carcinoma. Overall incidence of complication were higher in cases of malignant thyroid disease than benign thyroid disease. No complication was detected in solitary thyroid nodule.

**Table 6:** Incidence of complications for benign and malignant thyroid disease (n=30)

| Disease of thyroid gland | No of patient | Type of complication | Percentage of total No. of Patients |
|---|---|---|---|
| Multinodular goiter | 25 | Voice change | 36% |
| | | Temporary hypocalcaemia | 32% |
| | | Superior laryngeal nerve (SLN) palsy | 20% |
| | | Temporary RLN palsy | 16% |
| | | Respiratory obstruction | 4% |
| | | Neck hematoma | 4% |
| Papillary carcinoma of thyroid gland | 03 | Temporary hypocalcaemia | 100% |
| | | Superior laryngeal nerve (SLN) palsy | 66.7% |
| Solitary thyroid nodule (benign) | 02 | Voice change | 66.7% |

**Discussion:**

The present study was conducted to evaluate the outcomes of total thyroidectomy in 30 patients in the department of Surgery & ENT of Rangpur Medical College Hospital (RpMCH) during the period of 6 months from 13th June 2018 -13th December 2018.

In this study most common age group was 41-60 years (Table 1), and 28 patient (93.3%) were female (Table 2). Bhattacharyya and Fried in a study reported that mean patient age was 48.3 years and 81.8% of the patients were female among 517 patients who underwent total thyroidectomy as a primary procedure.[20] But Mridul et al. in a study conducted on Assam, India showed that, the commonest age group of patients who underwent different thyroidectomy procedure was 31-40 years, and majority of patients were female 90%.[21] In our study, complications were developed in 18 patients (60%). Among them, 5 patients developed multiple complications (16.7%). In cases of benign thyroid condition (MNG and solitary thyroid nodule) incidence of complication was 55.6% and in malignancy it was 100%. So, in our study, all of the carcinoma patients developed one or more complications. In case of multinodular goiter incidence was 60% and in case of solitary benign nodule no complication occured. Among 5 patients who developed multiple complications, four patients were operated for MNG (16%) and one patient for papillary carcinoma of thyroid (33.3%) (Table 5). Rehamet.al. on a study showed that, overall complications rate after total thyroidectomy was 91.2%.[22]

Antonio et al. showed that the incidence of complications after total thyroidectomy for MNG was 21%[23]. Meehmet et al. showed that the incidence of complications after total thyroidectomy for differentiated thyroid cancer was 22%[33]. In comparison among different studies, it was seen that, complications rate was varied from study to study and complication rate was higher in small scale study than larger scale study. As our study was a small scale study it showed higher rates of complications.

The present study showed that voice change 40% and temporary hypocalcaemia (36.7%) were the most common complications after the procedure. Other complications were superior laryngeal nerve palsy (23.3%), temporary RLN palsy (13.3%), neck hematoma/hemorrhage (3.3%), respiratory obstruction (3.3%), temporary hypocalcaemia with RLN palsy (2/30) (6.7%), temporary hypocalcaemia with SLN palsy (6.7%), airway obstruction plus hematoma (3.3%), (Table 4.). No patient developed seroma, wound infection or thyrotoxic storm. There was no mortality after the procedure. Voice change was the most common complications in our study (40%). In our study, we utilized subjective voice assessment according to patient's complaints postoperatively who had normal voice preoperatively. Page et al. studied on subjective voice assessment after total thyroidectomy procedure and found voice change in 49%[25]. Similarly during a prospective

study of 54 patients, 30% patients reported early subjective voice changes and 14% reported late (3 months) changes.[26]

AII patients who had voice changes were assessed by indirect laryngoscopy or fiberoptic laryngoscopy on the early postoperative period. Four patients who were suspected for recurrent layngeal nerve (RLN) palsy due to hoarseness of voice & dysphagia, found unilateral RLN Palsy on laryngoscopy. Interestingly all four unilateral RLNI was happened with the patients operated for MNG.

Antonio et al. in their study showed the incidence of recurrent laryngeal nerve injuries were 8.6% which was conducted on patients with MNG who underwent total thyroidectomy procedure.[23] Reham et al. at a study showed only RLN palsy in two cases (5.9%) and RLN palsy with hypocalcaemia in four cases (11.8%).[22] A study conducted by Hazem et al. showed transient URLN palsy in two cases (14.2%) and transient BRLN palsy in two cases (14.2%).[27]

In this study, incidence of superior laryngeal nerve palsy was 23.3% (Table 4) and it was the main cause of voice change (58.3% in total patients).

Several studies have suggested that majority of post-thyroidectomy voice complaints results from trauma to the external branch of superior laryngeal nerve (EBSLN), with reported rates ranging from 12 to 58%.[28,29,30]

In our study, one patient developed airway obstruction due to tracheomalasia (3.3%). This patient was operated for huge multinodular goiter. Tracheostomy was needed & it was done on 1St POD. Ayandipo et al. studied on airway complications and outcome after thyroidectomy. They showed hematoma in 4 (0.8%) patients, tracheomalasia in 27(5.3%) patients.[I7] Bhattacharyya and Fried. showed incidence of hematoma was 1.0%.[20] In our study temporary hypocalcaemia was developed in 11 patients (36.7%).

In the present study, 8 patients with multinodular goiter (32%) and 3 patients with papillary carcinoma of thyroid (100%) developed symptomatic hypocalcaemia. Arumugan et al. found postoperative hypocalcaemia approximately 35%. Joon et al showed that, transient symptomatic or biochemical hypocalcaemia developed in 62 patients (55.3%) and permanent hypocalcaemia in 2 patients (1.8%).[31]

This study was done within a short period of time, so sample size was small. As there was lack of facilities of high-tech technology, some complications could only be assessed by subjective assessment.

**Conclusion:**

Complication rates after total thyroidectomy has been well studied for many years at different centers. It seems that it varies from center to center, but total thyroidectomy is accepted worldwide as a choice of procedure for malignant thyroid disease, MNG & some other benign disease. In the present study complication rates were higher than some other studies. If we take consideration of the limitations of the present study this rate could be well judged.

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# Detection of Chronic Kidney Disease in Adult Rural Population

**Md. Abdul Muqueet[1], Prof. Harunur Rashid[2], Sakina Anwar[3]**

**Abstract:**
**Context:** To find out the exact prevalence of CKD in rural area this study was done on the background of CKD is a major public health problem worldwide and a significant cause of morbidity and mortality. **Methods:** A multistage sampling following simple random sampling procedure was done to choose the study area and a total 1265 adult population ranging from 15-65 years of both sexes were studied. Height, weight of the subjects was measured and body surface area was calculated. Multistik test of urine was done for proteinurea and serum creatinine was estimated. **Results:** The study revealed 60.1% participants were young and middle aged (15-40 years). The mean age was 35.57 $\pm$ 12.98 years. The majority of the participants were female (63%). Multisticks test for urine demonstrated a total 76(6.0%) participants were proteinuric and among this 2.5% had isolated proteinuria. Proteinuria and MDRD equation depicted 238 (18.8%) were having CKD of them 1.7% in stage-1, 2.4% in stage-2, 14.0% in stage-3, 0.5% in stage-4 and 0.2% in stage-5. On the other hand, C-G equation revealed 226 (17.9%) having CKD. Of them 1.7% in stage-1, 2.1% in stage-2, 13.6% in stage-3, 0.3% in stage-4 and 0.2% were in stage-5. Ccr from Cockcroft-Gault equation was corrected for body surface area. Results from both equations were not significantly different. The compliance for follow up after 3 months was 72 (32%). Of them 57(79%) were confirmed as having CKD. **Conclusions:** The survey data revealed that CKD is not less common (18%) among the rural subjects. So, a nationwide screening programme is necessary to develop awareness of entire population and to find exact prevalence of CKD so that a cost effective preventive strategy could be adopted.

**Indexing words:** Chronic kidney disease, Body mass index, MDRD equation, C-G equation, Cockcroft-Gault equation

## Introduction:

Chronic kidney disease (CKD) by definition and classification is new working tool to label the functional status of kidney in spite of its variable causes. This makes easy to diagnose kidney disease at an earlier stages and point out the potential scope for proper intervention to slow the progression of deterioration of renal function and reduce the morbidity and mortality due to late diagnosis and/or referral.

Patients with CKD most often present with nonspecific complaints or are asymptomatic and are referred to a nephrologist because of abnormal blood or urine findings. Late nephrology referral and evaluation of patients with CKD are associated with greater morbidity and mortality. For this reason, referral of patients earlier has been suggested[1].

The Kidney Disease Outcome Quality Initiative (K/DOQI) clinical practice guidelines for CKD evaluation, classification and stratification published by National Kidney Foundation provide a framework designed to address the growing burden of CKD in the United States. Staging of CKD is based on estimation of renal function by GFR. GFR is calculated from serum Creatinine by Cockcroft-Gault and MDRD (Modification of Diet in Renal Disease) equation. Some study showed that there were significant number of patients with normal serum Creatinine level had abnormal GFR with Cockcroft-Gault values <50 mi/mm$^2$. This group of patients may remain unrecognized by primary care physician who rely on serum creatinine abnormality to identify renal insufficiency. As a result these patients are becoming burden for themselves and for the whole family. In most of the cases the affected

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family bears the financial burden years after years even after the death of the patient.

Proper intervention in early stage of CKD would slow the progression and reduce the rate of ESRD. So, in country like us it is very important to know the prevalence of CKD which emphasis the early detection and prevention. So, the study was aimed at to find out the prevalence of Chronic Kidney Disease (CKD) in adult rural population and association of some risk factors among them.

**Methods**

This cross sectional study was carried out in Nephrology department, Bangabandhu Seikh Mujib Medical University and Kidney Foundation. The study area was selected named Bongaon Union, a rural area of Savar thana 30 k.m. away from centre of Dhaka city. A total fifteen thousand population of both sexes, age between 15 and 65 years were included in the study. Persons having fever at the time of screening, recent history of fluid loss such as diarrhea, vomiting, trauma and pregnant women were excluded from the study. A total of twelve hundred sixty five population was screened from July 2003 to June 2005 A multistaged clustered sampling design was utilized by following simple random sampling procedure. First of all a Thana of Dhaka district was selected named Savar. This thana comprises with 12 Unions. Out of these 12 Union Bongaon Union was selected. According to local Union porishod authority there were about 15 thousand adult population who met the inclusion criteria. Among them 1265 participated in the study within mentioned period.

Local authority, Public leaders, Imam, Social workers motivated people to participate in this program. Leaflet distribution, miking, postering was done to create awareness about this program regularly.

Data were collected from all participants by direct interview and using structured questionnaire. Informed consent was obtained from all participants.

Data and samples were collected from a fixed centre in every Friday from 9:00 AM to 2:00PM.

Age, occupation, marital status, addresses were recorded as per statement of the participants at the time of interview.

Height, weight was measured following standard procedure and BMI was calculated.

Multisticks test of urine was demonstrated for proteinurea. Spot urine sample was collected in test tubes labeled with individuals registration no. for each participants and dipstick test was done on the spot using uripath seris reagent strips (plasmatec laboratory products, UK) for detection of urinary protein and sugar. Positive test was lebelled as + (30mg/dl), ++ (100mg/dl), +++ (300mg/dl), ++++ (1000mg/dl) depending on amount of proteinuria.

The serum creatinine was estimated by biochemistry auto analyzer.

**Kidney Function:**

Kidney function was stratified according to current national kidney foundation (NKF) guidelines on the evaluation, classification and stratification of chronic kidney disease[3].

**Definition of CKD:**

1. Kidney damage for ≥ 3 month, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either:
   - Pathological abnormalities or
   - Markers of kidney damage, including abnormalities in the composition of the blood or urine or abnormalities in imaging tests.
2. GFR < 60ml/min/1.73m$^2$ for ≥3 month, with or without kidney damage.

**CKD stage:**

Stage-I : eGFR ≥ 90ml/min/1.73m$^2$ and positive proteinuria.
Stage-II : eGFR 60-89 ml/min/1.73m$^2$ and positive proteinuria.
Stage-III : eGFR 30–59 ml/min/1.73m$^2$ .
Stage-IV : eGFR 15–29 ml/min/1.73m$^2$ .
Stage-V : eGFR <15 ml/min/1.73m$^2$ or on dialysis.

Creatinine clearance (Ccr) and glomerular filtration rate (GFR) was estimated from serum creatinine level by using prediction equations. Cockcroft-Gault equation provides useful estimates of Ccr in adults. Normalization of Ccr for body surface area allows more accurate evaluation of renal function. MDRD equation also provides estimated GFR which compared with Cockroft-Gault Ccr after correction of body surface area.

**Body surface area:**

Body surface area (BSA) can be determined from height and weight using a nomogram found in standard references.

$$\text{BSA } (m^2) = \sqrt{\frac{Weight(kg)XHeight(cm)}{3600}}$$

**Cockcroft-Gault equation:**

$$\text{Ccr(ml/min)} = \frac{(140 - Age)XWeightinKg}{72XSerumCreatinine(mg/dl)} \text{ X (0.85 if female)}$$

$$\text{Corrected Ccr (ml/min/1.73m}^2\text{)} = \frac{Ccr(ml/\min)X1.73}{BSA(m^2)}$$

**MDRD equation:**

Abbreviated Modification of diet in renal disease (MDRD) study equation provides useful estimates of GFR in adults.

GFR ((ml/min/1.73m$^2$) = 186.3X (Scr)$^{-1.154}$ X (Age)$^{-0.203}$ X (0.742 if female)

**Data processing and analysis:**

Data were analyzed through SPSS program. Continuous data were presented as mean and standard deviation from the mean. Chi-square, fishers exact test, Students t- test and Spearman s correlation test was used for statistical analysis. Results were presented in tabulated form, charts and diagrams along with statistical interpretation**.**

**Observations & results**

The findings derived from analysis of the collected data are furnished below:

**Distribution of proteinuria:**

Out of 1265 participants 21(1.66%) had DM with proteinuria, 33(2.6%) had HTN with proteinuria, while 3192.5%) had isolated proteinuria. A total of 76(6%) were proteinuric (Fig. 1).

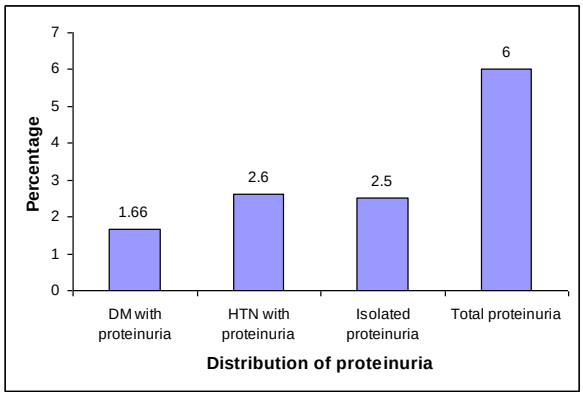



**Fig. 1:** Distribution of proteinuria among participants (n = 1265)

**CKD staging using uncorrected Ccr:**

CKD staging done by C-G equation using uncorrected Ccr, a citable proportion of the participants (34.2%) fell under CKD population (Table 2)

**Table 1: CKD staging by C-G equation using uncorrected CCr (n = 1265)**

| Staging | No | % |
|---|---|---|
| **Total CKD** | **432** | **34.2** |
| Stage 1 | 10 | 0.8 |
| Stage 2 | 35 | 2.8 |
| Stage 3 | 362 | 28.6 |
| Stage 4 | 23 | 1.8 |
| Stage 5 | 02 | 0.2 |
| **Normal** | **833** | **65.8** |

**CKD staging by different equation:**

No wide variation in staging of CKD by different equations was observed. The stage 3 occupied the highest position (Table 2).

**Table 2:** CKD staging by different equations (n = 1265)

| Staging of CKD | Equation | |
|---|---|---|
| | Cockcroft-Gault | MDRD |
| **Total CKD** | **226(17.9)*** | **238(18.8)** |
| Stage 1 | 22(1.7) | 21(1.7) |
| Stage 2 | 26(2.1) | 31(2.4) |
| Stage 3 | 172(13.6) | 178(14.0) |
| Stage 4 | 4(0.3) | 6(0.5) |
| Stage 5 | 2(0.2) | 2(0.2) |
| **Normal** | **1039(82.1)** | **1027(81.2)** |

*Figures in the parentheses denote corresponding **%**.

**Distribution of CKD:**

Comparison was made of the distribution of CKD between Cockcroft-Gault and MDRD equations for detecting CKD. The proportion of CKD detected by Cockcroft and MDRD equations were 17.9% and 18.8% respectively and no significant difference was observed between two equations in terms of CKD detection (p > 0.05) (Fig. 2).

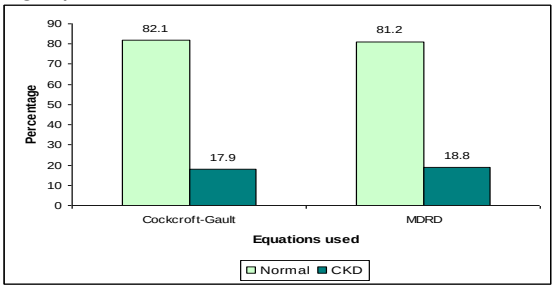



**Fig. 2:** Distribution of CKD among participants (n = 1265)

**Comparison of risk factors between CKD (C-G) and CKD (MDRD)**

The distribution pattern BMI and certain systemic diseases like HTN and DM in CKD population are almost similar whether CKD (C-G) or CKD (MDRD) equations are used for staging of CKD ($p > 0.05$) (Table 6).

**Compliance of participants:**

The compliance of the participants detected as having CKD in the first screening test. All the CKDs detected in the 1st round were instructed to attend at the 2nd follow up visit 3 months after 1st check up to have their serum checked for creatinine and urine for albumin. Of the 226 CKDs only 72 attended giving a compliance rate of 32% (Fig. 3).

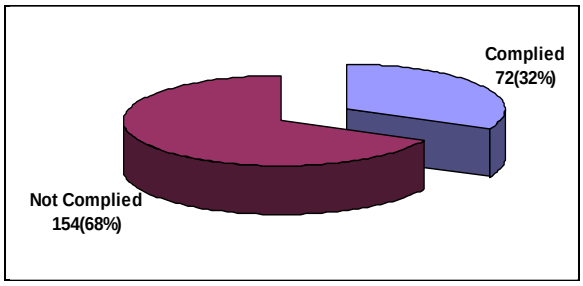



**Fig. 3:** Showing compliance of the participants (n = 226)

**CKD status 3 months after 1st detection:**

Out of 72 participants, 57 fulfilled the criteria of CKD giving rise a 79% of confirmed CKD (Fig. 4).

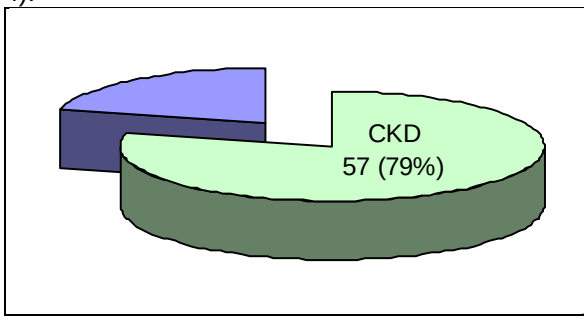



**Fig. 4:** CKD status 3 months after 1st detection (n = 72)

**Discussion:**

Among adults in rural population of Bangladesh the present study was done to examine the prevalence of chronic kidney disease (based on proteinuria and/or low GFR, estimated GFR was calculated from Cockcroft-Gault and MDRD equation.

Proteinuria is the cardinal manifestation of glomerulonephritis. Out of 1265 participants urine protein analysis using multisticks demonstrated that a total 76(6%) participants were proteinuric in the present study.

Glomerular filtration rate (GFR) is the singlemost best predictor of renal function in health and disease. Measuring GFR is expensive and cumbersome. Various methods of calculating estimated GFR (eGFR) from serum creatinine concentration have been studied, including Cockcroft-Gault and equation derived from the MDRD study population[4,5]. Both the equation are corrected for body surface area (BSA). Like our study several populations based study with the use of these equations found a surprisingly high prevalence of CKD. (a) The Third National Health and Nutritional Examination Survey (NHANES III)[6] for prevalence of low GFR in non diabetic Americans. (b) Prevalence of CKD and decreased kidney function in adult US population: NHANES III[7]. (c) Prevalence of CKD in Australian adults: The AusDiab kidney study[8]. (d) Prevalence study of CKD among Iceland adults[9]. High prevalence of CKD of all these study leading some authors to doubt the usefulness of these equation in epidemiological studies.[10,11,12]

In Iceland study a correction factor 0.84 is used in Cockcroft-Gault equation to estimate GFR form Ccr. But in the context of our study population the correction factor is yet to be determined. Other population based study did not use such correction factor. In the present study mean body surface area of the studied population was $1.49m^2 \pm 0.17m^2$ which was much lower than standard body surface area $1.73m^2$. To calculate estimated GFR (eGFR) from Cockcroft-Gault (C-G) equation, C-G Ccr (ml/min) was corrected for body surface area in every case. Detection of CKD using uncorrected Ccr (ml/min) from C-G equation without standardization of body surface area give rise inappropriately high prevalence (34.2%) of CKD. According to NKF: K/DOQI guideline unit of estimated GFR (eGFR) from prediction equation is ml/min/$1.73m^2$. So to detect CKD, Ccr from C-G equation should be corrected for body surface area. After correction, CKD prevalence was 17.9% which was comparable with CKD prevalence from MDRD equation (18.8%). MDRD equation calculates directly estimated GFR (eGFR).

Kunitoshi *et al*.,(2003) showed that proteinuria was a strong independent risk factor for developing ESRD[13]. Two community based screening program the Framinghum study[14] and the Okenowa study[15] demonstrated an approximately 10% prevalence of dipstick positive proteinuria in adults. The prevalence was higher in older than in younger and higher in woman than in man. In Hongkong a screening program on asymptomatic renal population found that prevalence of positive (> 1+) urine dipstick for protein is 3.2%[16].

NKF-K/DOQI guideline advocated using albumin-specific dipstick or albumin-to creatinine ratio in spot urine. But in our study we used dipstick for proteinuria and urine microscopy was not performed. Urinary tract infection was not evaluated for exclusion of proteinuria. In AusDiab kidney study[8] proteinuria was detected by protein to creatinine ratio and found that 2.4% was proteinuric. In Framingham cohort it is evident that proteinuria, even in casual urine specimens, carries substantial risk with the mortality rate increased threefold. In Bolivia a survey showed that 11% of apparently healthy subjects were proteinuric with dipsticks test.

Prevalence of CKD in our survey was 238 (18.8%) when MDRD equation was used. Out of which stage 1 (Proteinuria +GFR ≥90 ml/min) was 21(1.7%), stage 2 (proteinuria + GFR 60-89 ml/min) was 31(2.4%), stage 3 (GFR 30-59 ml/min) was 178(14.0%) stage 4(GFR 15-29 ml/min) was 6(0.5%) stage 5 (GFR <15 ml/min) was 2(0.2%).

Prevalence of CKD using MDRD in US adult population was 11%, out of which stage 1 was 3.3%, stage 2 (3%), stage 3 (4.3%), stage 4 (0.2%) and stage 5 (0.2%)[7]. In this NHANES III use of estimated GFR and Ccr equation, strengthened by appropriate calibration of serum creatinine level to the laboratory in which these GFR equations were developed. But in the study such calibration was not used.

Prevalence of CKD in this survey was 226 (17.9%) as Cockcroft-Gault equation was used. Out of which stage 1 was 22(1.7%), stage 2 was 26(2.1%), and stage 3 was 172 (13.6%) stage 4 was 4 (0.3%), stage 5 was 2 (0.2%). Prevalence of CKD using C-G equation in AusDiab kidney study was also 16%. According to NKF-K/DOQI CKD staging evidence of stage-I was 0.9%, stage-II was 2.0%, stage-III was 10.9%, stage-IV was 0.3% and stage-v was 0.3%[8].

In the present study the prevalence of individuals whose Ccr < 60ml/min/1.73m$^2$ by C-G equation was 14.1% and MDRD was 14.7% which was not different. But NHANES III showed the prevalence of individuals with CCR < 60 ml/min/1.73 m$^2$ (using C-G equation) was greater than those of estimated GFR < 60 ml/min/l.73m$^2$ using MDRD equation (7% versus 4.5%)[7]. This may be due to calibration of serum creatinine. In Iceland study eGFR < 60ml/min/1.73m$^2$ using MDRD equation the crude prevalence was 7.24%.

In the present study the prevalence of CKD with using both the formula revealed significantly high but the prevalence for both the formula was not different. A study of Bostom *et al.,*(2002) specifically evaluated the predictive performance of several GFR prediction equations in subject with CKD and normal serum creatinine[10]. They found that most accurate results were obtained with the Cockcroft-Gault equation, where as the most precise equation albeit biased, was the MDRD study equation. In the present study it was found that 12.1% of male and 12.6% of female with normal serum creatinine were detected as having CKD. In AusDiab kidney study Cockcroft-Gault estimates of creatinine clearance, when corrected for body surface area have been found to correlate well with gold standard measures of GFR[8]. From the above evidences use of both formula to find out the prevalence of CKD is justified.

In this study 11.9% of the CKD population were overweight and obese compare to 16.5% without CKD, although the difference between the two groups did not reach the level of significance (P=0.091) when using C-G equation. Also 15.1% of the CKD population were detected as overweight and obese compared to 15.8% of those without CKD and show no difference between the two groups (P=0.804) when using MDRD equation.

The AusDiab kidney study demonstrated hypertension (odds ratio: 5.4, 95% CI: 4.3, 6.9) were strongly predictive of proteinuria on univariate analysis and hypertension also predictive of renal impairment. The prevalence of reduced GFR <60ml/min/l.73 m$^2$ was fivefold more prevalent in those with hypertension compared to those without (P<0.00l).

According to NKF: K/DOQI guideline[3] CKD should be labeled if kidney damage with or without decreased GFR persist ≥ 3 months. In the follow up programme out of 226 CKD patient only 72 (32%) attended and complying to the advise. Out of these 72 person 57 (79%) met the CKD criteria after reevaluation. In other studies 18% of the participants showed compliance in KEEP study[17].

**Conclusion:**

The survey data revealed that CKD is not less common (18%) in the rural population. A similar survey conducted recently in the urban disadvantageous population also demonstrated a significant percentage of CKD. So to prevent or slow the progression of CKD, early detection and therapeutic intervention is the best way.

So, a nationwide screening programme is necessary to develop awareness of entire population and to find exact prevalence of CKD. As a result a cost effective preventive strategy could be adopted.

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# Relationship of Diabetes and Dyslipidemia with Neurological Disorders and Hypertension

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**Objectives:** To evaluate relationship of concurrent diabetes and dyslipidemia among patients with different neurological disorders and hypertension. **Methods:** This cross sectional analytical study was conducted in the Neurology Department of Rangpur Medical College Hospital from January 2016 to December 2018. 487 patients seen for any reason in OPD and indoor of Neurology department were enrolled into the study. Patients with previously known diabetes and dyslipidimia were excluded from this study. **Results:** Out of 487 subjects 307 (63.04%) males and 180 (36.96%) females. Stroke (45%) was the commonest cause of hospital visit. Among the total subjects, 209 (124 males and 85 females) were found to have diabetes and 147 subjects (99 males and 48 females) had dyslipidemia. 42.91% patients had diabetes, 30.18% had dyslipidemia, 18.27% subjects had diabetes and dyslipidemia, 31.41 % subjects had hypertension and diabetes, 19.50% subjects had hypertension and dyslipidemia, 20.73 % patients had stroke and DM, 10.47% patients had stroke and dyslipidemia, 34.90% had stroke with hypertension, and 12.73% had concomitant diabetes, dyslipidemia and hypertension. **Conclusion:** The relationship between hypertension and stroke with diabetes was stronger than that with dyslipidemia. Over all the metabolic profile was worse in subjects with diabetes than those without diabetes mellitus. Non-diabetic subjects had more favorable lipid status than those with diabetes.

**Indexing words**: Diabetes mellitus, Dyslipidemia, Hypertension, Stroke

**Introduction:**

The latest survival study with different treatment and rehabilitation models for cerebrovascular diseases (CVD) were not found to be beneficial[1]. Preventive strategies by risk factor modification are being considered to be more effective for both stroke recovery and patient survival. Recognizing and managing modifiable clinical and metabolic risk factors are thus important for both primary and secondary prevention of stroke. Though glucose metabolism is more clearly related to insulin than lipid metabolism, diabetes mellitus (DM) and dyslipidemia (DL) are common risk factors for atherosclerotic cerebrovascular and cardiovascular diseases[2,3,4]. It is unclear whether atherosclerotic vascular etiology is more related to DM or DL. In a certain population, their degrees of relationship with stroke may reflect their relative contributions and at the same time the relationship between DM and DL.

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In some studies DM was found to be associated with abnormal lipid levels[5] and again these two are more related to stroke[6]. Whether DM or DL is more important risk factor for stroke in the same population is not clearly defined in any previous study. So, the present authors have tried to find out the prevalence of DM and DL with neurological diseases in the same population.

**Methods:**

This study cross sectional study was conducted in the Neurology Department of Rangpur Medical College Hospital among the patients seen for any reason in Neurology OPD and indoor from January 2016 to December 2018. Patients with previously known diabetes and dyslipidimia were excluded from this study. All patients required to have an oral glucose tolerance test and a fasting lipid profile done along with a complete clinical profile including present and past history and a detailed clinical examination.

Fasting lipid profile and OGTT were done in the department of Biochemistry of Rangpur Medical College. ECG, CT scan and MRI were done from Rangpur Medical College Hospital. Patients with either normal or impaired OGTT (only Type 2

DM) and lipid profiles done simultaneously were enrolled in this study for data analysis.

487 patients fulfilling the selection criteria were enrolled into the study. Among the studied population, 307 were males and 180 females with male-female ratio 1.7:1. The Rangpur Medical College Ethical Committee and Thesis Protocol Review Committee approved the study protocol. For statistical analysis independent sample "t" test and chi square test was performed by computer based software Microsoft Excel to compare between various groups.

**Results**

It was observed that most common neurological problem was stroke. Out of total 487 subjects, 219 (45%) persons was involved in stroke and among them 157 (72%) were male and 62 (28%) were females (Table 1).

**Table 1:** Clinical presentation of 487 subjects

| Serial No | Presentation | Overall % (number) | Males % (number) | Females % (number) |
|---|---|---|---|---|
| 1 | Stroke | 45 (219) | 72 (157) | 28 (62) |
| 2 | Low back pain | 18 (88) | 50 (44) | 50 (44) |
| 3 | Headache | 12 (59) | 42 (25) | 58 (34) |
| 4 | Vertigo | 9.65 (47) | 74 (35) | 26 (12) |
| 5 | Muscle wasting | 3.29 (16) | 56 (9) | 44 (7) |
| 6 | Dementia | 3.08 (15) | 67 (10) | 33 (5) |
| 7 | Dysphasia | 2.67 (13) | 85 (11) | 15 (2) |
| 8 | Tremor | 2.67 (13) | 46 (6) | 54 (7) |
| 9 | Fainting/ LOCs* | 2.05 (10) | 50 (5) | 50 (5) |
| 10 | Miscellaneous | 1.44 (7) | 71 (5) | 29 (2) |
| | Total | 100 (487) | 63 (307) | 37 (180) |

*LOCs = Loss of consciousness

From Table 2, it was observed that females of the study group were involved at significantly earlier age than males. Body weight was significantly higher in males than females.

**Table 2:** Basic information of all subjects (n=487)

| Variables | All subjects (n=487) | Males (n=307) | Females (n=180) | t test |
|---|---|---|---|---|
| Age in years | 51.99±14.18 (487) | 54.11±14.15 (307) | 48.37±13.52 (180) | S |
| Weight in kg | 60.35±11.28 (365) | 62.48±10.40 (227) | 56.79±11.82 (138) | S |
| BP systolic (mm of Hg) | 155.81±27.94 (461) | 156.75±28.68 (290) | 154.21±26.60 (171) | NS |
| BP diastolic (mm of Hg) | 93.68±12.94 (461) | 94.27±13.19 (290) | 92.69±12.46 (171) | NS |
| Pulse pressure (mm of Hg) | 62.12±19.29 (461) | 62.48±19.31 (290) | 61.52±19.28 (171) | NS |
| Mean Arterial pressure (mm of Hg) | 114.39±17.00 (461) | 115.10±17.53 (290) | 113.19±16.02 (171) | NS |

NS: Not significant

$p<0.05$ was considered as significant

Student t test for different variables

Out of 487 subjects 209 (124 males and 85 females) were found to be diabetic on oral glucose tolerance test results.

Patients with normal glucose levels on fasting, 1 hour and 2 hour samples had a favorable lipid profile also. Those having impaired glucose levels at 1 hour or 2 hours after 75 gm glucose tended to have abnormal lipid values. 1 hr impaired values were more related with high TG levels and both 1 hr and 2 hr impaired levels were more related with high cholesterol and LDL levels.

**Table 3:** OGTT and fasting lipid profile of 487 subjects All values in mg/dl

| Age groups | Non-diabetic subjects (mean ± SD) (number ) | | | Diabetic subjects (mean ± SD) (number) | | | t-test |
|---|---|---|---|---|---|---|---|
| Sex | Males (183) | Females (95) | All ND (278) | Males (124) | Females (85) | All DM (209) | S |
| FPG | 95.20±12.31 | 91.85±15.76 | 94.05±13.65 | 135.16±55.51 | 130.73±44.89 | 133.36±51.39 | S |
| 1h PG | 147.80±17.49 | 147.59±20.27 | 147.73±18.45 | 233.18±75.49 | 239.63±68.44 | 235.80±72.61 | S |
| 2h PG | 131.75±18.52 | 130.09±18.83 | 130.57±18.60 | 200.17±134.16 | 200.79±124.62 | 200.42±66.40 | S |
| S Chol | 173.87±34.20 | 175.75±33.00 | 174.51±34.20 | 207.84±59.52 | 200.54±47.35 | 204.89±52.72 | S |
| S TG | 146.34±79.50 | 134.91±51.78 | 142.43±71.36 | 217.97±134.16 | 184.84±124.62 | 204.17±134.17 | S |
| LDL-C | 108.76±33.82 | 112.22±23.98 | 109.95±30.80 | 133.20±73.09 | 124.54±43.14 | 129.68±62.68 | NS |
| HDL-C | 37.14±7.63 | 38.02±9.04 | 37.44±8.13 | 42.70±9.25 | 41.10±8.56 | 42.05±9.25 | S |
| NHDL-C | 136.73±31.55 | 137.73±28.30 | 137.07±30.43 | 165.14±55.23 | 159.48±44.94 | 162.83±51.26 | |

NS: Not significant
p<0.05 was considered as significant

Table 4 shows the clinical and biochemical information of the subjects. It was observed that males were significantly commonly affected by stroke (51% vs 34%) but DM was found more commonly in females (38% vs 50%).

**Table 4:** Clinical and biochemical information of total (487) subjects

| Problems | Overall % (n) | Males % (n) | Females% (n) | Chi Square test |
|---|---|---|---|---|
| HTN | 67.14 (327) | 67.10 (206) | 67.22 (121) | NS |
| Stroke | 44.97 (219) | 51.14 (157) | 34.44 (62) | p<0.003 |
| DM | 42.91 (209) | 38.76 (119) | 50.00 (90) | p<0.02 |
| DL | 30.18 (147) | 32.24 (99) | 26.67 (48) | NS |
| DM or DL | 54.82 (267) | 53.09 (163) | 57.78 (104) | NS |

NS: Not significant
p<0.05 was considered as significant
Chi Square test for male and female groups

Table 5 expressed that in both HTN and stroke, incidence of DM was significantly higher than DL in total as well as in male and female subjects separately.

**Table 5:** Prevalence of HTN and stroke in DM and DL

| Variables | DM | | | DL | | | Chi Square test |
|---|---|---|---|---|---|---|---|
| | Overall % (n) | Sex | | Overall % (n) | Sex | | |
| | | Males % (n) | Females % (n) | | Males % (n) | Females % (n) | |
| HTN | 31.41 (153) | 28.66 (88) | 36.11 (65) | 19.50 (95) | 20.19 (62) | 18.33 (33) | p<0.001 |
| Stroke | 20.73 (101) | 22.80 (70) | 17.22 (31) | 10.47 (51) | 12.05 (37) | 7.78 (14) | p<0.001 |

NS: Not significant
p<0.05 was considered as significant
Chi Square test for all subjects in the non-diabetic and diabetic groups

**Discussion:**

Dyslipidemia is commonly highlighted as etiologic factor behind atherosclerosis related vascular diseases such as stroke. Various lipid lowering strategies are attempted for better survival with uncertain outcome[6]. Co-occurrence of DM, DL and HTN is much greater than would be predicted and a multifactorial program targeting all 3 risk factors is suggested[5].

In our study we found a preponderance in males with an M:F ratio of 1.7:1 with a lower age and weight in females (Table 2). Table 3 summarizes the laboratory reports of blood glucose and lipid status among the diabetic and non-diabetic subjects with significantly higher value of total cholesterol, TG, LDL-C, NHDL-C but not in HDL-C in diabetics than non-diabetics. Weycker et al[7] found that more than 50% patients with HTN also had DM and DL and a common risk factor was suggested. Jacobs et al[8] also reported a high prevalence of DL among DM subjects in US where 28.2% subjects were on treatment with lipid lowering agents but the LDL-C level did not differ by treatment status. Poor glycemic control is correlated with dyslipidemia and has very poor response to lipid lowering agents than those without diabetes[9] indicating the need for a better approach for diabetes. Furthermore a closer relationship of DM with HTN than that of DL indicates that the same factor causing DM is also causing DL.

In Table 4 of present study, it was found that about 67% of our subjects had HTN and no the sex difference was noted. About 45% subjects had stroke and among them 51.14% were males and 34.44% were females and the difference was significant ($p<0.003$), 31.62% subjects had IHD and among them 34.85% were males and 26.11% were females and the difference was significant ($p<0.05$). About 43% subjects had DM and among them 38.76% are males and 50.00% were females and the difference was significant ($p<0.02$). About 30% subjects had DL and among them 32.24% were males and 26.67% were females but the difference was not significant ($p>0.05$). About 55% subjects had either DM or DL but sex difference was not significant.

Table 5 shows that among the hypertensives 31.41 % had DM and 19.50% had DL and the difference was significant ($p<0.001$) indicating that HTN is more closely related to DM than with DL. Among the stroke patients 20.73% had DM and 10.47% had DL and the difference was significant ($p<0.001$). This indicates that stroke is more closely related to DM than with DL. Among the IHD patients 13.55% subjects had DM and 10.47% had DL but the difference was not significant ($p>0.05$) indicating an almost similar association of IHD with DM and DL.

As in the present study OGTT and lipid profile was performed at the same time on the same population and compared their biochemical profile on both clinical and laboratory grounds, it was found that association of DM with HTN and stroke were significantly greater (Table 2) than those with DL implicating the fact that DM comes first in the etiology of HTN and stroke. The common association of DM and DL[10] may however indicate a final common pathway to atherosclerosis. Diabetic vasculopathy may contribute to DL induced atherosclerosis[11]. Both DL and atherosclerosis can be induced by pro-inflammatory cytokines in insulin resistant states. Moreover a common etiology of DM and DL may be present [12].

Though insulin resistance is associated with DM in metabolic syndrome[13], further evidences suggest that insulin treatment of type-2 diabetes does not worsen DL rather a normal serum lipid level can be restored as long as body mass index (BMI) or weight can be kept within normal[14]. So, functional insulin deficiency can be regarded as the common etiology behind DM and DL and this can occur other neurological condition such as Dementia (considered as type -3 DM) and other neurodegenerative diseases[15,16] and immunological disorders[17] as because insulin is also essential for immunoglobulin production and normal cellular immunity[18].

**Conclusion**:

Neurological disorders of vascular etiology are closely related to hypertension, diabetes and dyslipidemia. The relationship of hypertension and stroke with diabetes were significantly stronger than that with dyslipidemia. Over all the metabolic profile was worse in subjects with diabetes than those with without diabetes mellitus. Non- diabetic subjects had more favorable lipid status than those with diabetes. As insulin directly lower glucose levels and insulin deficiency or dysfunction is indirectly related to abnormal lipid metabolism, a common etiology of diabetes and dyslipidemia may be responsible stroke and other neurological disorders.

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# Contraceptive Practice among the Rural Women at Reproductive Age in Bangladesh

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**Abstract:**

**Background**: This study was conducted with a view to finding out the prevalence and types of contraceptives used by rural women and its side effects in women's health. **Methods**: This cross-sectional study of seven days duration was conducted among 225 women of reproductive age in the rural area of Bangladesh. Every woman was interviewed face to face with a pre-formed questionnaire after taking informed consent**. Results:** About 49.8% women were in age group 26-35 years, majority (67.6%) had SSC-HSC level of education, 96.4% housewives, 40% had income tk 5001-10000 and 67.1% belonged to nuclear family. Contraceptive prevalence rate was 88.4% and most commonly used contraceptive was oral pills (64.9%) followed by injectable method 10.7%, condom 9.3%. The common side effects are headache (16.8%), nausea (14.1%), irregular menstruation (14.6%) and weakness (15.4%). There was no significant association of side effects with the use of hormonal contraceptive method. **Conclusion:** Though majority of women used contraceptive method emphasis is to be given on proper use of contraceptive methods for minimum adverse effects. Therefore there is a strong need for education and counseling of women about proper use of contraceptive for the sake of their good reproductive health.

**Indexing words:** Contraceptive practice, Rural area, Sirajganj, Bangladesh.

## Introduction:

WHO has defined family planning as a way of thinking and living that is adopted voluntarily upon the basis of knowledge, attitudes and responsible decisions by individuals and couples in order to promote the health and welfare of the family and thus contribute effectively to the social development of a country.[1] Family Planning efforts in Bangladesh began in early fifties under voluntary patronage of a group of social and medical workers post liberation period.[2] The government of Bangladesh wants to keep the population static and again have gone to two child norm. Demographers are of the view that the demographic goal of NRR can be achieved only if the CPR exceeds 60%.[3] The Bangladesh Family Planning Program is recognized as a success story in the contemporary Third World.[4] Unintended pregnancies increase the risk for poor maternal and infant outcomes.[5] Family planning has been widely acknowledged to intensify maternal death reduction, which is recommended by the World Health Organization as one of the six essential health interventions needed to achieve safe motherhood.[6] Family planning can reduce maternal mortality by reducing the number of pregnancies, the number of abortions, and the proportion of births at high risk.[7,8] Indian as well as Bangladeshi women have more children than desired and often too close together. Family Planning can have a positive impact on population growth, maternal mortality, and infant and new-born outcomes.[9] Therefore the result of this study would help the concerned authority to take necessary steps to improve contraceptive practice in rural area of Bangladesh.

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## Method:

This cross-sectional study was conducted during the period of 5th to 11th January 2019 among purposively selected 225 married women of reproductive age at the village Gobinathpur, Shahzadpur, Sirajganj with the view to finding out prevalence of contraceptive practice and its associated factors. The data were collected through pretested semi-structured questionnaire by face to face interview. The data thus collected

were checked & verified for any omission & inconsistency. Finally data were analyzed by SPSS program version 21 & chi-squire test were done. Then data were presented by necessary tables & charts.

**Results & Discussion**:

The table shows that almost half (49.8%) of women were within 26-35 years age group, 67.6% belongs to SSC-HSC educational level and housewife 96.4%. About 40% of the respondents had monthly income taka 5001-10000 and majority (67.1%) belongs to nuclear family. Similar study was conducted in India where 26-35 years wives were 46.0% which is comparable to the present study.[10] Another study conducted in rural area of Bangladesh by Khan and Jerifa showed that 69.8% lived in a nuclear family which is consistent to this study.[11]

**Table 1:** Socio-demographic characteristics of women (n= 225)

| Characteristics | n | % |
|---|---|---|
| **Age** | | |
| 15-25 years | 68 | 30.2 |
| 26-35 years | 112 | 49.8 |
| 36 years & above | 45 | 20.0 |
| **Educational status** | | |
| Illiterate | 28 | 12.4 |
| Primary-Secondary | 152 | 67.6 |
| SSC-HSC | 38 | 16.9 |
| Graduate-Masters | 7 | 3.1 |
| **Occupation** | | |
| Housewife | 217 | 96.4 |
| Service holder | 08 | 3.6 |
| **Monthly family Income taka** | | |
| 2001-5000 | 49 | 21.8 |
| 5001-10000 | 90 | 40.0 |
| 10001-20000 | 86 | 38.2 |
| **Types of Family** | | |
| Nuclear | 151 | 67.1 |
| Joint | 74 | 32.9 |

Figure 1 shows that, out of 225 respondents, 88.40% practiced some sort of contraceptive method. A study held in rural area of Bangladesh conducted by Das et al showed that 86.42% used contraceptve device which is consistent with this study.[12] Another study held in Myanmar conducted by Jirapongsuwan et al revealed that 73.3% of women of reproductive age used family planning method which is almost similar to this study.[13]

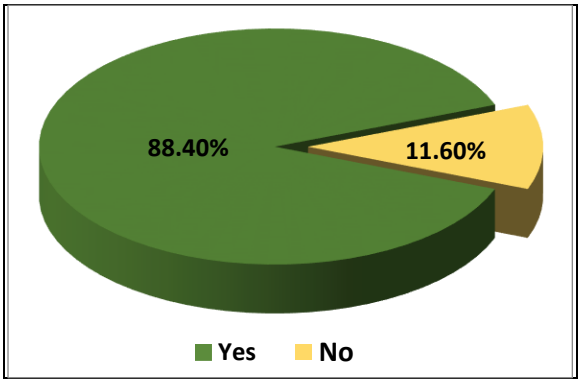



**Figure 1:** Distribution of respondents according to their use of contraceptive family method (n=225)

Table 2 shows that, two-thirds of the respondents (64.9%) used Oral pill followed by 9.3% used Condom, 10.7% injectable method and ECP 0.9%. A study held in Bangladesh conducted by Huda et al showed that 27% of the respondents used oral pill followed by 6.45 used condom 12.4% injectable method, 4.6% tubectomy, 1.2% vasectomy, 1.7% implants and 0.6% IUDs which is consistent to this study except oral pill.[14] Another study held in India conducted by Kashyap et al showed that 3% used emergency contraceptive pill which is almost similar to this study.[15]

**Table 2:** Distribution of respondents on the basis types of contraceptive use (n=199)

| Types | n | % |
|---|---|---|
| Oral Pill | 146 | 64.9 |
| Condom | 21 | 9.3 |
| Injectable method | 24 | 10.7 |
| Implant | 2 | 0.9 |
| IUDs | 2 | 0.9 |
| Vesectomy | 1 | 0.4 |
| Tubectomy | 1 | 0.4 |
| Emergency contraceptive pill | 2 | 0.9 |

Regarding side-effects of contracetives, Table 3 shows that, 18.8 % had headache followed by irregular menstruation in 14.6% and weight gain in 1.6%. A study held in rural area of Bangladesh conducted by Das et el showed that irregular menstruation in 43.3% and weight gain in 20.84% which is inconsistent with this study.[12]

**Table** 3: Side effects due to currently using family planning method

| Types | n | % |
|---|---|---|
| Headache | 36 | 18.8% |
| Nausea | 27 | 14.1% |
| Irregular menstruation | 28 | 14.6% |
| leucorrhoea | 17 | 8.9% |
| Weakness | 30 | 15.6% |
| Weight gain | 3 | 1.6% |
| Others | 51 | 26.6% |

Table 4 shows that there was no significant association between use of hormonal method and its various side effects.

**Table 4:** Association of side effects with hormonal contraceptives

| Side effects | Yes | No | Total | Significance |
|---|---|---|---|---|
| Headache | 31(39.2%) | 48(60.8%) | 79(100.0%) | $(\chi^2)$= 2.015 p= 0.733 |
| Nausea | 23(29.1%) | 56(70.9%) | 79(100.0%) | $(\chi^2)$= 3.810 p= 0.577 |
| Irregular menstruation | 23(29.1%) | 56(70.9%) | 79(100.0%) | $(\chi^2)$= 1.778 p= 0.879 |
| Weakness | 24(30.4%) | 55(69.6%) | 79(100.0%) | $(\chi^2)$= 2.598 p= 0.762 |
| Others | 40(50.6%) | 39(49.4%) | 79(100.0%) | $(\chi^2)$= 7.306 p= 0.199 |

Chi-square test was done to compare groups.

**Conclusion & recommendations:**

The study reveals that majority of the women at reproductive age practiced contraceptive method. This indicates a tremendous success of the family planning program in Bangladesh. But there are so many side effects among the women using family planning method. Even accurate use of contraceptive method is still in matter of question as most of the respondents are illiterate. So, the results of this study would help the concerned authority to take necessary steps to improve contraceptive practices in Bangladesh.

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# Assessment of Histomorphologiocal Changes in Gall Bladder Wall Operated for Chronic Cholecystitis

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**Abstract:**
**Context:** Chronic cholecystitis is a cause of morbidity and mortality throughout the world. Most of the cases of chronic cholecystitis are due to gall stone. The main objective of the study was to find out the histomorphological changes in gall bladder wall in chronic cholecystitis. **Methods:** This cross sectional study was conducted in the Department of Surgery in Dhaka Medical College, Dhaka from Nov 2005 to Oct. 2006 over a period of one year. A total of 104 patient were included in the study with diagnosis of chronic cholecystitis underwent cholecystectomy and the histopathological examination of the gallbladder was done in the Department of Pathology, Dhaka Medical College Hospital, Dhaka and final diagnosis made on histopathological report. **Results:** In the study of 104 patients, spectrum of charge in gallbladder wall ranges from minimal mucosal lesion, metaplastic change to malignant charge. Out of these 86(82.7%) diagnosed as chronic cholecystitis, followed by 8(7.7%) acute on chronic" cholecystitis, chronic cholecystitis in cholesterolosis (3.8%) chronic cholecystitis with metaplastic change 3(2.9%), carcinoma gallbladder (adenocarcinoma) 3(2.9%). **Conclusions:** The study revealed that metaplastic change and gall bladder carcinoma arise in the setting of chronic cholecystitis. Chronic gall bladder inflammation is likely a part of the cause of the malignant transformation to gall bladder cancer. Studying the spectrum of histomorphological changes certainly contribute to etiopathogenests and hence prevention.

**Indexing words:** Histomorphology, Gall Bladder, Chronic Cholecystitis

## Introduction:

Chronic cholecystitis is the most common form of symptomatic gall bladder disease and associated with gall stones in nearly every case.[1] It is probably inappropriate, although classical, to subdivide cholecystitis into chronic and acute calculous cholecystitis. They are part of same spectrum of disease and are related to inflammation within the gall bladder secondary to obstruction of the cystic duct by stones. With stone in a gall bladder it appears that there is always some degree of inflammatory change, but there is insufficient evidence to suggest that this is cause of symptom.[2] Chronic inflammation of gall bladder is most commonly due to stones and the term 'chronic cholecystitis' should be restricted to gall bladders containing gall stones with varying degrees of inflammation from mild mucosal/submucosal change to gross transmural fibrosis leading to a contracted fibrous encasement of the biliary calculi.[3]

The morphological changes in chronic cholecystitis are extremely variable and some times minimal. The serosa is usually smooth and glistening but often it is dulled by sub-serosal fibrosis following inflammation. Dense fibrous adhesions may remain as a sequelae of pre-existing acute inflammation. On sectioning, the wall is variably thickened rarely to more than thrice normal. The wall has an opaque gray white appearance and less flexible than normal. In uncomplicated cases, the lumen contains fairly clear green -yellow mucoid bile and usually stones. The mucosa itself is generally preserved. On histological examination, the degree of inflammatory reaction is variable. In more established cases there is marked sub-epithelial

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and sub- serosal fibrosis accompanied by mono nuclear cell infiltration. Inflammatory proliferation of the mucosa and fusion of the mucosal fold may give rise to buried crypts of epithelium within the gall bladder wall. Outpouching of the mucosal epithelium through the wall (Rokitansky - Aschoff's Sinuses) may be prominent; superimposition of acute inflammatory changes implies acute exacerbation of a previously chronically injured gall bladder. In rare instances, extensive dystrophic calcification within the gall bladder wall may yield a porcelain gall bladder notable for a markedly increased incidence of associated cancer.[4]

Diffuse calcification of the gall bladder considered to be the end stage of chronic cholecystitis has all been associated with carcinoma of gall bladder and an indication of early cholecystectomy[5]. However, most of the patients are unaware of the disease and remain asymptomatic for life. Only small percentage develops symptoms necessitating treatment. Cholecystectomy either open or laparoscopic is a treatment of choice in most patients. The diseased gall bladder shows a spectrum of histomorpholigical changes ranging from inflammation to malignancy. The present study aimed to analyze the change. To demonstrate the spectrum of changes in gall bladder wall in chronic cholecystitis, the present study was aimed at to demonstrate the histopathological changes in the gall bladder wall in chronic cholecystitis.

**Methods:**

This cross-sectional study was done in the Department of Surgery, Dhaka Medical College & Hospital, Dhaka, between the periods of November 2005 to October 2006. The study was done on one hundred and four patients (both sexes) who were preoperatively diagnosed as chronic cholecystitis admitted into Surgery Department undergoing operative treatment. Purposive convenience sample method was followed as per inclusion and exclusion criteria. Evaluations of the patients were done by based on history, clinical physical examination and necessary investigation. Patients with severe complicating medical illness, patient requiring emergency surgery, and patient with obvious malignancy were excluded from the study.

All patients were given an explanation of the study and informed consents were taken.

At first, a detailed history was taken and a thorough clinical examination was done to detect the cases of chronic cholecystitis. Subsequently necessary laboratory and other special investigations were carried out with all possible means- a preoperative diagnosis was made.

The final diagnosis was done based on operative findings and histopathological findings of the patients gall bladder suffering from chronic cholecystitis. Clinical diagnosis was correlated with operative findings and histopathological examination done in every case to see the histopathological changes.

Collected data was collated and appropriate statistical analysis were done using computer based SPSS (Statistical Program for Scientific Study) package.

**Results:**

Among the studied patients, 23(22.1%) were male and 81(77.9% were female with male and female ratio was 1:3.5. The mean age of the patients were 42.8±12.0 years ranging from 17 to 75 year. The mean age of the male patients was 42.9±11.8 years and that of female patients was 42.1±12.1 years.

The histological findings indicated that 78.8% had flattened mucosa and 21.2% ulcerated mucosa. Microscopic findings indicated that 84.6% had chronic cell infiltration in the lamina propria and muscle layer followed by 79.8% had perimuscular fibrosis and 2.9% had malignant cell. However, 12.5% had both had chronic infiltration of cell and malignant cell. In the serous layer, 82.7% had vascular congestion followed by chronic cell Infiltration (75.0%).

**Table 1:** Distribution of patients by histological findings (N=104)

| Histological finding | Frequency | Percent |
|---|---|---|
| **Mucosa** | | |
| Flattened | 82 | 78.8 |
| Ulcerated | 22 | 21.2 |
| **Lamina propria and muscle layer** | | |
| Chronic cell Infiltration (lymph. macro) | 88 | 84.6 |
| Perimuscular fibrosis | 83 | 79.8 |
| Both | 13 | 12.5 |
| Malignant cell | 3 | 2.9 |
| **Serous layer** | | |
| Vascular congestion | 86 | 82.7 |
| Chronic cell Infiltration (lymph. macro) | 78 | 75.0 |

Histological diagnosis indicated that 82.7% diagnosed as chronic cholecystitis followed by acute on chronic cholecystitis (7.7%), adenocarcinoma (2.9%), chronic cholecystitis

with cholesterosis (3.8%) and chronic cholecystitis with metaplastic changes (2.9%) that is 90.4% chronic cholecystitis and 9.6% diagnosed as carcinoma and metalastic changes.

**Table 2:** Distribution of patients by histological diagnosis (N=104)

| Histological findings | Frequency | Percent |
|---|---|---|
| Chronic cholecystitis | 86 | 82.7 |
| Acute on chronic cholecystitis | 8 | 7.7 |
| Adenocarcinoma | 3 | 2.9 |
| Chronic cholecystitis with cholesterosis | 4 | 3.8 |
| Chronic cholecystitis with metaplastic changes | 3 | 2.9 |
| **Total** | **104** | **100.0** |

**Discussion:**

Biliary disease, specially cholecystitis with cholelithiasis is very common in our country. An increased incidence of carcinoma also been observed in recent years. The primary objective of the study was to find out the histomorphological changes in gallbladder wall operated for chronic cholecystitis.

In this study, 104 patients were anatyzed irrespective of age a sex. Clinical and laboratory parameters, serological are ultrasonographic findings and the final diagnosis were done by histopathological findings.

All the patient with diagnosis of chronic cholecystitis underwent cholecystectomy and gallbladder histopathological study was done. Numerous and variable histomophological findings varying from minimal to gross alteration was found in the gall bladder wall.

Among the studied patient 23 (22.1 %) were male and 81 (77.9%) were female and male and female ratio was 1.3:5. The mean age of the patient were 42±12 years ranging from 17 to 75 years. The gallbladder diseases are more common in female and female are more sufferer than male findings are consistent with previously published reports.[6]

It is well known that cholelithiasis is more common is female and more than 90% of cases of chronic cholecystitis are associated with cholelithiasis.[7]

Considering the symptoms and signs 38.5% patient present with upper abdominal pain followed by nausea (9.6%), vomiting (6.7%), and fever (9.6%) and chill (9.6%). However no patient had anaemia, jaundice or palpable liver.

The ultrasonographic findings indicated that 38.5% patient has increased wall thickness followed by 61.5% patient has normal wall thickness. However 99% patients were gallstone detected ultrasonographically. The other parameters were within normal limit.

The morphological finding indicated that majority of the patient had bile stained velvety mucosa (85.6%) followed by atrophied (8.7%) and flattened (8.5%) mucosa and 99% had gallstone in resected gallbladder.

The histological diagnosis revealed that 82.7% diagnosed as chronic cholecystitis followed by acute on chronic cholecystitis (7.7%), chronic cholecystitis with cholesterolosis (3.8%), and chronic cholecystitis with metaplastic charge (2.9%), carcinoma gallbladder (adenocarcinoma) (2.9%) in decreasing order of frequency.

The histological finding revealed that 78.8% had flattened mucosa are 21.2% ulcerated mucosa. There were chronic inflammatory cell infiltration in the lamina propria and muscle layer 84.6% and perimuscular fibrosis 79.8%, malignant cell infiltration was 2.9%. In serous layer 82.7% was vascular congestion followed by chronic cell infiltration (75.0%).

In the study, out 104 patients it was found that chronic cholecystitis and other benign lesion were 101(97%) and only 3(2.9%) was malignant lesion.

In the study stone was found in 97% patient and carcinoma gallbladder was 2.9%. Gallstone are found in 65-90%of patients with carcinoma gallbladder.[8] However there may be several other important factor involved in the development of carcinoma gall gladder and only a small proportion of patient (1-3%) of all cholelithiasis patients develop carcinoma gall bladder. Two School of thought have emerged as to pathogenesis of carcinoma gallbladder due to gallstone disease, (i) Epithelial hyperplasia, (ii) Epithelial metaplasia leading to dysplasia, carcinoma in situ and invasive cancer current thinking favour the second hypothesis 1 that adenocarcinoma develops in displasia of metaplastic gallbladder.[8]

Carcinoma gall bladder is rare but highly lethal disease. In present study, there were only 3 cases (2.9%). Different studies have reported different incidence of carcinoma gallbladder ranging from1% to 12.4%. Even to day, with multiple diagnostic tests available, gall bladder

cancer is usually first recognized during a laparotomy performed for a presumptive diagnosis of benign gall bladder disease.

However, the study was conducted in a short period of time and included limited number of patients in surgical department of Dhaka Medical College Hospital, Dhaka and selected by convenience sampling may not represent the actual histopathological change in gallbladder wall in chronic cholecystitis of the whole country. Although findings of the present study consistent with the findings of the different published studies, a large number of patients should be studied in different centers to correlate with this study.

**Conclusion:**

The study revealed that in chronic cholecystitis histomorphological changes ranging from minimal mucosal lesion, metaplastic change to malignant change. Cholecystectomy seems to be best prevention of carcinoma gallbladder in any case of cholecystitis with cholelithiasis symptomatic or not in absence of any contraindication. A selective approach to histopathology of gallbladder is justifiable.

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# Management of Fracture of Distal End of Femur with Locking Compression Plate

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**Abstract:**

**Context:** The fractures of the distal end of femur are one of the commonest fractures found and represent 6-8% of all the femoral fractures treated by orthopedic surgeons. These fractures can be treated by different methods and near anatomical reduction is the most important to obtain near good functional results. The aim of the study was to evaluate the surgical management of fractures of distal end of femur with locking compression plate. **Methods:** A longitudinal clinical study was carried out Department of orthopedics, Shaheed M. Monsur Ali Medical College, Sirajgonj. In this study 50 patients with closed distal femoral fractures (distal fifteen cm of femur) were studied. All the cases were treated between January-2017 and December -2018 at this institution and followed for a minimum of 12 months. Age of the patients was ≥20 yrs. All the fractures in this series were post-traumatic fresh fracture of distal end femur with or without osteoporotic changes and managed surgically by locking compression plate. **Results:** In postoperative complications, 4(8.0%) patients had superficial infection, 8(16.0%) had knee stiffness (which was corrected by vigorous physiotherapy), 1(2.0%) had deep seated infection and 2(4.0%) had delayed union. According to Neer's scoring system, 42(84.0%) patients were excellent, 6(12.0%) were good and 2(4.0%) were poor outcome. **Conclusion:** Locking compression plate is an excellent fixation system for distal end femoral fractures. Device provides good angular stability and helps in early mobilization.

**Indexing words:** Fracture of distal end of femur, Locking compression plate (LCP)

## Introduction:

The fractures of the distal end of femur are one of the commonest fractures found. Incidence of distal end of femur fractures is 37 per 1,00,000 person[1] comprises about 6-8% of all the femoral fractures treated by orthopedic surgeons. The most common high-energy mechanism of injury is a traffic accident (53%) and the most common low-energy mechanism is a fall at home (33%).[2,3] In the past two decades there has emerged another injury group coming out of periprosthetic fractures.[3] Near anatomical reduction is most important in these fractures to obtain near good functional results. A variety of treatment options are proposed for distal femoral fractures of the treatment with distal femoral LCP has yielded good results.[4] There are various options for operative treatment like plating techniques that require compression of the implant to the femoral shaft (blade plate, dynamic condylar screw, non-locking condylar buttress plate), antegrade nailing, retrograde nailing, sub muscular locked internal fixation and external fixation.[5] Locking compression plates with its innumerous advantage is of great use in such circumstances.[5,6] Locking compression plate has the advantage of combination of conventional compression plating and locked plating techniques which enhances the plate osteosynthesis.[5,6,7] Anatomically precontoured built reduces soft tissue problems and acts as internal fixator.[7,8] In addition, a locking compression plate has got distinct advantages of unicortical fixation and least chance of plate back out as the screw gets locked to the plate.[9] The study was undertaken to evaluate the outcome of management of distal femoral fractures using LCP which may be helpful to find the solutions for the age-old problems and complications associated with management of these complex fractures.

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**Methodology:**

A longitudinal clinical study was carried out Department of Orthopedics, Shaheed M. Monsur Ali Medical College, Sirajgonj. In this study 50 patients with closed distal femoral fractures (distal fifteen cm of femur) were studied. All the cases were treated between January 2017 and December 2018 at our institution and followed for a minimum of 12 months. All the fractures in this series were post-traumatic fracture of distal end femur (distal 15 cms of femur). Patients who were aged ≥20 yrs had fresh distal femoral fractures with or without osteoporotic changes and managed surgically were included in the study. Patients with open distal femoral fractures; children with distal femoral fractures in whom, growth plate is still open; patients lost in follow-up; patients managed conservatively for other medical reasons; distal femoral fractures with neurovascular compromise were excluded from the study. The plate and screws are manufactured from 316L stainless alloy with gun drilling technique. The locking compression plates (4.5 mm precontoured) are available from 8 hole to 12 hole. After following proper surgical preparation, fracture reduction was achieved by traction and counter traction with gentle manipulation during surgery, in few cases Steinmann pin was used for reduction as joystick method. Condyles were fixed with 2 mm Kirschner wires initially along with plate after reduction and fixed with 6.5 mm cancellous screws into the condyles and 4.5 mm locking screws into the shaft. This has been confirmed intraoperatively under image intensifier. Patients post operative care was maintained as per hospital protocol. Patient was mobilized on 3rd or 4th day postoperatively with knee exercises. Non-weight bearing was started after first post-operative week till 6 weeks depending on the fracture pattern. Partial weight and full weight bearing exercises started depending on healing process till fracture union respectively.



**Figure 1**: Locking compression plate and screws.

**Results:**

Majority (42.0%) patients belonged to age 21-30 years. Majority (88.0%) patients were male and 6(12.0%) were female. Majority (90.0%) patients had fracture of right side and 5(10.0%) left side. Majority (92.0%) cases the type of injury was due to RTA and 4(8.0%) cases were due to self fall (Table 1).

**Table 1:** Demographic characteristics of the study patients

| Variables | Number of patients | Percentage |
|---|---|---|
| **Age (years)** | | |
| 21-30 | 21 | 42.0 |
| 31-40 | 18 | 36.0 |
| 41-50 | 7 | 14.0 |
| 51-60 | 4 | 8.0 |
| **Sex** | | |
| Male | 44 | 88.0 |
| Female | 6 | 12.0 |
| **Side of fracture** | | |
| Right | 45 | 90.0 |
| Left | 5 | 10.0 |
| **Type of injury** | | |
| Road traffic accident | 46 | 92.0 |
| Self fall | 4 | 8.0 |

Almost one fourth (24.0%) patients were Mullers type A1 followed by 6(12.0%) were A2, 8(16.0%) were A3, 8(16.0%) were B1, 5(10.0%) were B2, 4(8.0%) were C1, 5(10.0%) were C2 and Mullers type C3 (Table 2).

**Table 2:** Type of fracture lower end of femur of the study patients

| Type of fracture | Number of patients | Percentage |
|---|---|---|
| A1 | 12 | 24.0 |
| A2 | 6 | 12.0 |
| A3 | 8 | 16.0 |
| B1 | 8 | 16.0 |
| B2 | 5 | 10.0 |
| C1 | 4 | 8.0 |
| C2 | 5 | 10.0 |
| C3 | 2 | 4.0 |

Majority (70.0%) patients used 8-12 holed plate and 15(30.0%) used 5-7 holed plate for lower end of femur (Table 3).

**Table 3:** Plate size of the study patients

| Plate size (Holed) | Number of patients | Percentage |
|---|---|---|
| 8-10 | 15 | 30.0 |
| 11-12 | 35 | 70.0 |

In postoperative complications, 4(8.0%) patients had superficial infection, 8(16.0%) had knee stiffness (which was corrected by vigorous physiotherapy), 1(2.0%) had deep seated infection and 2(4.0%) had delayed union (Table 4).

**Table 4:** Post operative complications of the study patients

| Post operative complications | Number of patients | Percentage |
|---|---|---|
| Superficial infection | 4 | 8.0 |
| Knee stiffness | 8 | 16.0 |
| Deep seated infection | 1 | 2.0 |
| delayed union | 2 | 4.0 |

The radiological union was found 35(70.0%) patients in 3 month and 15(30.0%) in 6 month (Table 5).

**Table 5:** Radiological union of the study patients

| | Number of patients | Percentage |
|---|---|---|
| 3 month | 35 | 70.0 |
| 6 month | 15 | 30.0 |

Mean time of partial weight bearing was found 12.4±1.1 weeks and complete weight bearing was found 22.2±1.6 weeks (Table 6).

**Table 6:** Weight bearing of the study patients

| Weight bearing | Mean | ±SD |
|---|---|---|
| Partial weight bearing (weeks) | 12.4 | ±1.1 |
| Complete weight bearing (weeks) | 22.2 | ±1.6 |

According to Neer's scoring system, 42(84.0%) patients were excellent, 6(12.0%) were good and 2(4.0%) were poor outcome (Table 7).

**Table 7:** Functional result (Neer's score) of the study patients

| | Number of patients | Percentage |
|---|---|---|
| Excellent | 42 | 84.0 |
| Good | 6 | 12.0 |
| Poor | 2 | 4.0 |



**Figure 2:** Implant used in fracture of distal femur



**Figure 3:** (A and B) Follow-up with range of motion and incision site.

**Discussion:**

In this study it was observed that the majority (42.0%) patients belonged to age 21-30 years. Majority (88.0%) patients were male and 6(12.0%) were female. Majority (90.0%) patients had fracture of right side and 5(10.0%) left side. Majority (92.0%) cases the type of injury was due to RTA and 4(8.0%) cases were due to self fall. Ajaz et al[10] observed similar results where they showed majority (40.0%) patients belonged to age 31-40 years and 12(80.0%) patients were male. Almost three fourth (73.0%) patients had fracture of right side and 14(93.0%) patients the type of injury was due to RTA. Ravish et al[1] also reported out of 25 patients in their study, 17 were male patient (68%) and 8 were female patients (32%). The average age of the patients was between 25-45 years. In 20 (80%) cases the type of injury was due to RTA and 5 (20%) cases were due to self fall. Gupta and Dande[11] reported all cases were fresh, 78 patients were males and 22 patients were females. The median age was 47 years ranging from 20-70 years. 65 of the fractures were caused by road traffic accidents and 25 were due to fall, 10 were due to assault. 60 patients were with fracture on right side and 40 on left side. Vikranth et al[4] reported majority (30.0%) patients belonged to age 20-30 years and 20(66.7%) patients were male. Bhimani et al[12] also reported the patients' ages ranged from 18 to 74 years with a mean age of 44 years. Twenty fractures involved the right side and ten involved the left side. The causes of fractures were motor vehicle accident in nineteen patients and a domestic fall in remaining eleven.

In the current study showed that almost one fourth (24.0%) patients were Mullers type A1 followed by 6(12.0%) were A2, 8(16.0%) were

A3, 8(16.0%) were B1, 5(10.0%) were B2, 4(8.0%) were C1, 5(10.0%) were C2 and Mullers type C3. Ajaz et al[10] observed that majority (60.0%) patients were Mullers type C2, 3(20.0%) were A1 and 3(20.0%) were C3. Gupta and Dande[11] reported 5 cases were Mullers type A1; 25 was Mullers type A2; 20 were Mullers type A3; 10 was Mullers type C1 20 were type C2 and remaining 20 were Mullers type C3. Bhimani et al.[12] observed according to Muller's classification of distal femur five were Muller's type A1; nine Muller's type C1; ten Muller's type C2 and six Muller's type C3.

In the present study, in majority (70.0%) patients 8-10 holed plate was used and in 15(30.0%) 4-7 holed plate was used for lower end of femur. Bhimani et al[12] reported the size of the plate used for fixation varied from 4 holed to 12 holed depending on fracture pattern. But commonly used size was 7-9 holed plates. Ajaz et al[10] in more than two third (67.0%) patients used 8-10 holed plate. Gupta and Dande[11] reported the size of plate was selected based on the type of fracture. 6 and 8 holed plates were used more commonly for lower end of femur.

In the present study, postoperative complications were occurred in some patients. Among them 4(8.0%) patients had superficial infection, 8(16.0%) had knee stiffness (which was corrected by vigorous physiotherapy), 1(2.0%) had deep seated infection and 2 (4.0%) had delayed union. Agarwal et al[13] found that late postoperative complications included chronic infection (10%), knee stiffness (10%), malalignment (10%). Ajaz et al[10] reported 6(40.0%) patients had superficial infection and 1(7.0%) had delay union. Ravish et al[1] reported 2 patients had superficial infection, 3 patients had wound gaping, 12 patients had knee stiffness and bent implant was seen in 1 patient. In study of Gupta and Dande[11], very few patients had significant varus/valgus malalignment with 5 patients had superficial infection which was treated with debridement and antibiotics. Implant failure occurred in 2 patients, delayed union in 2 patients. Bhimani et al[12] two patients (7%) had superficial infection which was managed conservatively with intravenous antibiotics. They observed one patient each with varus and valgus malalignment.

In the present study, the radiological union was found in 35(70.0%) patients in 3 month and 15(30.0%) in 6 month. Agarwal et al[13] reported the radiological union was noted in 46.67% patients each at three months and six months. Ajaz et al[10] two third (66.66%) patients were found <16 weeks of radiological union. Ravish et al[1] reported the average time taken for radiological union was between 20-24 weeks. Gupta and Dande[11] observed 73 Patients (73%) showed radiological union within 18 weeks. In Vikranth et al[4] study 22 patients showed radiological union within 16 weeks and 7 cases united within 24 weeks. Bhimani et al[12] also reported 26 (87%) showed radiological union within 20 weeks. Mean time for Radiological union was 16 weeks.

In the present study, the mean time of partial weight bearing was found 12.4±1.1 weeks and complete weight bearing was found 22.2±1.6 weeks. Ravish et al[1] reported time of partial weight bearing was 12 weeks and full weight bearing was 22 weeks. In Bhimani et al[12] partial weight bearing was started at an average 6-8 weeks after surgery when there were early signs of callus formation. Full weight bearing was started on an average 12-14 weeks after surgery as per union seen on roentogram and patient's tolerance.

In this study observed that according to Neer's scoring system, 42(84.0%) patients were excellent, 6(12.0%) were good and 2(4.0%) were poor outcome. Agarwall et al[13] reported all types of fractures had excellent outcome except type C1 and C2 where 55.56% and 66.66% of patients had excellent outcome respectively. Ajaz et al[10] reported 3(20.0%) patients were excellent, 9(60.0%) were good and 3(20.0%) were poor outcome. Ravish et al[1] stated according to Neer's scoring system, 7(28%) cases were excellent, 14(56%) were good, 3(12%) were fair, 1(4%) were poor. In Gupta and Dande[11] study on 100 fractures around knee, 65 patients showed excellent result. 20 patients showed good outcome, 10 patients showed fair outcome and 5 patient showed poor outcome. Vikranth et al[4] reported restoration of anatomy was excellent in 18 patients (60%), good in 8 patients (26.6%), fair in 2 patients (6.7%) and poor outcome in 2 patients (6.7%). Bhimani et al[12] reported Neer's scoring system as excellent in 19(64%), good in 6(20%), fair in 4(13%) and poor in 1(3%).

**Conclusion:**

Locking compression plate is an excellent fixation system for distal end femoral fractures. Device provides good angular stability and helps in early mobilization.

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# JOURNAL OF RANGPUR MEDICAL COLLEGE

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