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# GREEN LIFE MEDICAL COLLEGE JOURNAL

**Vol. 3, No. 2, July 2018**


## Journal Committee




**Address of Correspondence**

Executive Editor, Green Life Medical College Journal
31 and 31/1, Bir Uttam K.M. Shafiullah Sarak, Dhanmondi, Dhaka-1205
Tel: 9612345-50 Ext. 1251
E-mail: ashraf.ahmeddrcme@gmail.com; Website: www.greenlife.edu.bd

# ABOUT THE JOURNAL


| | | |
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| Full Name of the Journal | : | Green Life Medical College Journal |
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**AIMS & SCOPE:**

The Green Life Medical College Journal is an english language scientific papers dealing with clinical medicine, basic sciences, epidemiology, diagnostic, therapeutics, public helath and healthcare in relation to concerned specialities. It is an official journal of Green Life Medical College and is published bi-annually.

This Joural is recognized by Bangladesh Medical & Dental Council (BM&DC).

The Green Life Medical College Journal of Bangladesh intends to publish the highest quality material on all aspects of medical science. It includes articles related to original research findings, technical evaluations and reviews. In addition, it provides readers opinion regarding the articles published in the journal.

**INSTRUCTION TO AUTHORS:**

**Papers:**

The Green Life Medical College Journal (published bi-annually) accepts contributions from all branches of medical science which include original articles, review articles, case reports, and letter to the Editor.

The articles submitted are accepted on the condition that they must not have been published in whole or in part in any other journal and are subject to editorial revision. The editor preserves the right to make literary or other alterations which do not affect the substance of the contribution. It is a condition of acceptance that the copyright becomes vested in the journal and permission to republish must be obtained from the publisher. Authors must conform to the uniform requirements for manuscripts submitted to biomedical journals (JAMA 1997; 277: 927-34).

**Legal considerations:**

Authors should avoid the use of names, initials and hospital numbers which may lead to recognition of a patient. A table or illustration that has been published elsewhere should be accompanied by a statement that permission for reproduction has been obtained from the author(s) or publisher(s).

**Preparation of manuscript:**

Each manuscript should indicate the title of the paper, and the name(s) and full address(es) of the author(s). Contributors should retain a copy in order to check proofs and in case of loss. Two hard copies of each manuscript (double-spaced) should be submitted. If a manuscript is accepted for publication in the GMCJ, the editor responsible for it and may request a soft copy (a CD or via internet) for the revision. Each paper will be reviewed for possible publication. The Editor may wish to see the raw data (electronic form) if necessary.

In preparing the manuscript, use double spacing throughout, including title, abstract, text, acknowledgement, references, table and legends for illustrations and font type and size 'Times New Roman 12'. Begin each of the following sections on a separate paper. Number pages consecutively.

**The standard layout of a manuscript:**

- Title page
- Abstract, including Keywords
- Introduction
- Methods
- Results
- Discussion
- Acknowledgements
- Funding
- List of references
- Tables & Figures
- Illustrations

The pages should be numbered in the bottom right-hand corner and the title page being page one, etc. Start each section on a separate page.

**Title page:**

A separate page which includes the title of the paper. Titles should be as short and concise as possible (containing not more than 50 characters). Titles should provide a

reasonable indication of the contents of the paper. This is important as some search engines use the title for searches. Titles in the form of a question, such as 'Is drinking frequent coffee a cause of pancreatic carcinoma?" may be acceptable.

The title page should include the name(s) and address(es) of all author(s). Details of the authors' qualifications and post (e.g., professor, consultant) are also required. An author's present address, if it differs from that at which the work was carried out, or special instructions concerning the address for correspondence, should be given as a footnote on the title page and referenced at the appropriate place in the author list by superscript numbers ([1, 2, 3] etc.) If the address to which proofs should be sent is not that of the first author, clear instructions should be given in a covering note, not on the title page.

**Abstract:**

The 'Abstract' will be printed at the beginning of the paper. It should be on a separate sheet, in structured format (Introduction/Background; Methods; Results; and Conclusions) for all Clinical Investigations and Laboratory Investigations. For Reviews and Case Reports, the abstract should not be structured. The Abstract should give a succinct account of the study or contents within 350 words. The results section should contain data. It is important that the results and conclusion given in the 'Abstract' are the same as in the whole article. References are not included in this section.

**Keywords:**

Three to six keywords should be included on the summary page under the heading Keywords. They should appear in alphabetical order and must be written in United Kingdom English spelling.

**Introduction:**

The recommended structures for this section are:

- Background to the study/Introduction
- What is known/unknown about it
- What research question / hypothesis you are interested in
- What objective(s) you are going to address

The introduction to a paper should not require more than about 300 words and have a maximum of 1.5 pages double-spaced. The introduction should give a concise account of the background of the problem and the object of the investigation. It should state what is known of the problem to be studied at the time the study was started. Previous work should be quoted here but only if it has direct bearing on the present problem. The final paragraph should clearly state the primary and, if applicable, secondary aims of the study.

**Methods:**

The title of this section should be 'Methods' - neither 'Materials and methods' nor Patients and methods'. The Methods section should give a clear but concise description of the process of the study. Subjects covered in this section should include:

- Ethics approval/license
- Patient/population
- Inclusion/exclusion criteria
- Conduct of the study
- Data handling
- Statistics
- Cognitive Task Analysis (CTA)

**Ethical clearance:**

Regardless of the country of origin, all clinical investigators describing human research must abide by the Ethical Principles for Medical Research Involving Human Subjects outlined in the Declaration of Helsinki, and adopted in October 2000 by the World Medical Association. This document can be found at: http://ohsr.od.nih.gov/guidelines/helsinki.html. Investigators are encouraged to read and follow the Declaration of Helsinki. Clinical studies that do not meet the Declaration of Helsinki criteria will be denied peer review. If any published research is subsequently found to be non-compliant to Declaration of Helsinki, it will be withdrawn or retracted. On the basis of the Declaration of Helsinki, the Green Life Medical Journal requires that all manuscripts reporting clinical research state in the first paragraph of the 'Methods' section that:

- The study was approved by the appropriate Ethical Authority or Committee.
- Written informed consent was obtained from all subjects, a legal surrogate, or the parents or legal guardians for minor subjects.

Human subjects should not be identifiable. Do not disclose patients' names, initials, hospital numbers, dates of birth or other protected healthcare information. If photographs of persons are to be used, either take permission from the person concerned or make the picture unidentifiable. Each figure should have a label pasted on its back indicating name of the author at the top of the figure. Keep copies of ethics approval and written informed consents. In unusual

circumstances the editors may request blinded copies of these documents to address questions about ethics approval and study conduct.

The methods must be described in sufficient detail to allow the investigation to be interpreted, and repeated if necessary, by the reader. Previously documented standard methods need not be stated in detail, but appropriate reference to the original should be cited. However, any modification of previously published methods should be described and reference given. Where the programme of research is complex such as might occur in a neurological study in animals, it may be preferable to provide a table or figure to illustrate the plan of the experiment, thus avoiding a lengthy explanation. In longitudinal studies (case-control and cohort) exposure and outcome should be defined in measurable terms. Any variables, used in the study, which do not have universal definition should be operationalised (described in such terms so that it lends itself to uniform measurement). Where measurements are made, an indication of the error of the method in the hands of the author should be given. The name of the manufacturer of instruments used for measurement should be given with an appropriate catalogue number or instrument identification (e.g. Keyence VHX-6000 digital microscope). The manufacturer's town and country must be provided, in the case of solutions for laboratory use, the methods of preparation and precise concentration should be stated.

**Single case reports:**
Single case reports of outstanding interest or clinical relevance, short technical notes and brief investigative studies are welcomed. However, length must not exceed 1500 words including an unstructured abstract of less than 200 words. The number of figures/tables must not be more than 4 and references more than 25.

**Animal studies:**
In the case of animal studies, it is the responsibility of the author to satisfy the board that no unnecessary suffering has been inflicted on the animal concerned. Therefore, studies that involve the use of animals must clearly indicate that ethical approval was obtained and state the Home Office License number or local equivalent.

**Drugs:**
When a drug is first mentioned, it should be given by the international non-proprietary name, followed by the chemical formula in parentheses if the structure is not-well known, and, if relevant, by the proprietary name with an initial capital letter. Dose and duration of the drug should be mentioned in sufficient details. If the drug is already in use (licensed by appropriate licensing authority), generic name of the drugs should preferably be used followed by proprietary name in brackets.

Present the result in sequence in the text, table and figures. Do not repeat all the data in the tables and/or figures in the text. Summarize the salient points. Mention the statistics used for statistical analysis as footnote under the tables or figures. Figures should be professionally drawn. Illustration can be photographed (Black and White glossy prints) and numbered.

**Discussion:**
Comments on the observation of the study and the conclusion derived from it. Do not repeat the data in detail, already given in the results. Give implications of the findings, their strengths and limitations in comparison to other relevant studies. Avoid un-qualified statements and conclusions which are not supported by the data. Avoid claiming priority. New hypothesis or implications of the study may be labeled as recommendations.

Letters are welcome. They should be typed double-spaced on side of the paper in duplicate.

**References:**
References should be written in Vancouver style, numbered with arabic numerals in the order they appear in the text. The reference list should include all information, except for references with more than six authors, in which case give the first six names followed by et al.

**Examples of correct forms of references:**
Dorababu M, Prabha T, Priyambada S, Agrawal VK, Aryaa NC, Goel RK. Effect of Azadirachta indica on gastric ulceration and healing of bacopa monnierang in experimental NIDDM rats. *Indian J Exp. Biol 2004; 42: 389-397.*

**Chapter in a book:**
Hull CJ. Opioid infusions for the management of postoperative pain. In: Smith G, Covino BG, eds. Acute Pain. London: Butterworths. 1985,1 55-79.

All manuscripts for publication should be addressed to the executive editor.

**LETTER TO THE EDITOR:**
Any reader can provide feedback regarding published articles by writing letter to editor. The reader can also share any opinion in relation to medical science.

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**Professor M.A. Azhar**
Editor-in-chief
Green Life Medical College Journal and
Principal
Green Life Medical College

# ABOUT THE COLLEGE

## INTRODUCTION

In 2005, about fifty distinguished physicians of the country started a hospital to give specialized care in the private sector. They named it Green Life Hospital and it turned out to be a great success. So in 2009, they decided to establish a medical college which will be a non-government, non-profit, self-financing project and will serve the humanity.

This College came into existence in 2009. The college commences its activities with the enrollment of 51 students in the 1st batch in 2010. Since inception, the college has undergone tremendous development and became a splendid centre for learning and development. At present we are enrolling 110 students each year. Among them, numbers of seats are reserved for overseas students.

We continue to evaluate and improve our programme to ensure the best medical education for the students. Our educational strategy is to create a conducive learning environment and to steer our students to acquire adequate knowledge, skills and temperament to practice medicine and be a competent health care professional group.

Green Life Medical College (GMC) is approved by the Ministry of Health and Family Welfare (MOHFW), Government of Bangladesh and Bangladesh Medical and Dental Council (BMDC) and affiliated to the University of Dhaka.

## AIMS AND OBJECTIVES OF THE COLLEGE

**Aims:**

To create a diverse and vibrant graduate scholars in medical discipline and to create highly competent and committed physicians for the country.

**Objectives:**

- To provide an appropriate learning environment where medical students can acquire a sound theoretical knowledge and practical skills with empathetic attitude to the people.
- To carry out research in medical sciences to scale up the standard of medical education in the country.

## LOCATION

The campus is located at 31 and 31/1, Bir Uttom K. M. Shafiullah Sarak (Green Road), Dhanmondi, Dhaka. The location is at the heart of the mega city Dhaka and is facilitated with very good communication networks.

The Medical College and the Hospital complexes have been raised in a multistoried fully air-conditioned building with an arrangement of approximately 500 patients. The building is equipped with state-of-the-art infrastructure, excellent with an out-patient department and adequate in-patient facilities.

## *EDITORIAL*

# Substance abuse

Substance abuse refers to the harmful or hazardous use of psychoactive substances, including alcohol and illicit drugs. Psychoactive substance use can lead to dependence syndrome - a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the drug.[1]

Substance abuse, also known as drug abuse, is a patterned use of a drug in which the user consumes the substance in amounts or with methods which are harmful to themselves or others, and is a form of substance-related disorder.

In addition, substance abuse can simply be defined as a pattern of harmful use of any substance for mood-altering purposes.[2]

Substance abuse prompts chemical alterations in the brain that affect memory, behavior and the perception of pleasure and pain. Conscious decisions turn into compulsive actions, and major health, financial and social consequences often follow.[3]

Health effects of most substance abuse will cause strain on the organs, as well as the venous and respiratory system after prolong use. The physical effects of substance abuse include organ damage, hormone imbalance, cancer, prenatal and fertility issues, gastrointestinal disease and HIV/AIDS. Also, the neurological and emotional effects of substance use include depression, anxiety, memory loss, aggression, mood swings, paranoia and psychosis. In addition, lung, kidney and heart diseases are common among the drug addicts who smokes drugs (amphetamine), tobacco and marijuana. Injection of drugs also leads to infectious, transmission of diseases like HIV / AIDS and hepatitis. Mental disorders and cancer are also common diseases to substance abusers. In extreme cases, drug abuse leads to death.

Economically, a lot of money and time is driven out in solving health problem and adverse social effects related to drug abuse. Substance abuse is also highly associated with criminal activities and violence that poses a significant security threat to the society.

An article written by Kamrul Hassan published in the Dhaka Tribune stated that according to the Association for the Prevention of Drug Abuse (Manas), in Bangladesh, the number of drug addicts is around 6,600,000, while according to the Department of Narcotics Control (DNC) reports the number is around 5,000,000. But according to the National Institute of Mental Health (NIMH) report published in the year of 2017, more than 7,000,000 people suffers from drug addiction. Also, according to report of the Department of Narcotics Control (DNC), in Bangladesh, in 2013, the addicts were buying drugs by paying 600 crore per month which is a big amount of money.[4]

Therefore, the country needs to address the problem of substance abuse seriously to safe the people specially the young generation from the ill effects of substance abuse and economic loss of the country. Accordingly, the concerned authority of the government of Bangladesh has taken action against the peddler, seller and consumers of drugs. The approach of managing of substance abuse should be medically supervised and alcohol detox program. Every education institutes from primary to university level in Bangladesh, must involve in the drug abuse awareness program, where students and faculty members of the institutes should take active part in the all-out activities to obtain information among themselves and disseminate the ill effect of substance abuse on individual health and economy loss of individual as well a country. Also, a network among the organizations both public and private who are working on management and rehabilitation of the substance abusers.

In addition, a topic on substance use, abuse, dependence or addition, its ill effect on health should be in the undergraduate medical education curriculum and the method of teaching learning and assessment should be integrated vertically.

In conclusion, a coordinated approach should be taken to create awareness and educating the people on the dangers and consequences of substance abuse. Also, need to engage the young people in sports, arts and cultural recreational activities and ensuring the productive and constructive use of leisure time. There should be a program for enabling the parents and families to recognize the early warning signs in relation to substance abuse in the electronic and the print media. Moreover, the communities

should be empowered to understand and proactive in dealing with the challenges of the substance abuse, and its link with crime, HIV/AIDS and other conditions. As substance abuse or drug addiction is a significant health and social problem so that should be looked into and resolved before it gets out of hand.

***Journal of Green Life Med. Col. 2018; 3(2): 61-62***

**Prof. Dr. Ashraf Uddin Ahmed**
Executive Editor, Green Life Medical College Journal
Head, Department of Community Medicine
Chairperson, Medical Education Unit (MEU) and
Medical Skill Center (MSC), Green Life Medical College.

## References

1. Substance abuse - World Health Organization. Available from: www.who.int/topics/substance_abuse/en/ Cited 2018, April, 14.
2. By Buddy T | Reviewed by Richard N. Fogoros, MD , An Overview of Substance Use. Available from: https://www.verywellmind.com/substance-use-4014640 https://en.wikipedia.org/wiki/Substance_abuse Cited 2018, February,
3. Consequences Addiction – Summit behavioral Health. Available from: www.summitbehavioralhealth.com/resources/articles/consequences-of-addiction/Cited 2018, May, 10.
4. Kamrul Hassan, Is it time to decriminalize drug use in Bangladesh? Available from: www.dhakatribune.com/ Cited 2018, June, 14.

## ORIGINAL ARTICLE

# Protective Effect of Peanut (Arachis Hypogaea L.) and Its Combination with Propranolol on Serum Troponin-I, LDL & HDL levels in Isoproterenol Induced Cardiotoxic Rats

NAZ F[1], JAHAN N[2], SULTANA N[3], AKTER F[4]

**Abstract**

***Introduction:*** *Cardiotoxicity (CT) can be developed due to prolonged use of higher doses of some drugs, exposure to some chemicals, toxins or infectious agents and also by some disease conditions. Natural plant foods such as peanut (Arachis hypogaea L.) may have free radical scavenging and lipid lowering activity, thereby can be used for the prevention and management of heart disease. To observe the protective effect of peanut (Arachis hypogaea L.) and its combined action with propranolol on serum troponin-I, LDL and HDL levels in isoproterenol induced cardiotoxic rats.*

***Methods:*** *This experimental study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka in 2012. For this purpose, 20 Wistar albino rats, age 85- 100 days, weighing 120 to 150g (initial body weight) were included in the peanut treated group. They were sub-divided into CT-ISO-P (Cardiotoxic group with isoproterenol after peanut treatment) and CT-ISO-C (Cardiotoxic group with isoproterenol after combined treatment of peanut and propranolol). Age and weight matched 30 Wistar albino rats without any peanut supplementation were taken and sub-divided into three sub-groups, BC (Baseline control), CT-ISO (Cardiotoxic group with isoproterenol) and CT-ISO-PRO (Cardiotoxic group with isoproterenol after propranolol treatment). Each sub-group consisted of 10 rats. After taking final body weight all the rats were sacrificed on 22$^{nd}$ day. Blood was collected from heart & supernatant serum was preserved in deep freeze until analysis. For assessment of cardiac enzyme status, serum troponin-I was estimated by using immunoassay method and for assessment of lipid status serum LDL and HDL were estimated by using standard method. The statistical analysis was done by one way ANOVA and Bonferroni test as applicable.*

***Results:*** *In this study, percent change from initial body weight to final body weight was significantly ($p<0.01$) lower both in CT-ISO-P and CT-ISO-C as compared to that of BC. Again, the mean serum troponin-I was significantly ($p<0.01$) higher in CT-ISO, CT-ISO-PRO, CT-ISO-P, CT-ISO-C in comparison to that of BC. Moreover, this level was significantly ($p<0.05$) lower in CT-ISO-PRO, CT-ISO-C in comparison to CT-ISO. Furthermore, serum LDL level was significantly ($p<0.05$) higher and HDL level was significantly ($p<0.05$) lower in CT-ISO in comparison to BC. Again, serum LDL level was significantly ($p<0.05$) lower in CT-ISO-P, CT-ISO-C in comparison to CT-ISO. Moreover, serum HDL was significantly ($p<0.01$) higher in CT-ISO-C in comparison to CT-ISO and CT-ISO-P.*

***Conclusion:*** *The present study revealed that peanut can restored serum troponin-I, LDL and HDL towards normal level in isoproterenol induced cardiotoxic rats. However, the combined therapy of peanut and propranolol showed synergistic effect on lowering serum troponin-I and LDL levels where as elevating serum HDL level.*

***Key words:*** *Peanut, Propranolol, Isoproterenol, Cardiac enzyme, Blood lipid.*

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1. Dr. Farah Naz, Associate Professor, Department of Physiology, Green Life Medical College, Dhaka.
2. Dr. Nasim Jahan, Professor & Head, Department of Physiology, Enam medical college, Shavar, Dhaka.
3. Dr. Nayma Sultana, Professor & Head, Department of Physiology, Sir Salimullah Medical College, Mitford, Dhaka.
4. Dr. Fatema Akter, Assistant Professor, Department of Physiology, Medical College for Women & Hospital. Uttara, Dhaka.

**Address of Correspondence**: Farah Naz, Associate Professor, Department of Physiology, Green Life Medical College, Dhaka. Email: nazf188@gmail.com.

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**Introduction:**

Cardiotoxicity (CT) is the electrophysiological dysfunction of heart and myocardial damage.[1] It may be caused by chemotherapy treatment with cytotoxic drugs such as doxorubicin, epirubicin, cisplatin etc., adverse effects of heavy metals intake like lead, cadmium etc, and an incorrectly administered drug such as high dose of isoproterenol and also by some cardiotoxins.[2]

Isoproterenol (ISO) is a sympathomimetic non-selective β-adrenergic receptor agonist used to produce myocardial

injury in experimental animals for evaluation of various cardioprotective agents.[3] High dose of isoproterenol causes severe oxidative stress in the myocardium resulting in infarction, it also generate free radicals and stimulate lipid peroxidation.[4] Thus elevates different cardiac biomarker enzyme levels in serum like troponin-I, creatine phosphokinase-MB & lactate dehydrogenase due to cell necrosis.[5] Loss of myocardial integrity, widespread cell necrosis were observed by some investigators after using high dose of isoproterenol in their study.[6]

However, propranolol (PRO) is a non-selective â-blocker used in patients with hypertension, ischemic heart disease, cardiac arrhythmias and other cardiovascular diseases.[7] But long term use of propranolol may produce dyslipidemia, bradycardia, insomnia, light-headedness etc.[8]

Arachis hypogaea L. known as peanut belongs to the family of fabaceae have been valued for their high nutritional content throughout the world for many years.[9] Peanuts are energy dense foods that are particularly rich in fat, mostly unsaturated fatty acids and this unsaturated fatty acid of nuts through its lipid lowering effect may be responsible for their protective effects against ischemic heart disease.[10] Peanuts are also a rich source of vitamin-B, vitamin-E, magnesium, copper, phosphorus, plant protein, arginine, dietary fiber and numerous bioactive substances like flavonoids, resveratrol and plant sterols.[11] Peanut consumption is relatively safe but approximately 1% in the general population showed nut allergy.[12]

Some researchers observed that consuming about an ounce of peanuts every day can reduce the risk of heart diseases by up to half.[13] Moreover, some other researchers found that consumption of peanut 5 times per week (about 155g of nuts/week) reduced the risk of death from coronary heart diseases by 35%.[14] Recently in an experimental study some researchers observed significant improvement in the serum troponin-I level in rats treated with isoproterenol.[15] Some other researchers observed that peanut oil significantly reduces LDL-cholesterol level[16] and also improved HDL-cholesterol level[17].

Therefore, the present study has been designed to observe the protective effect of peanut (Arachis hypogaea L.) and its combination with propranolol on serum troponin-I, LDL and HDL levels in isoproterenol induced cardiotoxic rats.

**Methods:**

This experimental study was conducted in the Department of Physiology, Sir Salimullah Medical College (SSMC), Mitford, Dhaka from January to December 2012. The protocol of this study was approved by Institutional Ethics Committee (IEC) of SSMC. Twenty Wistar albino rats, age 85-100 days, weighing 120 to 150g (initial body weight) were included in the experimental group (with peanut). They were sub-divided into CT-ISO-P (Cardiotoxic group with isoproterenol after peanut treatment) and CT-ISO-C (Cardiotoxic group with isoproterenol after combined treatment of peanut and propranolol). Age and weight matched 30 Wistar albino rats without any peanut supplementation was taken as control and sub-divided into three sub-group, BC (baseline control), CT-ISO (Cardiotoxic group with isoproterenol) and CT-ISO-PRO (Cardiotoxic group with isoproterenol after propranolol treatment). Each subgroup consisted of 10 Wistar albino rats. Before grouping all the animals were acclimatized for 14 days under 12 hour dark and light cycle. During this study they had free access to food and water *ad libitum*. Each group consisted of 10 rats and was given basal diet for 21 consecutive days. In addition to this, animals of CT-ISO-PRO were given propranolol (10mg/kg body weight; orally) for last seven (from 15$^{th}$ to 21$^{st}$ day of study period) consecutive days, animals of CT-ISO-P were given peanut extract (500mg/kg body weight; orally) for 21 consecutive days (started from 1$^{st}$ day of study period), animals of CT-ISO-C were given both peanut extract (500mg/kg body weight; orally) for 21 consecutive days (started from 1$^{st}$ day of study period) and propranolol (10mg/kg body weight; orally) for last seven (from 15$^{th}$ to 21$^{st}$ day of study period) consecutive days. All the groups of animals except baseline control group were given isoproterenol subcutaneously (150mg/kg body weight/day) for last two (at 20$^{th}$ & 21$^{st}$ day of study period) consecutive days. After acclimatization and before giving any supplementation, body weights of all the rats were measured (initial bw). After giving isoproterenol, propranolol and peanut all the animals including the baseline control rats, were anaesthetized with the help of chloroform (30%) and sacrificed on 22$^{nd}$ day. Before anaesthetized the rats on 22$^{nd}$ day again body weights of rats (final bw) were taken. Then their blood sample was collected from the heart and supernatant serum was preserved in deep freeze until analysis. For the assessment of myocardial status serum tropinin-I was measured by using immunoassay method[18] in the department of biochemistry, BSMMU. To find out the blood lipid status serum LDL-cholesterol and HDL-cholesterol were measured by standard method[19] in department of physiology SSMC. Statistical analysis were done by one way ANOVA and Bonferroni test by using SPSS windows, version 16.

**Results:**

The percent change of body weight from final to initial was significantly ($p<0.01$) lower both in CT-ISO-P and in CT-ISO-C as compared to that of baseline control (Table I).

Again, the mean serum troponin-I was significantly ($p<0.01$) higher in CT-ISO, CT-ISO-PRO, CT-ISO-P, CT-ISO-C in comparison to that of BC. Moreover, this level was significantly ($p<0.05$) lower in CT-ISO-PRO, CT-ISO-C in comparison to CT-ISO. Furthermore, serum LDL level was significantly ($p<0.05$) higher and HDL level was significantly ($p<0.05$) lower in CT-ISO in comparison to BC. Again, serum LDL level was significantly ($p<0.05$) lower in CT-ISO-P, CT-ISO-C in comparison to CT-ISO. Moreover, serum HDL was significantly ($p<0.01$) higher in CT-ISO-C in comparison to CT-ISO and CT-ISO-P (Table II).

**Table I**

*Body weight in different groups of rats (n=50)*

| Parameters | Without peanut | | | With peanut | Combined |
|---|---|---|---|---|---|
| | BC | CT- ISO | CT- ISO-PRO | CT- ISO-P | CT-ISO-C |
| Initial body wt (g)(Day 1) | 128.89±6.01 | 132.78±10.93 | 134.33±10.03 | 135.73±5.35 | 134.44±8.08 |
| Final body wt (g)(Day 22) | 137.11±6.43 | 147.83±11.06*** | 152.02±10.33** | 142.63±5.45*+ | 135.78±7.63•++o |
| % of change from final (F) to initial (I) body wt[(F-I)/Ix100] | 6.39±1.67 | 6.73±1.08 | 6.06±0.93 | -1.64±1.07^— | -3.24±4.46^^”- |

Values are means ±SD. Statistical analysis was done by ANOVA test and then Bonferroni test. For final body wt (***$p<0.01$, **$p<0.01$ & *$p<0.05$ BC vs CT-ISO, CT-ISO-PRO & CT-ISO-P) (•$p<0.01$ CT-ISO vs CT-ISO-C) ($^{+}p<0.05$ & $^{++}p<0.01$ CT-ISO-PRO vs CT-ISO-P & CT-ISO-C) ($^{o}p<0.01$ CT-ISO-P vs CT-ISO-C). For % change of body wt (^$p<0.01$ & ^^$p<0.01$ BC vs CT-ISO-P & CT-ISO-C) ($^{“}p<0.01$ CT-ISO vs CT-ISO-C) ($^{-}$ $^{-}p<0.01$ & $^{-}p<0.01$ CT-ISO-PRO vs CT-ISO-P & CT-ISO-C). BC = Baseline control CT-ISO = Cardiotoxic group with isoproterenol CT-ISO-PRO = Cardiotoxic group with isoproterenol after propranolol treatment CT-ISO-P = Cardiotoxic group with isoproterenol after peanut treatment CT-ISO-C = Cardiotoxic group with isoproterenol after combined treatment of peanut and propranolol.

**Table II**

*Serum troponin-I, LDL and HDL levels in different groups of rats (n=50)*

| Parameters | Without peanut | | | With peanut | Combined |
|---|---|---|---|---|---|
| | BC | CT-ISO | CT-ISO-PRO | CT-ISO-P | CT-ISO-C |
| Serum troponin-I (ng/ml) | 1.63±0.20 (1.39-1.89) | 5.69±1.69 (3.41-8.59)* | 4.77±1.48 (2.95-7.23)*^ | 5.04±1.59 (3.26-8.29)* | 4.16±1.15 (2.54-6.35)*^ |
| Serum LDL(mg/dl) | 113.11±36.40 (63-189) | 130.22±32.60 (85-198)$^{o}$ | 109.55±32.28 (70-176) | 87.75±29.37 (58-152)+ | 89.67±26.30 (52-127)+ |
| Serum HDL(mg/dl) | 49.67±4.55 (43-58) | 40.33±8.22 (25-52)$^{o}$ | 45.44±5.81 (33-55) | 50.88±3.44 (45-55) | 58.56±4.61 (54-69)$^{oo}$++# |

Statistical analysis was done by ANOVA test & then Bonferroni test was performed to compare between groups. Figures in parenthesis indicate ranges. For serum troponin-I level (*$p<0.01$ BC vs CT-ISO, CT-ISO-PRO, CT-ISO-P & CT-ISO-C) (^$p<0.05$ CT-ISO vs CT-ISO-PRO & CT-ISO-C). For blood lipid LDL, HDL levels ($^{o}p<0.05$ & $^{oo}p<0.01$ BC vs CT-ISO & CT-ISO-C) (+$p<0.05$ & ++$p<0.01$ CT-ISO vs CT-ISO-P, CT-ISO-C) (#$p<0.01$ CT-ISO-P vs CT-ISO-C). BC = Baseline control CT-ISO = Cardiotoxic group with isoproterenol CT-ISO-PRO = Cardiotoxic group with isoproterenol after propranolol treatmen CT-ISO-P = Cardiotoxic group with isoproterenol after peanut treatment CT-ISO-C = Cardiotoxic group with isoproterenol after combined treatment of peanut and propranolol.

**Discussion:**

In the present study, the percent changes of body weight were almost similar to the findings reported by the various investigators from different countries.[20]

Again, in this study serum troponin-I was significantly higher in CT-ISO (Cardiotoxic group with isoproterenol), CT-ISO-PRO (Cardiotoxic group with isoproterenol after propranolol treatment), CT-ISO-P (Cardiotoxic group with isoproterenol after peanut treatment) and CT-ISO-C (Cardiotoxic group with isoproterenol after combined treatment of peanut and propranolol) in comparison to BC (Baseline control group). Moreover, this level was significantly lower in CT-ISO-PRO (Cardiotoxic group with isoproterenol after propranolol treatment) and CT-ISO-C (Cardiotoxic group with isoproterenol after combined treatment of peanut and propranolol) in comparison to that of CT-ISO (Cardiotoxic group with isoproterenol). Furthermore, serum LDL level was significantly higher and HDL level was significantly lower in CT-ISO (Cardiotoxic group with isoproterenol) in comparison to that of BC (Baseline control group). Whereas serum LDL level was significantly lower in CT-ISO-P (Cardiotoxic group with isoproterenol after peanut treatment) and CT-ISO-C (Cardiotoxic group with isoproterenol after combined treatment of peanut and propranolol) in comparison to CT-ISO (Cardiotoxic group with isoproterenol). On the other hand serum HDL level was significantly higher in CT-ISO-C (Cardiotoxic group with isoproterenol after combined treatment of peanut and propranolol) in comparison to CT-ISO (Cardiotoxic group with isoproterenol) and CT-ISO-P (Cardiotoxic group with isoproterenol after peanut treatment). Almost similar findings were also observed by different researchers by using different nuts & herbal plants.[20,21] On the contrary, some researchers observed that low dose of Tylophora indica herbal plant leaves failed to show any cardiac enzyme lowering effect.[22] Some investigators also observed reduced level of serum HDL after walnut consumption.[23]

It has been postulated that, administration of high dose of isoproterenol subcutaneously induced marked inflammatory changes in the myocardium and visible ischemic lesion[24]. However, rats that received isoproterenol at the dose of 150mg/kg body weight showed diffuse myocardial necrosis and leakage of myocardial enzymes[20].

Also, high dose of isoproterenol causes lipid peroxidation of myocardial membrane through production of cytotoxic free radicals[4]. Isoproterenol also enhanced lipid biosynthesis in the myocardium by cardiac cAMP formation, which in turn leads to myocardial necrosis,[20] mobilizes lipids from adipose tissue resulting in hypercholesterolemia.[21] Some investigators reported that isoproterenol produces a number of biochemical and electrophysiological disturbances in the heart tissue[5]. Again, high dose of isoproterenol causes degeneration and necrosis of myocardial fibers due to increased production of free radicals.[22,24]

In addition, some investigator suggested that propranolol causes dephosphorylation of myosin light chain kinase thereby decreases generation of oxygen free radicals[24] but long term use of propranolol causes a significant decrease in HDL level and increase in LDL level due to the lipoprotein lipase inhibitory activity and lecithin-cholesterol acyl transferase (LCAT) lowering activity of propranolol.[25]

Furthermore, some other investigators observed that resveratrol, a poly-phenol phytoalexin present in peanut provide protection to myocardium via antioxidant activity.[26] Again, some investigators observed that peanut consumption significantly improve the antioxidant-oxidant status by increasing glutathione peroxidase (GSH) and decreasing thiobarbituric acid reactive substance (TBARS) levels.[23] High level of L-arginin and vitamine E content of peanut also have antioxidant activity and scavange oxygen free radicals thereby preserve normal levels of myocardial enzymes.[15,24] However, Oleic acid which is the predominant mono-unsaturated fatty acid in peanut prevents LDL oxidation and reduces risk of cardiovascular disease[27]. The flavonoids and phytosterols of peanut show cardioprotective effect by lowering blood cholesterol levels.[28]

In the present study, cardiotoxicity and dyslipidemia was observed in rats treated with isoproterenol as evidenced by elevated levels of serum troponin-I, LDL and lower level of serum HDL.

Moreover, lower levels of serum troponin-I, LDL and higher level of serum HDL were observed in CT-ISO-P (Cardiotoxic group with isoproterenol after peanut treatment) and CT-ISO-C (Cardiotoxic group with isoproterenol after combined treatment of peanut and propranolol) of the present study suggested the cardioprotective role of peanut against isoproterenol induced cardiotoxicity. Moreover, in this study combined therapy of peanut and propranolol showed synergistic cardioprotective effect than when they were used alone. These effects are most likely due to mono-unsaturated fatty acid content, anti-oxidant and free radical scavenging activity of peanut and

propranolol. However, the exact mechanism involved in the cardioprotective activity of peanut against isoproterenol induced cardiotoxicity in rats cannot be find out from this type of study.

**Conclusion:**

From this study, it can be concluded that peanut can lower serum troponin-I, LDL levels and increasing HDL levels due to its inhibition of generating and free radicals scavenging activity. However, combined therapy of peanut with propranolol showed synergistic effect on preventing cardiotoxicity by reducing free radical induced myocardial damage. It is also expected that the result of this study would make peanut acceptable among the people as a rich source of nutrients with medicinal value for the prevention of coronary heart diseases.

**References:**

1. Huang C, Zhang X, Ramil JM, Rikka S, Kim L, Lee Y, Gude NA, Thistlethwaite PM. Juvenile exposure to anthracyclines impairs cardiac progenitor cell function and vascularization resulting in greater susceptibility to stress induced myocardial injury in adult mice. Circulation 2010; 121(5): 675-683.
2. Schimmel K, Richel D, Brink RVD, Guchelaar HJ. Cardiotoxicity of cytotoxic drugs. Cancer Treatment Review 2004; 30: 181-191.
3. Sushma KS, Jaydeep A, Kumar JSS. Effect of carnitine on malondialdehyde, taurine and glutathione levels in heart of rats subjected to myocardial stress by isoproterenol. Ind J Exp Biol 1989; 27: 134-137.
4. Senthilkumar H, Anandan R, Devaki T, Santhoshkumar M. Cardioprotective effects of Picrorrhiza kurrora against isoproterenol induced myocardial stress in rats. Fitoterapia 2001; 72: 402-405.
5. Sasikumar SC, Devi SCS. Protective effect of Abana. A polyherbal formulation on isoproterenol induced myocardial infarction in rats. Indian Journal Pharmacol 2000; 32:198-201.
6. Sing PN, Athar MS. Simplified calculation of mean QRS vector (mean electrical axis of heart) of electrocardiogram. Indian Journal Physiol Pharmacol 2003; 47:212.
7. Asdaq SMB, Inamdar MN. Pharmacodynamic and pharmacokinetic interactions of propranolol with Garlic (Allium sativum) in rats. Evidence Based Complementary and Alternative Medicine 2011; Article ID. 824042: 11.
8. Hoffman BB. Adrenoceptor antagonist drugs in Katzung BG. Basic and Clinical Pharmacology. 8th ed. The McGraw Hill Companiesz: Amarica 2001; 138-152.
9. Higgs J. The beneficial role of peanuts in the diet-part 2. Nutrition & Food Science 2003; 33(2): 56-64.
10. Sabate J. Does nut consumption protect against ischemic heart disease?. European Journal of Clinical Nutrition 1993; 47(1): S71-S75.
11. Griel AE, Eissenstat B, Juturu V, Hsieh G, Kris-Etherton PM. Improved diet quality with peanut consumption. J Am Coll Nutr 2004; 23(6): 660-668.
12. Crespo JF, James JM, Fernandez-Rodriguez C, Rodriguez J. Food allergy: nuts and tree nuts. Br J Nutr 2006; 96: 95-102.
13. Fraser GE, Sabate J, Beeson WL, Strahan TM. A possible protective effect of nut consumption on risk of CHD. Archives of Internal Medicine 1992; 152: 1416-1424.
14. Hu FB, Stampfer MJ, Manson JE, Rimm EB, Colditz GA, Rosner BA, Speizer FE, Hennekens CH, Willett WC. Frequent nut consumption and risk of coronary heart disease in women: prospective cohort study. British Medical Journal 1998; 317: 1341-1345.
15. Manodeep C, Mohammed Basheeruddin AS, Suresh N, Kumar RR. The potential of interaction of hydro alcoholic extract of Semecarpus anacardium nut with propranolol in ischemia reperfusion induced myocardial damage using isolated rat heart. International Research Journal of Pharmacy 2010;1(1):161-170.
16. Sales RL, Coelho SB, Costa NMB, Bressan J, Iyer S, Boateng LA, Lokko P, Mattes RD. The effects of peanut oil on lipid profile of normolipidemic adults:a three country collaborative study. The Journal of Applied Research 2008; 8(3):216-225.
17. Asdaq SMB, Sowmya SK. Effect of hydroalcoholic extracts of Tylophora indica leaves in isoprenaline induced myocardial damage in rat heart. IJPT 2010; 9(1): 15-20.
18. Panteghini M. Role and importance of biochemical markers in clinical cardiology. European Heart Journal 2004; 25:1187-1196.
19. Ajitha M, Rajnaryana K. Role of oxygen free radicals in human disease. Indian Drugs 2001; 38: 545.
20. Chakraborty M, Asdaq SMB. Interaction of Semecarpus anacardium L. with propranolol against isoproterenol induced myocardial damage in rats. Indian Journal of Experimental Biology 2011; 49: 200-206.
21. Upaganlawar A, Gandhi H, Balaraman R. Isoproterenol induced myocardial infarction: protective role of natural products. Journal of Pharmacology and Toxicology 2011; 6(1): 1-17.
22. Wolter F, Akoglu B, Clausnitzer A, Stein J. Downregulation of the cyclin D1/Cdk4 complex occurs during resveratrol induced cell cycle arrest in colon cancer cell lines. J Nutr 2001; 131: 2197-2203.
23. Emekli-Alturfan E, Kasikci E, Yarat A. Peanuts improve blood glutathione, HDL-cholesterol level and change tissue factor activity in rats fed a high cholesterol diet. Eur J Nutr 2007; 46: 476-482.
24. Teerlink JR, Pfeffer JM, Pfeffer MA. Progressive ventricular remodeling in response to diffuse isoproterenol induced myocardial necrosis in rats. Circ Res 1994; 75: 105-113.
25. Metcalfe J, Simpson CN. Adrenergic mechanisms in control of plasma lipid concentrations. British Medical Journal 1982; 284: 1145-1148.
26. Ellsworth JL, Kushi LH, Folsom AR. Frequent nut intake and risk of death from coronary heart disease and all causes in postmenopausal women: the lowa women's health study. Nutr Metab Cardiovasc Dis 2001; 11: 372-377.
27. Kris-Etharton PM, Hu FB, Ros E. The role of tree nuts and peanuts in the prevention of coronary heart disease: Multiple potential mechanisms. J Nutr 2008; 138: S1746-S1751.
28. Awad AB, Chan KC, Downie A, Fink CS. Peanuts as a source of beta-sitosterol, a sterol with anticancer properties. Nutrition and Cancer 2000; 32: 2: 238-241.

## ORIGINAL ARTICLE

# Bordetella Infection In Children And Adults Having Cough For More Than Two Weeks

YESMIN K [1], ALAM MS[2], SARKER M[3], FARAH S[4]

*Abstracts*

***Introduction:*** **B. pertussis** ***and*** **B. parapertussis** ***cause whooping cough in human which is one of the major health problems in the world and transmitted person to person by close contact with aerosolized droplets. Pertussis is still a major infection worldwide and one of the important cause of death in malnourished children. Adults with waning vaccine-induced immunity are and also increasingly suffering from pertussis.***

***Methods: This cross sectional study was done from January 2009 to June 2010 in Microbiology department of Dhaka Medical College on Bordetella infection in children and adults having cough for more than two weeks. The nasopharyngeal swabs were collected from 290 patients for culture and 101 serum samples were tested by slide agglutination test to detect anti-*** **Bordetella** ***antibody.***

***Results: Culture of nasopharyngeal swabs revealed 1 (0.63%)*** **B. pertussis** ***and 5 (3.84%)*** **B. parapertussis** ***from a child and adults respectively. Among the study population, 31(30.70%) were positive and 70 (69.30%) were negative for antibody against*** **B. pertussis.** ***In anti-*** **Bordetella** ***antibody positive cases, 14 (93.33%) children had duration of cough for 2-3 weeks, 7 (43.75%) adults had duration of cough for 3-4 weeks and 1 (6.25%) adult had more than 6 weeks.***

***Conclusion: Pertussis is a common cause of persistent cough in adults and should be considered in differential diagnosis. The children presenting to primary health care center with a cough lasting for more than 2 weeks, a diagnosis of whooping cough should be considered.***

***Key words:*** **Bordetella** ***pertussis, cough, Charcoal blood agar media, anti-Bordetella antibody.***

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**Introduction:**

Cough is the most frequent symptom of respiratory infection and about 12% of the general population have chronic cough. Cough may be caused by several factors including infection by microorganisms. [1] *B. pertussis* and *B. parapertussis* cause whooping cough in human which is one of the major health problems in the world and transmitted person to person by close contact with aerosolized droplets. [2] Pertussis is still a major infection worldwide and one of the important cause of death in malnourished children. It has been estimated that over 5 million cases of pertussis occur each year worldwide and 0.6 million were reported deaths.[3] In majority cases, the disease is endemic, with epidemics occurring every 4 years in late winter and spring.[4] It is a widely held belief that pertussis is an exclusive childhood disease while in reality it may affects all age groups.[5]

Pertussis is one of the causes of persistent cough. Approximately 13-20% have cough in adolescents and adults due to *B. pertussis* infection.[2-3] Adults with waning vaccine-induced immunity are and also increasingly suffering from pertussis.[4] Recently, an increase in reported cases of *pertussis* in adolescents and adults has been noted in many countries despite high immunization rates in childhood period. The clinical presentation in adolescents, adults and vaccinated individuals may be atypical, with paroxysmal cough of short duration or

1. Dr. Kazi Yesmin, Associate Prof. Department of Microbiology, Green Life Medical College.
2. Dr. Md. Sahbub Alam, Assistant Prof. Department of ENT, Faridpur Medical College
3. Dr. Moushumi Sarker, Assistant Prof. Department of Microbiology, Mugda Medical College,
4. Dr. Shayela Farah, Associate Prof. Department of Community Medicine, Dhaka Community Medical College

**Address of Correspondence**: Dr. Kazi Yesmin, Department of Microbiology, Green Life Medical College, Dhanmondi, Dhaka-1205, E-mail: kaziyesmin@gmail.com.

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simply a persistent cough.[5-6] It has been suggested that up to 30% of adults with a prolonged cough may be due to pertussis.[7] The affected adolescents and adults act as reservoirs of the disease to the vulnerable population of infants.[8] Seroepidemiological studies suggest that pertussis is a common and frequently unrecognized infection in adults.[9-12]

**Methods:**

This cross sectional study included 290 patients of all age groups attending at Medicine and Pediatrics OPD of Dhaka Medical College Hospital and Dhaka Shishu Hospital with symptom of cough for more than two weeks. Data regarding age, sex, monthly income, level of education, DPT vaccination and duration of cough were collected by using a predesigned data collection sheet. Specimens of nasopharyngeal swab were collected and were inoculated immediately in different culture media. All the Charcoal blood agar media were incubated at $35^0$C in aerobic condition up to 7 days and adequate humidity was maintained by placing a flask of water on the floor of incubator and inspected regularly every morning. All organisms were identified by their colony morphology, staining characteristic, hemolysis on blood agar, pigment production, motility and other relevant biochemical tests as per standard methods. Isolated *B . pertussis* was confirmed by using specific anti- *B. pertussis* antiserum. Detection of Anti-*B. pertussis* IgG antibody in serum were made by slide agglutination test.

**Result:**

A total of 290 patients with history of cough for more than 2 weeks were selected for the study. The highest number of patients were 48 (16.55%) in the age group of 1-4 years followed by 45 (15.52%) in the age group of 5-9 years (Table I).

**Table I**

*Distribution of the study population by age (n =290)*

| Age group | No. of cases | Percentage |
|---|---|---|
| < 1 years | 37 | 12.75 |
| 1 – 4 years | 48 | 16.55 |
| 5 - 9 years | 45 | 15.52 |
| 10 - 18 years | 30 | 10.34 |
| 19 - 29 years | 40 | 13.79 |
| 30 - 39 years | 20 | 06.81 |
| 40 - 49 years | 27 | 09.33 |
| 50 - 59 years | 17 | 05.84 |
| ≥60 years | 26 | 09.06 |
| Total | 290 | 100.0 |

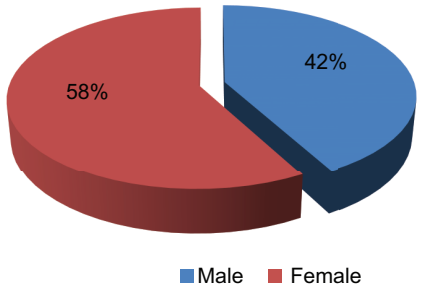


**Fig.-1:** *Distribution of the study population by sex*

Figure 1. shows the sex distribution of the study population. Among 290 patients, 122 (42%) were males and 168 (58%) were females with a male female ratio of 3:4.

**Table II**

*Duration of cough among the study population*

| Duration of cough | No. of cases | Percentage |
|---|---|---|
| 2 - 3 weeks | 158 | 54.50 |
| 3 - 4 weeks | 75 | 25.90 |
| 5 - 6 weeks | 21 | 7.20 |
| > 6 weeks | 36 | 12.40 |
| Total | 290 | 100.00 |

Table II shows the distribution of the study subjects by duration of cough. Among the study population, 158 (54.50%) had cough for 2-3 weeks, 75 (25.90%) had cough for 3-4 weeks, 21 (7.20%) had cough for 5 - 6 weeks and 36 (12.40%) had cough for more than 6 weeks.

**Table III**

*Distribution of study population in relation to history of DPT vaccination*

| History of vaccination | No. of cases | Percentage |
|---|---|---|
| Vaccinated | 183 | 63.10 |
| Non- vaccinated | 60 | 20.70 |
| Couldn't recall | 47 | 16.20 |
| Total | 290 | 100.00 |

Table III shows the distribution of the respondents by history of vaccination against pertussis. Among the study subjects 183 (63.10%) received vaccination, 60 (20.70%) didn't receive the vaccination and 47 (16.20%) couldn't recall about the history of vaccination.

**Table IV**

*Status of vaccination among 183 populations*

| Status of vaccination | No. of cases | Percentage |
|---|---|---|
| 1 dose | 15 | 08.20 |
| 2 doses | 18+2* | 10.90 |
| 3 doses | 148 | 80.90 |
| Total | 183 | 100.00 |

*2 cases did not complete vaccination schedule.

Table IV shows the vaccination status against pertussis (DPT) among the 183 population with history of vaccination, 148 (80.90%) had completed the full course of vaccination, 20 (10.90%) completed up to 2nd dose, 15 (8.02%) received only the 1st dose and 2 (1.09%) cases did not complete vaccination schedule.

Table V shows isolation of different organisms among children and adults. The most common isolated organism was *Neisseria* spp. among children (n=69; 43.12%) and *Staphylococcus* spp. among adults (n=43; 33.08%).

Table VI shows the distribution of study participants by serology result. Among the study participants, 31(30.70%) were positive and 70 (69.30%) were negative for antibody against *B. pertussis*.

Table VII shows duration of cough among anti-*Bordetella* antibody positive cases. Among study population, 14 (93.33%) children had duration of cough for 2-3 weeks, 7 (43.75%) adults had duration of cough for 3-4 weeks and 1 (6.25%) adults had more than 6 weeks.

**Table V**

*Rate of isolation of different organisms among children and adults*

| | Children | | | Adults | | |
|---|---|---|---|---|---|---|
| Growth | Single | Mixed | Total | Single | Mixed | Total |
| *B. pertussis* | 1 | 0 | 1(0.63) | 0 | 0 | 0 (0.00) |
| *B. parapertussis* | 0 | 0 | 0 (0.00) | 5 | 0 | 5 (3.84) |
| *Staph. aureus* | 5 | 4 | 9(5.62) | 16 | 0 | 16(12.31) |
| *S. pneumoniae* | 15 | 2 | 17(10.62) | 4 | 0 | 4(3.08) |
| *N. meningitidis* | 25 | 3 | 28(17.50) | 3 | 0 | 3(2.31) |
| *H. influenzae* | 1 | 0 | 1(0.63%) | 0 | 0 | 0 (0.0) |
| *Staphylococcus* (Coag -ve) | 12 | 10 | 22(13.75) | 26 | 1 | 27(20.77) |
| *Streptococcus* (others) | 24 | 6 | 30(18.75) | 14 | 0 | 14(10.77) |
| *Neisseria* (others) | 34 | 7 | 41(25.62) | 16 | 1 | 17(13.08) |

Figures in parentheses represent percentage

Note- *Streptococcus* (other) - Other than *S. pneumoniae* *Neisseria* (others) - Other than *N. meningitides*

**Table VI**

*Results of anti-Bordetella antibody test in children and adults (n=101)*

| | Children | Adults | Total |
|---|---|---|---|
| Serology positive | 15 (30) | 16 (31.38) | 31 (30.70) |
| Serology negative | 35 (70) | 35 (68.62) | 70 (69.30) |
| Total | 50 (100) | 51 (100) | 101(100) |

Figures in parentheses represent percentage

**Table VII**

*Duration of cough among anti-Bordetella antibody positive cases (n=101)*

| | 2-3 weeks | 3-4 weeks | 5-6 weeks | >6 weeks | Total |
|---|---|---|---|---|---|
| Children | 14 (93.33) | 1 (6.67) | 0 (0.00) | 0 (0.00) | 15 (100) |
| Adults | 5 (31.25) | 7 (43.75) | 3 (18.75) | 1 (6.25) | 16 (100) |

Figures in parentheses represent percentage Chi-square – 9.04, df 3, p = 0.023 (statistically significant)

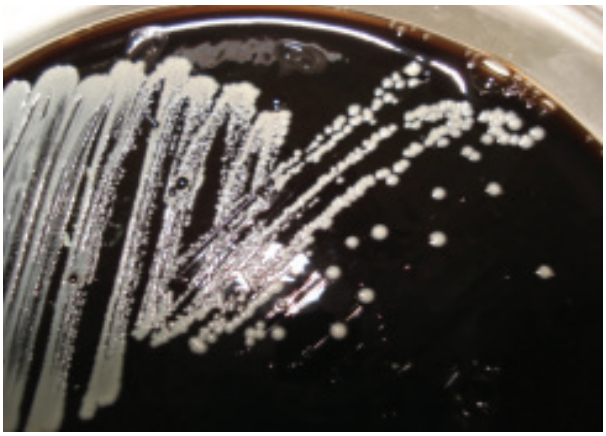

**Fig.-5:** *Pure culture of Bordetella spp. in the charcoal blood agar media.*

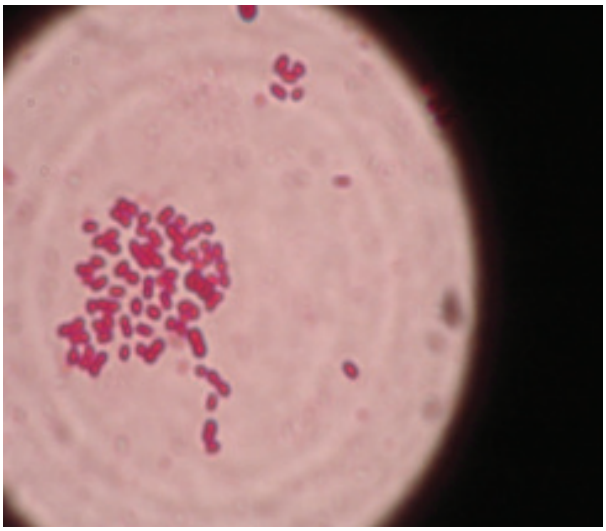

**Fig.-6:** *Gram stained smear showing Bordetella spp. from culture.*

**Discussion:**

In the present study *B. pertussis* was isolated from only one child suffering from protein energy malnutrition (PEM). The child had taken only two doses of DPT vaccine. Isolation of *B. pertussis* indicates that the organism exit in the community. In our study, *B. parapertussis* was isolated in 5 (3.84%) adults. Similar prevalence was observed by He *et al.* (1998) who reported that culture positivity of *B. parapertussis* was 3.4% in children and adults.[13]

In this study, *B. pertussis* was not isolated in culture in adults. However, 31.37% of adults were sero-positive. In United State, Wright *et al* (1995) demonstrated that no subject was culture positive for *B. pertussis*, but 21% subjects met the serological criteria for pertussis infection.[14] In a study carried out in United State reported that adults with cough illness of more than 2 weeks duration found a prevalence of 12.4%; however, only a single serum sample was tested detected IgG antibodies.[15] The laboratory diagnosis of pertussis in adults is difficult because of the usual delay in the clinical suspicion. [16]

Maximum adults (43.75%) with positive serology for IgG/IgM against *B. pertussis* had cough for 3-4 weeks and 14 (93.33%) seropositive children had duration of cough for 2-3 weeks (Table-XV). Cherry (1998) studied on prolonged cough illness in adolescents and adults and reported that between 12% to 32% were positive for *B. pertussis* infection.[17-19] A study in China on multicentral clinical investigations of pertussis in children and adolescents with persistent cough found that about 11.3% patient were B. pertussis positive who had cough for more than 2 weeks.[20]

To evaluate the pertussis infection in Canada among adolescents and adults who had cough related illness of 7- 56 days durations researchers found that 19.9% had either laboratory - confirmed pertussis or laboratory evidence of pertussis.[21] In both Canada and the United States, Guris *et al* reported the highest incidence of pertussis cases among infants and also found the rapid increase in incidence among adolescents and adults.[22] Pertussis has been shown to be an important cause of cough illness in college students, military recruits, referrals to pulmonary specialist and visitors to hospital emergency departments.[23-25] In India, about 9.52% patients were culture positive for *B. pertussis* and 14.28% patients were positive by direct fluorescence antibody test.[26]

There have been increasing reports of pertussis out breaks in adult's population in many western countries and vaccination of this group is being planned.[27] Like many other developing countries of the world, morbidity and mortality rate due to pertussis is likely to be high in South Asian countries such as Pakistan, India, Bangladesh and Sri Lanka as well as countries of African continent. [28-30] There is also a very high possibility of occurrence of adult's pertussis case in this region. Further, there is an overall lack of data related to laboratory confirmed cases of pertussis from these regions. The main reason behind this under reporting may be due to lack of adequate diagnostic facilities, poor surveillance systems and unawareness of the physicians to the incidence of the infections in adult population. Widespread use of DPT vaccination has resulted in a shift in the incidence of pertussis to adolescents and adults.[31] It has been estimated that almost 20- 50% of all persistent cough cases in adults are caused by the *B. pertussis*.[32-33] Adult pertussis is both a significant health problem as well as an economic burden in both developing as well as developed countries.[34]

In spite of good immunization coverage, the developed countries have shown a shift in the epidemiology of the disease to the adolescent and the adult age group, leading to a revision of their vaccination policies. The anticipation and early recognition of this change in the epidemiology is important because the affected adolescents and adults act as reservoirs of the disease to the vulnerable population of infants, for whom the disease can be life threatening.[35]

Previous research in several countries had shown that pertussis is endemic among the adolescents and adults. [11-12] It is suggested that a universal program of adolescent and adult boosters would decrease the propagation of *B. pertussis* in these age groups and possibly could lead to the elimination of the organism from the population. With the availability of vaccine, booster doses in adolescents have been introduced in Canada, Austria, Australia, France, Germany and the US, and many other countries are considering similar expansion of their immunization programs at present.

**Conclusion:**

Although the immunization rate of DPT is high, *B. pertussis* is still an important etiological factor associated with persistent cough; pertussis is a common cause of persistent cough in adults and should be considered in differential diagnosis. The children presenting to primary health care center with a cough lasting for more than 2 weeks, a diagnosis of whooping cough should be considered. Insufficient data are available in association between prolong cough with pertussis. Further research on Microbiological works are being needed in order to established an etiological association between B. pertussis and B. parapertussis in the causation of prolonged cough among adults and adolescent so that booster doses pertussis vaccine can be employed in order to prevent pertussis.

**References:**

1. Balows A, Duerden BI. Bacterial infections of the respiratory tract. In: Balows A, Duerden BI editors. Topley's & Wilson's Microbiology and Microbial infections, 9th edition, New York: Arnold; 1999: pp.324-325.
2. Viljanen MK, He Q, Arvilommi H, Aittanen B, Mertsola J. Whooping cough caused by *B. pertussis* and *B. parapertussis* in an immunized population. *JAMA,* 1998; 280: 635-637.
3. Ryan KJ, Ray CG. *Haemophilus & Bordetella.* In: Ryan KJ, Ray CG, editors. Sherris Medical Microbiology, 4th edition, New York: McGrew Hill; 2004: pp.401-407.
4. Winter K, Harriman K, Zipprich J. California pertussis epidemic, 2010. *J Pediatr* 2012; 129: 968-970.
5. Heininger U. Pertussis immunization in adolescents and adults. Springerlink, New York, 2008; 609: 72-97.
6. Singh M, Lingappan K. Pertussis infection in adults with persistent cough. *JAMA,* 1995; 273: 1044-1046.
7. Strebel P, Nordin J, Edwards K. Population-based incidence of pertussis among adolescents and adults, Minnesota, 1995–1996. *J Infect Dis,* 2001; 183: 1353 –1359.
8. Bisgard L. Children with pertussis inform the investigation of other pertussis cases among contacts. *JAMA*, 2004; 7: 21.
9. Cromer BA, Goydos J, Hackell J, Mezzatesta J, Dekker C, Mortimer EA. Unrecognized pertussis infection in adolescents. *Am J Dis Child,* 1993; 147: 575 –577.
10. Devile IG, Cherry ID, Christenson PD. Frequency of unrecognized *Bordetella pertussis* infections in adults. *Clin Infect Dis,*1995; 21: 639 -642.
11. Rota MC, Asiello CM, D'Amelio R. Prevalence of markers of exposure to *Bordetella pertussis* among Italian young adults. *Clin Infect Dis,*1998; 26: 297- 302.
12. Cattaneo IA, Reed GW, Haasa DH, Wills MI, Edwards KM. The seroepidemiology of *Bordetella pertussis* infections: a stdy of persons ages 1 -65 years. *J Infect Dis* 1996; 173: 1256- 59.
13. He Q, Edelman K, Arvilommi H, Mertsola. Protective role of immunoglobulin G antibodies to filamentous hemagglutinin and pertactin of *B. pertussis* and *B. parapertussis* infection. *Eur J Clin Microbiol Infect Dis,* 1996; 15: 793-798.
14. Wright SW, Edwards KM, Decker MD, Zeldin MH. Pertussis Infection in adults with persistent cough. *JAMA,* 1995; 273: 1044–1046.
15. Rosenthal S, Strebel P, Cassiday P, Sanden G, Brusuelas K, Wharton M. Pertussis infection among adults during the 1993 outbreak in Chicago. *J Infect Dis,* 1995; 171 :1650 –1652.
16. Cherry JD. Epidemiological, clinical, and laboratory aspects of pertussis in adults. *Clin Infect Dis,* 1998; 28: 112–7.
17. Birkebaek NH, Kristiansen M, Seefeldt T. *Bordetella pertussis* and chronic cough in adults. *Clin Infect Dis,* 1999; 29: 1239 –1242.
18. 4Gilberg S, Njamkepo E, Du Chatelet IP. Evidence of *Bordetella pertussis* infection in adults presenting with persistent cough in a French area with very high whole-cell vaccine coverage. *J Infect Dis,* 2002; 186: 415 –418.
19. Nennig ME, Shinefield HR, Edwards KM, Black SB, Fireman BH. Prevalence and incidence of adults pertussis in urban population.*JAMA,* 1996; 275: 1672-1674.
20. Lin L, Poh KL, Lim TK. Multicenter clinical investigation of pertussis in children and adolescents with persistent cough. *Zhonghua Er Ke Za Zhi*. 2010; 48 (10): 748 – 752.
21. Linda DS, Scott AH, John SS, Merrilyn A, Annette M, Bruce S et al. Pertussis is a frequent cause of prolonged cough in adults and adolescents. *Clin Infect Dis,* 2001; 32 ( 12): 1691-1697.

22. Guris D, Strehel PM, Bardenheier R. Changina epidemiology of pertussis in the United State: increasing reported incidence among adolescent and adults, 1990-1996. *Clin Infect Dis*, 1999; 28: 1230-7.

23. Jansen DI, Gray GC, Putnam SD, Iynn E, Meade RD. Evaluation of pertussis in U.S. Marine Corps trainees. *Clin Infect Dis,*1997; 25: 1099 – 107.

24. Wright SW, Edwards KM, Decker MD. Incidence of pertussis infection in healthcare workers. *Infect Control Hosp Epidemiol* 1999; 20: 120 – 3.

25. Rohertson PW, Goldhera H, Laryie RH, Smith DD, Whyhin IR. *Bordetella pertussis* infection: a cause of persistent cough in adults. *Med J Aust* 1987; 146: 522 – 5.

26. Dahiya S, Kapil A, Kabra SK, Mathur P, Sood S, Lodha R et al. Pertussis in India. *J Med Microbiol* 2009; 58 (5): 688 – 689.

27. Bassinet L, Matrat M, Njamkepo E, Aberrane S, Housset B, Guiso N. Nosocromial pertussis out breaks among adults patients and healthcare workers. *Infect Control Hosp Epidemiol* 2004; 25: 995- 997.

28. Zaidi AKM, Avasthi S, De Silva HJ. Burden of infectious diseases in South Asia. *Brit Med J* 2004; 328: 811- 815.

29. Shears P. Emerging and reemerging infections in Africa: the need for improved laboratory services and disease surveillance. *Microb Infect* 2000; 2: 589- 595.

30. World Health Organization. Global Burden of Diseases 2004.

31. Bamberger ES, Srugo I. What is new in pertussis. *Eur J Pediatr* 2007; 167: 133- 136.

32. Cherry JD. The epidemiology of pertussis: A comparison of the epidemiology of the disease pertussis with the epidemiology of *Bordetella pertussis* infection. *Pediatrics* 2005; 115: 1222- 1227.

33. Hoey J. Pertussis in adults. *Can Med Assoc J* 2003; 168: 453- 454.

34. Weir E. Resurgence of *Bordetella pertussis* infections. *Can Med Assoc J* 2002; 167: 1146.

35. Bisgard L. Children with pertussis inform the investigation of other pertussis cases among contacts. *JAMA*, 2004; 7: 21.

*ORIGINAL ARTICLE*

# Problems in Initiation and Continuation of Exclusive Breastfeeding in Term Neonate

AHMED QN[1], RAHIM CFMM[2], MONI SC[3], MALEK A[4]

***Abstract***

***Introduction: Breastfeeding (BF), the "Gold standard" of infant feeding should be initiated within the first hour of life and exclusive breastfeeding (EBF) needs be to established and sustained for six completed months of age (WHO,UNICEF). Several physical, mental & sociocultural factors create barriers in current breast feeding practice. The objectives of this study was to evaluate problems in initiation of breastfeeding in term neonates within first hour of life and to identify the difficulties in continuing EBF in early puerperium.***

***Methods: We conducted this observational study for one year from March 2015 to August 2016 in a maternity. Mothers with term pregnancy, who delivered in the maternity, within the time period and have a post-natal follow up were included. A pre-designed semi-structured questionnaire using open and close ended questions was used to collect information just after delivery and on third day of puerperium. Data were tabulated and analyzed to identify the reasons for non-initiation of EBF by one hour and problems in its continuation.***

***Results: Total 592 mothers were included in this study. One third (36.36%) of the mothers could not initiate breastfeeding in first hour, despite adequate counseling. Reasons behind are flat nipple, inverted nipple - 34%, lack of knowledge - 31.4%, operative pain and other illness - 22%, pre-lacteal feeding - 17.3%, delay in shifting from OT or labour room-10.6%, sick baby, congenital anomaly in baby - 6%, wrong ritual, feeding from another mother - 5.7%. Majority of mothers (89.69%) fed their children with colostrum. Irrespective of breast feeding initiation time after birth or person who helped, 14.86% mothers were found not to continue EBF at postnatal visit. The identified causes found were- mixed feeding - 29.7%, thought that baby not getting enough milk - 24%, lack of proper knowledge - 23%, over anxious grandparents - 11%, feeding from another mother - 5.7%, lack of privacy - 10.7%, time consuming - 4.9%, difficult and lack of confidence- 6.9%, apprehension of not getting maternity leave - 2.5%, previous breastfeeding was painful throughout - 6.3%, sleepiness of the babies at feeding time- 6.3%.***

***Conclusion: Lack of knowledge, nipple disorder, prelacteal feeds, operative pain and others are the predominate factors that interfere with breast feeding initiation within one hour of age. Mixed feeding practice & not enough milk, over anxious family members, are the common barriers in establishing & sustaining EBF.***

***Key words: Exclusive breastfeeding, Gold standard of infant feeding, Term neonate***

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1. Dr. Qumrun Nassa Ahmed, Assistant Professor, Department of Obs. and Gynae, Green Life Medical College, Dhaka, Bangladesh.
2. Dr. Choudhury Faisal Md. Manzurur Rahim, Deprtment of Medicine, Dhaka Medical College Hospital, Dhaka, Bangladesh.
3. Dr. Sadeka Choudhury Moni, Assistant Professor, Department of Neonatology, BSMMU, Dhaka, Bangladesh.
4. Dr. Abdul Malek, Assistant Professor, Department of Paediatric, Green Life Medical College, Dhaka, Bangladesh.

**Address of Correspondence**: Dr. Qumrun Nassa Ahmed, Assistant Professor, Department of Obstetrics and Gynaecology, Green Life Medical College, Dhaka, Bangladesh. Email: qumrunmow@yahoo.com

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**Introduction:**

Breast feeding is the first fundamental right of a human being. It provides a unique biological and emotional basis for the health and cognitive development of the children. WHO recommends mothers worldwide to exclusively breastfeed their infants for first six months to achieve optimal growth, development and health. Thereafter, they should be given nutritious complementary foods and continue breastfeeding up to the age of two years or beyond.

"Exclusive breastfeeding" is defined as no other food or drink, not even water, except breast milk (including milk expressed or from a wet nurse) for 6 months of life, but allows the infant to receive ORS, drops and syrups (vitamins, minerals and medicines). Colostrum, A sticky white or yellow fluid secreted by the breasts during the second half of pregnancy and for a few days after birth, before breast milk comes in. It is high in protective antibodies that boost the newborn's immune system and recommended to be given within the first hour after birth.[1]

Breastfeeding offers infants and young children complete nutrition, early protection against illness (like- diarrhea, otitis media, gastrointestinal infections, respiratory tract infection and allergies), and promote growth and development of the baby.[2] It also reduce infant mortality[3] and health problems in later childhood like Inûammatory Bowel Disease, obesity.[4] Breast milk improves significantly Intelligence Quotient, Brain size compared to artificial feeds.[5] Continuation of breastfeeding for six months can reduce risk for clinical asthma, skin problems, diabetes, and respiratory problems, and also reduced risk for serious colds, ear and throat infections, respiratory problems, and childhood leukemia and lymphoma. The beneficial effect of breastfeeding depends on breastfeeding initiation, its duration, and age at which the breast-fed child is weaned.

Benefits for the mother from breastfeeding includes more rapid involution of the uterus, healthier weight, and reduced risk for postpartum depression, rheumatoid arthritis, hypertension, type 2 diabetes, myocardial infarction, and the metabolic syndrome.[6]

Despite Government and institutional support for breastfeeding, recognized barriers for exclusive breastfeeding includes lack of knowledge, contrary social norms, inadequate family and social support, embarrassment, lactation problems, and conflicts with employment and child care.[7] In our country breastfeeding practices also influenced by rural and urban residence, cultural and economic factors, psychological status, nipple abnormality, pre-lacteal feed, religious value and literacy especially low level of mother's education.

By assessing the knowledge, attitude and practices of lactating mothers regarding their child's feeding, an overview can be obtained about the areas which need modifications and hence specific intervention strategies can be made to correct where problems.[8,9]

**Methods:**

It is a cross sectional study. Study population were postnatal mothers admitted into the maternity for delivery both vaginal and caesarian. Sample of 592 mothers were included, among them 132 (22.3%) had some or more complains. The study was conducted in a renowned maternity clinic at Mirpur in Bangladesh. for 1 year. Study population were postnatal mothers both primi and multi, age between 18 to 40 years, delivered by both vaginally and abdominally who at 37 completed weeks to 41 weeks stayed for at least 72 hour after delivery at the maternity thus to help in breastfeeding mother of those neonate who are- preterm, gross congenitally abnormal, and severely ill. A semi-structured questionnaire using open and close ended questions was prepared. Patient's individual view is also included.

A pre-designed questionnaire was used to collect face to face interview. Every mother were counseled for early initiation and exclusive breastfeeding by service provider and they mothers were observed at early puerperium "who could initiate or not breastfeeding at first hour of life". And they were interviewed and breastfeeding process were observed on next postnatal visit to find out "who still could not establish breast feeding and can't continue exclusive breastfeeding and the reason behind" with the aid of the questionnaire.

All the data were tabulated and quantitative data were analyzed using SPSS 17.0 to derive percentages, proportions and chi-square tests and results were presented in narratives and tables. The significance level for all statistical analysis was set at 0.05. Patient's knowledge, attitude and practices regarding Breast feeding are analyzed to identify the most common reasons for not initiation and continuation of exclusive breast feeding.

**Results:**

Total 592 mothers were included at their early puerperium. Majority of the mothers (32.6%) in the study belong to age group 26-30 years.

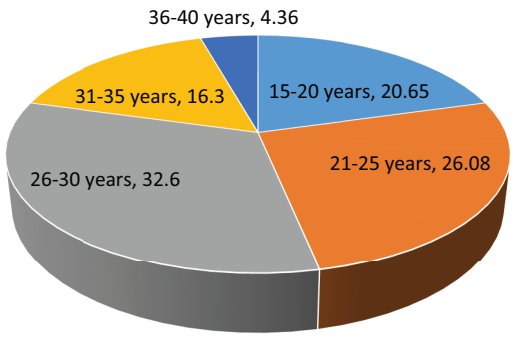


**Fig.-1 :** *Distribution of mother by age.*

According to parity 54.3% of mothers were primi para and 45.7% mothers were multi para. Among the study population 20.7% mother were service holder and only 8.7% women were self-employed. Rests of the mothers (72.7%) were homemaker.

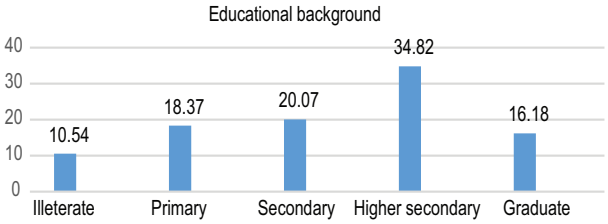


**Fig.-2:** *Educational background of the study population.*

Only 16.5% of the cases belong to poor category and 68.1% at middle socio-economic category. Only 15.4% of the mothers belong to high and upper middle group of socio-economic status.

All mother were counseled about breastfeeding during late antenatal period and after delivery. Just after birth every mother were taught and help to initiate breast feeding by the service provider in 42.4%, by their attendant in 33.7%. Mother herself initiated breastfeeding in 22.8% cases. In spite of all, in 63.6% mother can initiate breastfeeding in first hour of life, and 36.7% mother need more time to initiate breastfeeding. Causes for not to initiation of breastfeeding within first hour of life includes- nipple disorders, lack of proper knowledge irrespective to parents and other family members, and some wrong idea and attitudes.

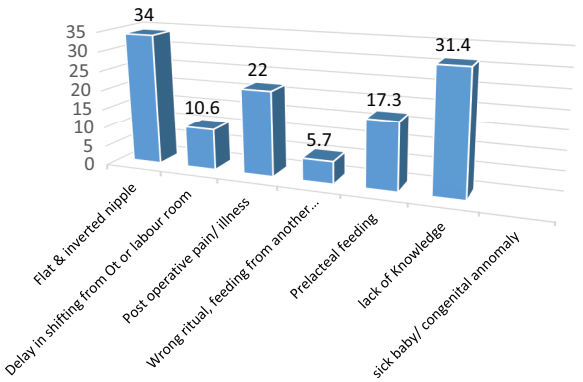


**Fig.-3:** *Causes of not initiation of breast feeding in 1st hour*

Majority of mothers (89.7%) fed their children with colostrum. Irrespective of breast feeding initiation time after birth or person who helped, 14.86% mothers was found not to continue EBF at next postnatal visit. The identified causes were put in the following table.

**Table-1**

*Distribution of patients according to causes for not continuation of exclusive breast feeding.*

| Distribution of causes | Percentage |
|---|---|
| Mixed feeding | 29.7% |
| Thought that baby not getting enough milk | 24% |
| Lack of proper knowledge | 23% |
| Over anxious grand-parents | 11% |
| Feeding from another mother | 3.7% |
| Lack of privacy | 10.7% |
| Time consuming | 4.9% |
| Difficult and lack of confidence | 6.9% |
| Apprehension of not getting maternity leave | 2.5% |
| Previous breastfeeding was painful throughout | 6.3% |
| Sleepiness of the babies at feeding time | 6.3% |

**Discussion:**

This study upgrades and documents mother's perception and attitude towards delay in timely breastfeeding initiation and interference with EBF. Although many mothers had heard some breastfeeding promotional messages from the media and other sources, but these were not sufficient to influence their practices and were also not convincing for other family members. This resulted in big gaps in initiating breastfeeding within first hour of life, feeding colostrum and not giving other pre-lacteal feed for the first three days of puerperium when milk let down was yet to start. It also influence in exclusive breastfeeding for first six months. According to The State of Policy and Program on Infant and Young Child Feeding (IYCF) guidelines 2015, Government of Bangladesh recommends that initiation of breastfeeding should begin immediately after birth, preferably within one hour.[10] Though, all of the mothers delivered in the hospital, only 63.6% of the mothers stated that they had initiated breastfeeding within 1st hour, which is slightly higher than national report from Bangladesh Demographic and Health Survey (BDHS) 2014. According to BDHS percentage of babies' breastfed within one hour of birth is 57%.[11] It may be because here all the mothers had delivered in a maternity and were under supervision of Doctors, Nurses, and other health service providers. But here also it was not cent percent, and most common reasons for delay in initiation of breastfeeding were; delay in shifting the mothers from labor room, Caesarean delivery and it's pain, various nipple disorders, low maternal knowledge and lack of education and some family restriction and misconceptions. Our result

of early initiation of breastfeeding 63.64% is higher than the studies conducted from different parts of the world ranging from 6.3% to 31%.[12,13,14] On the contrary, few studies demonstrated higher rate of breastfeeding initiation 38%[15], 53%[16] and 72.2%.[12] These findings indicate health professionals to be made aware about the importance of initiating early breastfeeding is an urgent concern.

In the present study, 86.7% of the mothers were aware of breastfeeding and 89.4% mothers knew that they should continue breastfeeding up to 2 years of life. This finding is consistent with one study conducted in India, where they found it 85.2% of mothers were aware of EBF and 68% mothers felt that they should continue breastfeeding till the age of 2 years.[17] Maternal education has been described as one of the strongest determinants of the practice of EBF,[18] but a contrast result was found in another study, where they showed literacy status had little impact on initiation of breastfeeding.[19] However, an early initiation was observed in comparatively more educated mother.[20] Studies indicate that mothers with higher family income had better attitudes towards breastfeeding and similar finding was observed in our study sample.[21,22] Mothers older than 25 years and homemakers had more positive attitudes toward exclusive breast feeding. This finding is consistent with previous reports that showed high rates of awareness of EBF among older groups[23] and homemakers.[24]

It is known that the institutional delivery enhance the early initiation and continuation of breastfeeding.[23,25] We are committed for early and exclusive breastfeeding to all newborns. However, all is not well with our children's health. A report of World Breast Feeding Trends Initiative 2015 shows that only 57% of the newborns get the opportunity of early breast feeding in Bangladesh the early breastfeeding in Bangladesh.[26]

Our finding showed, majority of mothers did not discard colostrum and they fed it to their newborn. Also, the study suggested that the enhancement in maternal literacy may be proved helpful to initiate breastfeeding as earliest as possible, and practice of colostrum feeding by them, like another study.[27]

In a study they found that 71.7% infants were given pre-lacteal feeds. Among pre-lacteal feeds honey (25%) was commonest followed by other substances like water (18%) etc.[28]

**Limitation of the study:**

The present study has certain limitations such as cross sectional in nature, all the participants were at early postpartum and small sample size that made difficult to generalize the findings. The data for this study were taken from a single center, thus providing a small study number and impacting on the generalisability of the findings. As the study was conducted in a maternity with in the capital, so the exact scenario could not be visualized from the result of the study. Moreover, whether these mothers continued breast feeding for two years or not could not be evaluated due to lack of further follow up. However, despite of these limitations, the present study findings may be helpful to the clinicians and nursing professionals in designing the interventions to promote breast feeding practices in future.

**Conclusion:**

Our study findings showed that some correctable physical barrier, inadequate knowledge, and huge knowledge-to-practice gaps continue to exist in breastfeeding behaviors, mostly due to lack of awareness as to why the recommended breastfeeding practices are beneficial, the risks of not practicing them, as well as how to practice them. And also health workers' interactions for promoting and supporting optimal breastfeeding are extremely low, may be due to increased workload without rationalizing the manpower. Thus, it is important to provide prenatal education and counseling to mothers and family members on breast feeding, strengthening the public health education campaigns to promote breast feeding, increase number of institutional deliveries, implications for public health policy and program implementation.

**References:**

1. WHO, Breastfeeding. Available from: http://www.who.int/topics/breastfeeding/en/. [Last accessed on 2015 Aug 11].
2. American Academy of Pediatrics Section on Breastfeeding. (2012). Breastfeeding and the use of human milk. Pediatrics, 129(3), e827e841. doi:10.1542/peds.2011-3552.
3. Hanson LÅ. Human milk and host defence: immediate and long term effects. ActaPaediatrica 88(s430): 42-6 (1999).
4. Hess C, Ofei A, Mincher A. Breastfeeding and childhood obesity among africanamericans: a systematic review. MCN Am J Matern Child Nurs. 2015;40(5): 313–19. [PubMed].
5. Isaacs EB, Fischl BR, Quinn BT, Chong WK, Gadian DG, Lucas A. Impact of breast milk on intelligence quotient, brain size, and white matter development. Pediatric research 2010;Apr 1;67(4):357-62.
6. Che Zem J, Friesen C, and Boettcher J. Breastfeeding knowledge, breastfeeding confidence and infant feeding plans: Effects on actual feeding practice. J Obstetr Gynecol Neonat Nurs. 2003;32(1):42-7.

7. Centers for Disease Control and Prevention [CDC], 2013; Teich, Barnett, &Bonuck, 2014; U.S. Department of Health and Human Services, 2011).

8. Oommen A, Vatsa M, Paul VK, Agarwal R. Breastfeeding practices of urban and rural mothers. Ind Paediatr. 2009;46:891-4.

9. Brodribb W. Barriers to translating evidence based breastfeeding information into practice. Acta Paediatrica. 2011;100(4):486-90.

10. IYCF. National guideline on Infant and Yong Child Feeding, 2015. WBTi- World Breastfeeding Trends Initiative.

11. Bangladesh Demographic and Health Survey (BDHS), 2014. The DHS Program, National Institute of Population Research and training, Ministry of Health and Family Welfare, Dhaka, Bangladesh.

12. Oche MO, Umar AS, Ahmed H. Knowledge and practice of exclusive breastfeeding in Kware, Nigeria. Afr Health Sci, 2011; 11:518-23.

13. Oche MO, Umar AS. Breastfeeding Practices of Mothers in a Rural Community of Sokoto, Nigeria. Niger Postgrad Med J, 2008; 15:101-4.

14. Chaudhary RN, Shah T, Raja S. Knowledge and practice of mothers regarding breast feeding: a hospital based study. Health Renaissance, 2011; 9:194200.

15. Raval D, Jankar DV, Singh MP. A study of breast feeding practices among infants living in slums of Bhavnagar city, Gujarat, India Health line, 2011;2:78-83.

16. Chandrashekhar TS, Joshi HS, Binu V, Shankar PR, Rana MS, Ramachandran U. Breastfeeding initiation and determinants of exclusive breastfeeding-a questionnaire survey in an urban population of western Nepal. Public Health Nutr, 2007; 10:192-7.

17. Vijayalakshmi P, Susheela T, Mythili D, RN, RM, BSN, MSN, Clinical instructor, College of Nursing: Knowledge, attitudes, and breast feeding practices of postnatal mother. I. J. Health Sciences, Q. U, Vol. 9, No. 4 (Oct-Dec 2015).

18. Dubois L, Girard M. Social determinants of initiation, duration and exclusivity of breastfeeding at the population level. The results of a longitudinal study of child development in Quebec (ELDEQ 19982002). Can J Public Health. 2003; 94:3005

19. Ansari MA, Khan Z, Khan IM. Hospital based study on breastfeeding practices in Aligarh. Ind J Prevent Soc Medic. 2007;38(1-2):69-74.

20. Kumar A, Verma P, Singh VS, Kansal S. Breastfeeding practices in rural eastern uttarpradesh: a descriptive cross-sectional study. Indian J PrevSoc Med. 2011; 42(2): 193-8.

21. Shi L ZJ, Wang Y, Guyer B. Breastfeeding in rural China: association between knowledge, attitudes, and practices. J Hum Lact, 2008; 24:377-85.

22. Weiqi C. Breastfeeding knowledge, attitude, practice and related determinants among mothers in Guangzhou, China. West cluster: University of Hong Kong.2010.

23. Hawkins SS, Stern AD, Baum CF, Gillman MW. Evaluating the impact of the Baby-Friendly Hospital Initiative on breast-feeding rates: a multi-state analysis. Public Health Nutr. 2015 Feb;18(2):189–97.

24. Mbada EC AE, Joel OF, Folasade CO-A, Funmilola AF, Abiola OO, et al. Knowledge, attitude and techniques of breastfeeding among Nigerian mothers from a semi-urban community. BMC Research Notes, 2013;6:552.

25. Dongre AR, Deshmukh PR, Rawool AP, Garg BS. Where and how breastfeeding promotion initiatives should focus its attention? A study from rural wardha. Indian J Community Med Off Publ Indian Assoc Prev Soc Med. 2010;35(2):226–29.

26. World Breastfeeding Trends Initiative (WBTI) 2015. Arrested Development, all is not well with our Children's health. Available from:http://www.worldbreastfeedingtrends.org / GenerateReports/report/WBTi-India-Report-2015.pdf. [Last accessed on 2015 Sep 16].

27. Tiwari V, Singh A. Knowledge attitude and practice of mothers regarding breast feeding in an urban area of Faizabad district (UP). Ind J Prevent Soc Medic. 2007;38(1-2):18-22.

28. Mandal PK, Sardar JC, Chatterjee C, Lahiri SK, Ghosh P. A study of breast feeding practices among infants in a rural area of West Bengal. Ind J Prevent Soc Medic. 2007;38(1-2):28-31.

*ORIGINAL ARTICLE*

# Association of Serum Ferritin with Severity and Hospital outcome of Acute Ischemic Stroke Patients in a Tertiary Care Hospital in Bangladesh

RAHMAN MM[1], AKHTER M[2], RAHIM CFMM[3], RAHMAN MA[4]

*Abstract*

***Introduction:*** *According to the World Health Organization and other leading stroke experts, stroke claims 6.2 million lives each year. An estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths. Stroke is the second cause of disabilities in low mid income countries. Dementia and stroke account for one third of all long term disabilities worldwide. In Fenton reaction, Fe (11) catalyzes the formation of extremely reactive hydroxyl radicles. Interaction with lipids may initiate the formation of oxidized LDL that ultimately leads to the development of foam cells and progression of atherosclerosis. Davalos et al. (2015) conducted a study among the patients with ischemic stroke and relation of iron load with prognosis of stroke and it was found that depending upon CSS, serum ferritin values were greater in the poor outcome group. This study is intended to be conducted among the patients with acute stroke to determine the role of ferritin in depending severity and outcome of acute ischemic stroke to evaluate the association of serum ferritin with severity and hospital outcome of acute ischemic stroke.*

***Methods:*** *Study was carried out in Dhaka Medical College, during January 2016 to December 2016. The severity of stroke of the admitted patients were investigated to clarify etiologic factors for stroke. Computed tomography, MRI were performed within the first 72 hours and repeated if needed and followed up in the clinical course. Ferritin levels were measured using immunoassay technique within 24 hours of admission.*

***Results:*** *Out of 134 patients, only 34 patients were improved. Comparison between level of serum ferritin and MRI, there was no patient having serum ferritin raised in case of normal MRI but in 26 (29.5%) had serum ferritin raised in abnormal MRI group. In comparison of serum ferritin with outcome the difference was statistically significant between two groups. On admission within 24 hours the mean difference of CSS score was not statistically significant between normal serum ferritin level and raised serum ferritin level but in subsequent follow-up the difference of CSS score was statistically significant ($p<0.05$) between normal serum ferritin level and raised serum ferritin.*

***Conclusion:*** *Elevated values of serum ferritin may be used as a reliable index of acute stroke for prediction of severity and prognosis of acute stroke.*

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1. Dr. Md. Mahbubor Rahman, Department of Medicine, Dhaka Medical College Hospital
2. Dr. Mahbooba Akhter, Department of Biochemistry, Dhaka Medical College
3. Dr. Choudhury Faisal Md. Manzurur Rahim. Department of Medicine, Dhaka Medical College Hospital
4. Dr. Md. Ashikur Rahman, Department of Medicine, Dhaka Medical College Hospital

**Address of correspondence:** Dr. Md. Mahbubor Rahman, Department of Medicine, Dhaka Medical College Hospital, Dhaka, E-mail: mahbuborrahmanmd@gmail.com

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**Introduction:**

According to the World Health Organization and other leading stroke experts, stroke claims 6.2 million lives each year. An estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths. Of these deaths, an estimated 7.3 million were due to coronary heart disease and 6.2 million were due to stroke.[1] Worldwide, it is estimated that six people die from stroke every 60 seconds.[2] From 2000 to 2008, the overall stroke incidence rates in low to middle income countries, exceeded that of high-income countries, by 20%.[3]

Stroke is the second cause of disabilities in low-mid income countries. Dementia and stroke account for one third of all long-term disabilities worldwide. The WHO Global Burden of Disease (2004) Update (re-published in 2008) provides data on stroke disabilities (moderate to severe disabilities) worldwide.[4] In developing countries ischemic stroke represents the majority of stroke subtypes and ischemic stroke is the most frequent event (72% of all stroke) in Bangladesh.[5]

In the Fenton reaction, Fe (II) catalyzes the formation of extremely reactive hydroxyl radicals. Interaction with lipids may initiate the formation of oxidized LDL that ultimately leads to the development of foam cells and progression of atherosclerosis. Additionally, iron could also play a role in vascular disease by activating platelets via a protein kinase C mechanism.[7] although its initial focus was on ischemic heart disease, the hypothesis may also apply to cerebrovascular disease.

During reperfusion after cerebral infarction, there is a marked increase in oxygen-radical production as well as a release of iron ions, leading to progressive tissue damage and cellular death.[8] In CVD, oxygen superoxide radicals increase the amount of iron in the cytosole during oxidative stress by enabling the release of iron from ferritin.[9,10] Ferrous iron-mediated free radical mechanism is assumed to play an important role in acute stroke.[11]

Davalos et al.[12] conducted a study among the patients with ischemic stroke and relation of iron load with prognosis of stroke and it was found that depending upon CSS serum ferritin values were greater in the poor outcome group (218±156 mg/L versus133±125 jig/L;P=.004),a correlation between ferritin values and degree of worsening or improvement of the CSS score on day 30 was found (P=.002).

This study is intended to be conducted among the patients with acute stroke to determine the role of serum ferritin in predicting severity and outcome of acute ischemic stroke. During the study period and in hospital course stroke severity was scored by CSS and definite outcome recorded as morbidity and mortality.

**Methods:**

This cross sectional analytical study was carried out among 134 the ischemic stroke patients admitted due to acute ischemic stroke in medicine depertment of Dhaka Medical Collage, Dhaka, during January' 2016 to December' 2016. Patients with suspected or diagnosed as ischemic stroke and those who had hypertension, first 24 hours with clinical, CT scan & MRI of brain findings of acute ischemic stroke were included in this study. During study, patients were divided into two groups, improved (neurological deficit with normal serum ferritin level) and deteriorated group (neurological deficit with raised serum ferritin level). Patients who presented after 24 hours of Ischemic stroke, patients with liver disease like NASH and patients with severe anemia were excluded from the study. Informed written consent was taken from the patient or patient's guardian after informing the procedure of treatment, anticipated result, possible advantages, disadvantages and complications' considering all ethical issues and the protocol was approved by ethical committee of Dhaka Medical College & Hospital. Purposive sampling according to availability of the patients and strictly considering the inclusion and exclusion criteria's.

Stroke severity at admission was determined by Canadian Stroke Scale (CSS) (Cote et al., 1986). Functional outcome of patients was measured by CSS on day 1, 2, 3, 7 and at the time of discharge by Canadian Stroke Scale. Laboratory tests (blood cell count, biochemical studies including random blood glucose, CRP, lipid profiles , serum electrolytes and 12-lead electrocardiography was performed in all patients. Computed tomography (CT), MRI were performed within the first 72 h and repeated when it was necessary and followed up in the clinical course. Ferritin levels of the sera was measured using immunoassay technique within 24 hours of admission (Access, Beckman, Chaska, MN, USA). On admission, the patient's age, sex, height and approximate weight was recorded by using a prescribed data sheet. In this study serum ferritin is measured and correlated with morbidity and mortality. CSS neurological deficit measured by the following methods:- Scoring at admission by alertness, orientation, facial muscle weakness, arm muscle weakness and leg muscle weakness in on admission, in 24 hrs, 48 hrs, 7$^{th}$ day and at the discharge of the patients. Severity is assessed by following scoring, mild ≥8, moderate 5-7 and severe ≤4 (In CSS scoring is 23 ). In this study serum ferritin is measured and correlated with morbidity and mortality.

**Statistical Analysis**

Statistical analyses was carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean, standard deviation, and categorical variables as frequencies and percentages. The differences between groups was analyzed by unpaired t-test or chi-square ($\chi^2$) test and shown with cross tabulation and also the Pearson correlation coefficient was used for testing associations. A p-value <0.05 was considered as significant.

**Results:**

This study was conducted on 134 patients who were divided into two groups. The mean age was found 60.6±11.7 years in improved group and 65.1±13.8 years in deteriorated group. The mean CSS score was 4.7±1.6 on admission in improved and 3.8±2.0 in deteriorated group which was statistically significant ($p<0.05$). The serum ferritin level was 148.3±32.6 µg/l in improved group and 292.5±34.1 µg/l in deteriorated group which was also statistically significant ($p<0.05$) .Regarding serum ferritin with outcome, serum ferritin raised in 107 patients, 21(19.6%) patients found in improve group and (80.4%) in Deteriorated group. Out of 134, 27 patients had normal serum ferritin level, 13(48.1%) patients in improve group and (51.9%) in Deteriorated group. The difference was statistically significant ($p<0.01$) between two groups. Serum ferritin level was found to be higher in patients with severe neurologic deficit in deteriorated group, according to initial CSS score (Fig. 2). In univariate analysis, serum ferritin and CSS score at admission were significantly high in the diseased group but not significant in age and sex of the patients or nature (Table I). On admission the mean difference of CSS score was not statistically significant ($p>0.05$) between normal serum ferritin level and raised serum ferritin level but in subsequent follow-up (Table III) the difference of CSS score was statistically significant ($p<0.05$) between normal serum ferritin level and raised serum ferritin.

**Table I**

*Clinical and biochemical characteristics c with outcome (n=134)*

| Serum ferritin | Outcome | | P value |
|---|---|---|---|
| | Improved (n=34) Mean±SD | Deteriorated (n=100) Mean±SD | |
| Age (years) | 60.6±11.7 | 65.1±13.8 | 0.090$^{ns}$ |
| Female | 21 | 54 | 0.430$^{ns}$ |
| CSS on admission | 4.7±1.6 | 3.8±2.0 | 0.018$^{s}$ |
| Serum ferritin level | 148.3±32.6 | 292.5±34.1 | 0.001$^{s}$ |

CSS= Canadian Stroke Scale

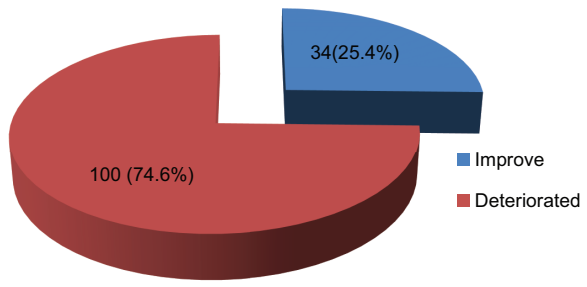


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**Table II**

*Comparison between serum ferritin with outcome (n=134)*

| Serum ferritin | Outcome | | | | Total | P value |
|---|---|---|---|---|---|---|
| | Improved (n=34) | | Deteriorated (n=100) | | | |
| | n | % | n | % | | |
| Raised | 21 | 19.6 | 86 | 80.4 | 107 | 0.001$^{s}$ |
| Normal | 13 | 48.1 | 14 | 51.9 | 27 | |
| Total | 34 | 25.4 | 100 | 74.6 | 134 | |

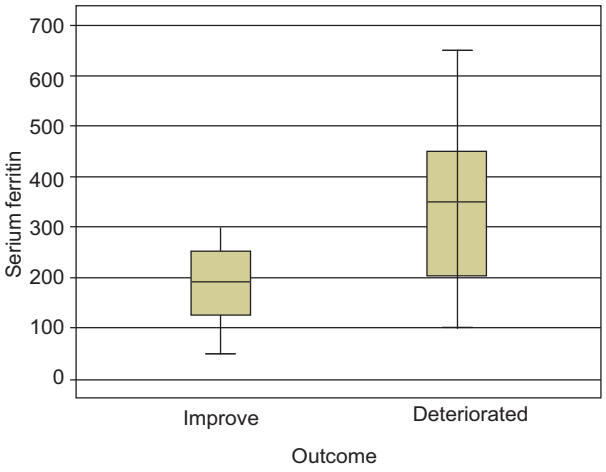


**Fig.-2:** *Boxplot shows a significant difference in mean serum ferritin level (µg/l) according to level of conscious on admission.*

**Table III**

*Comparison between serum ferritin with CSS Score (n=134)*

| | CSS Score Normal(n=27) Mean±SD | Serum ferritin Raised (n=107) Mean±SD | P value |
|---|---|---|---|
| On admission CSS score | 4.71±1.88 | 3.88±1.93 | 0.116$^{s}$ |
| Range (min, max) | 2 , 9 | 0, 8 | |
| At 24 hours | 4.84±2.07 | 3.84±1.78 | 0.012$^{s}$ |
| CSSscore Range (min, max) | 2, 9 | 2, 8 | |
| At 48 hours | 4.80±2.14 | 3.91±1.85 | 0.032$^{s}$ |
| CSS score Range (min, max) | 2 , 9 | 2, 8 | |
| At 7$^{th}$ days | 5.27±2.58 | 3.66±2.40 | 0.002$^{s}$ |
| CSS score Range (min, max) | 1, 9 | 1, 15 | |
| At discharge | 6.03±3.09 | 3.73±2.50 | 0.001$^{s}$ |
| CSS scoreRange (min, max) | 1.5, 1.9 | 2.51, 14 | |

s= significant, ns= not significant p value reached from un-pair test

**Discussion:**

Stroke is one of the foremost causes of morbidity, mortality and a socioeconomic challenge. This is particularly true for developing countries like Bangladesh, where health support system including the rehabilitation system is not within the reach of ordinary people. It is crystal clear that, this devastating condition not only affects the patient but also their family.[5]

In present study it was observed that majority (36.6%) patients were in 7th decade and the mean age was found 63.96±13.41 years. Similarly, in our country, Hossain et al. [5] observed most (69.0%) of the patients were between 51-70 years of age. In another study in Bangladesh Iqbal et al. [13] found maximum patients (30%) were in between the group of 51-60 years age and next prevalence group was 61-70 years (22%) ages.

In this current study it was also observed that more than half (54.5%) patients were male and 45.5% female, where the present found male to female ratio was 1.2:1, which is closely similar with Islam et al. [14] observed in Bangladeshi population, where they found the ratio of male : female patients was 3•44 : 2•41.

Risk factors for stroke are characteristic for an individual or for a population, indicate that the individual or population has an increased risk of stroke compared with an individual or a population, without that characteristic. In this current study it was observed that that majority (56.7%) patients had history of DM, 37.3% Hypertension, 12.7% had previous history of stroke, 9.0% had convulsion, 5.2% had death of any family member from stroke and 3.7% had fever.

A study was done by Latif et al.(2015),BIRDEM on 165 cases of diabetic patients and showed that all of them developed stroke within 10 years duration of DM. Hypertension was the most common modifiable risk factor in 60.0% observed by Hasan et al.[16]

Gentile et al. [17] obtained in their study that comorbid diagnoses included diabetes 39.0% in their study patients. Stollberger et al. [18] found 30% patients had a history of diabetes mellitus. Stollberger et al. [18] found that 66.0% patients were hypertensive. Basu et al. [19] and Gentile et al. [17] showed that 74.0% and 73.8% patients were known hypertensive respectively, which is higher with the current study.

About the laboratory investigations it was observed in this series that 79.9% had raised Serum ferritin level. Erdemoglu and Erdemoglu and Ozbakir [20] reported that increased serum ferritin levels correlate to severity of stroke and the size of the lesion. In this current study all patients had abnormal findings in CT scan of Brain, 99.3% had abnormal MRI 12.7% abnormal serum electrolytes, 3.7% had abnormal serum creatinine and 0.7% patients had abnormal ECG.

In this study regarding the level of consciousness 94.8% was drowsy, 74.4% was disoriented, receptive aphasia was 51.1% and expressive aphasia 24.8% of the patients. Toni et al. [21] found 51.0% of the study patients had an impaired level of consciousness and 49.0% had impaired limb strength and/or speech. In another study Cote et al. [22] found all patients were alert or drowsy and more than 50% were disoriented. Half the patients had normal speech as defined by the speech scale, 23.0% of the patients were classified as having an expressive deficit and twenty-seven percent had a receptive disorder and more than 84% of the patients had at least one motor deficit present.

In this study it was observed that 37.3% patients had face weakness, 35.8% patients had significant and mild Arm proximal weakness, 78(58.2%) patients had significant Arm distal weakness, 58.9% patients had significant leg proximal weakness and 51.1% patients had significant distal leg weakness. In this series it was observed that 68.7% patients had asymmetrical facial weakness and 31.3% symmetrical facial, 99.3% unequal arms, equal 0.7% and all patients had unequal leg weakness.

Regarding the CSS Score, it was observed in this present study that almost three fourth (71.6%) patients were severe according to CSS score on admission, 73.1% became severe at 24 hours, 70.9% severe at 48 hours, 71.6% severe at 7th days, 67.9% were severe at discharge. The mean CSS score was 4.0±1.9 with range from 0.4 to 9.0 on admission, 4.0±2.5 with range from 1.5 to 9.0 at 24 hrs, 4.1±1.9 with ranged from 1.5 to 9.0 at 48 hrs, 4.0±2.5 with range from 1.3 to 15.0 and 4.2±2.8 with ranged from 0.2 to 14.0. The mean difference of CSS score was almost alike in different follow-up with on admission CSS score. Similarly, Erdemoglu and Ozbakir (2002) observed on admission, the mean CSS score was 4.8 ± 0.4 with median 4.5, which is comparable with the current study.

Regarding the outcome, it was observed in this present study that 25.4% patients improved, 21.6% deteriorated, 3.7% expired and 49.3% patients remain unchanged. Davalos et al. [23] found 49.0% were in the good outcome group and 51.0% in the poor outcome group. In the 21 patients in whom serum ferritin was not measured, mortality 24.0% and poor clinical outcome 48.0% were similar to those of the patients included in the study.

Regarding the association between serum ferritin with MRI it was observed in this present study that patients who had raised serum ferritin level all were abnormal finding in MRI evaluation.

High serum ferritin levels within the first 24 hours of hospitalization for an acute ischemic stroke are related to a poor prognosis, independent of the stress response. (Davalos et al. [23]). In this study it was observed that almost two third (61.8%) patients had serum ferritin raised in improve group and 86.0% had serum ferritin in deteriorated group. The difference was statistically significant (P<0.05) with outcome. Davalos et al. [12] found that depending upon Canadian stroke Scale Serum ferritin values were greater in the poor outcome group (218± 156 Mg/L versus133±125 jig/L; p<0.05). Serum ferritin (odds ratio, 4.6; 95% CI, 1.1 to 19) were related to poor outcome. Choi et al. [24] found that a high ferritin level remained an independent predictor of HT(Hemorrhagic Ttansformation) in the patients with acute ischaemic stroke (P<0.05). Serum ferritin levels higher than 171.8 ng/ml were independently associated with hemorrhagic transformation. Armengou et al. [25] and Erdemoglu et al. [20] studies showed that the serum ferritin concentrations are not modified in the acute phase of ischaemic stroke during the first 48 h after a vascular event, and there is a lack of correlation between ferritin and acute phase reactants in blood such as C-reactive protein (CRP). Therefore, serum ferritin can provide a reliable index of iron stores in patients with acute stroke who are without infectious or inflammatory diseases.

In this present study it was observed that the mean CSS score was found 4.71±1.88 in serum ferritin normal group and 3.88±1.93 in serum ferritin raised group on admission. The mean CSS score was found 4.84±2.07 in serum ferritin normal group and 3.84±1.78 in serum ferritin raised group 24 hrs. The mean CSS score was found 4.80±2.14 in serum ferritin normal group and 3.91±1.85 in serum ferritin raised group at 48 hrs. The mean CSS score was found 5.27±1.58 in serum ferritin normal group and 3.66±2.4 in serum ferritin raised group at 7th day. The mean CSS score was found 6.03±3.09 in serum ferritin normal group and 3.73±2.50 in serum ferritin raised group at discharge. On admission the mean difference of CSS score was not statistically significant (P>0.05) between normal serum ferritin level and raised serum ferritin level but in subsequent follow-up the mean difference of CSS score was statistically significant (P<0.05) between normal serum ferritin level and raised serum ferritin.

**Conclusion:**

Stroke cases in Bangladesh has significantly increased in number over the past decades. Adverse outcome from these cases are also rising due to the low number of neurologists and specialized hospitals in the countries. The study was undertaken to evaluate the role serum ferritin in prediction of severity and outcome of acute ischemic stroke. Majority of the patient having acute stroke in 7$^{th}$ decade, male predominant and came from average socio-economic status.DM and hypertension were common previous history of acute ischemic stroke in patients. Most of the patients were drowsy, focal neurological deficit and Arcns senilis during clinical observation. More than one fourth patients were improved, near a half of the patients remain unchanged, almost one fourth deteriorated and 3.7% expired. Serum ferritin is significantly associated with mortality

**References:**

1. World Health Organization, 2011. Global status report on no communicable diseases 2010. Geneva.
2. World Health Report 2007. Geneva: World Health Organization.
3. Truelsen T, Heuschmann PU, Bonita R, Arjundas G, Dalal P, Damasceno A, Nagaraja D, Ogunniyi A, Oveisgharan S, Radhakrishnan K, Skvortsoya VI. Standard method for developing stroke registers in low-income and middle-income countries: experiences from a feasibility study of a stepwise approach to stroke surveillance (STEPS Stroke). The Lancet Neurology. 2007 Feb 28;6(2):134-9.
4. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, Moran AE, Sacco RL, Anderson L, Truelsen T, O'Donnell M. Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010. The Lancet. 2014 Jan 24;383(9913):245-55.
5. Hossain AM, Ahmed NU, Rahman M, Islam MR, Sadhya G, Fatema K. Analysis of sociodemographic and clinical factors associated with hospitalized stroke patients of Bangladesh. Faridpur Medical College Journal. 2011;6(1):19-23.
6. Streinberg D, Parthasarathy S, Carew TE, Khoo JD, Witztum JL. Beyond cholesterol. Modification of low density lipoprotein that increases its atherogenecity. N. Eng. J. Med. 1989:320-915.
7. Pratico D, Pasin M, Barry OP, Ghiselli A, Sabatino G, Iuliano L, FitzGerald GA, Violi F. Iron-dependent human platelet activation and hydroxyl radical formation. Circulation. 1999 Jun 22;99(24):3118-24.
8. White BC, Sullivan JM, DeGracia DJ, O'Neil BJ, Neumar RW, Grossman LI, Rafols JA, Krause GS. Brain ischemia and reperfusion: molecular mechanisms of neuronal injury. Journal of the neurological sciences. 2000 Oct 1;179(1):1-33.

9. Reif DW. Ferritin as a source of iron for oxidative damage. Free Radical Biology and Medicine. 1992 Jan 1;12(5):| 417-27.

10. Sorond FA, Ratan RR. Ironing-out mechanisms of neuronal injury under hypoxic–ischemic conditions and potential role of iron chelators as neuroprotective agents. Antioxidants and Redox Signaling. 2000 Sep 1;2(3):421-36.

11. Bishop GM, Robinson SR. Quantitative analysis of cell death and ferritin expression in response to cortical iron: implications for hypoxia–ischemia and stroke. Brain research. 2001 Jul 13;907(1):175-87.

12. Davalos A, Castillo J, Marrugat J, Fernandez-Real JM, Armengou A, Cacabelos P, Rama R. Body iron stores and early neurologic deterioration in acute cerebral infarction. Neurology. 2000 Apr 25;54(8):1568-74.

13. Iqbal MJ, Siddiqui MM, Islam QT, Hossain A, Mustafa E, Shipa MR, Rahman MY, Sina H. Association between acute stroke and metabolic syndrome. Journal of Medicine. 2010; 11(2):124-7.

14. Islam N, Moniruzzaman M, Khalil I, Basri R, Alam MK, Loo KW, Gan SH, 2012, 'Burden of stroke in Bangladesh. International Journal of Stroke © 2012 World Stroke', *Panorama*, vol.11, pp. 25-9.

15. Latif ZA, Zaman SM, Barua A, Ahad A, Rahim SA. Study of stroke between normotensive and hypertensive NIDDM cases in BIRDEM, Dhaka. Bangladesh journal of Neuroscience. 1990;6:52-9.

16. Hasan SR, Ghouri AS. Frequency of known risk factors of stroke and its outcome in patients admitted in sindh government Qatar hospital Karachi. Pakistan Journal of Medical Sciences. 2007 Jul 1;23(4):634.

17. Gentile NT, Seftchick MW, Huynh T, Kruus LK, Gaughan J. Decreased mortality by normalizing blood glucose after acute ischemic stroke. Academic emergency medicine. 2006 Feb 1;13(2):174-80.

18. Stöllberger C, Exner I, Finsterer J, Slany J, Steger C. Stroke in diabetic and non diabetic patients: Course and prognostic value of admission serum glucose. Annals of medicine. 2005 Jan 1;37(5):357-64.

19. Basu S, Sanyal D, Roy K, Bhattacharya KB. Is post-stroke hyperglycemia a marker of stroke severity and prognosis: A pilot study. Neurology Asia. 2007 Jun;12:13-9.

20. Erdemoglu AK, Ozbakir S. Serum ferritin levels and early prognosis of stroke. European Journal of Neurology. 2002 Nov 1;9(6):633-7.

21. Toni D, Fiorelli M, Gentile M, Bastianello S, Sacchetti ML, Argentino C, Pozzilli C, Fieschi C. Progressing neurological deficit secondary to acute ischemic stroke: a study on predictability, pathogenesis, and prognosis. Archives of Neurology. 1995 Jul 1;52(7):670-5.

22. Cote R, Hachinski VC, Shurvell BL, Norris JW, Wolfson C. The Canadian Neurological Scale: a preliminary study in acute stroke. Stroke. 1986 Jul 1;17(4):731-7.

23. Davalos A, Fernandez-Real JM, Ricart W, Soler S, Molins A, Planas E, Genis D. Iron-related damage in acute ischemic stroke. Stroke. 1994 Aug 1;25(8):1543-6.

24. Choi KH, Park MS, Kim JT, Nam TS, Choi SM, Kim BC, Kim MK, Cho KH. The serum ferritin level is an important predictor of hemorrhagic transformation in acute ischaemic stroke. European journal of neurology. 2012 Apr 1;1 9(4):570-7.

*25.* Armengou A, Dávalos A, Fernandez-Real JM, Castillo J. Serum ferritin concentrations are not modified in the acute phase of ischemic stroke. Stroke. 1998 Jan 1;29(1):258-60.

*ORIGINAL ARTICLE*

# Frequency of Diabetic Retinopathy in Type 2 Diabetic Patients Having Microalbuminuria in a Tertiary Level Hospital in Bangladesh

HOSSAIN KN[1], AHMED JU[2], UDDIN KN[3]

***Abstract***

***Introduction: Diabetes Mellitus is one of the most common non-communicable disease which can damage the microvasculature of both retina and kidney simultaneously. This study was performed to find out the frequency of retinopathy in diabetic patients having microalbuminuria. This study aimed to determine the frequency of diabetic retinopathy in type 2 diabetic patients having microalbuminuria and to find out the association of diabetic retinopathy with the duration of diabetes, glycemic status, age and sex predominance and presence of co-morbidities.***

***Methods: This cross sectional study included 60 diabetic patients having microalbuminuria in BIRDEM General Hospital, Dhaka from July to December, 2013. Microalbuminuria was defined as urine albumin-creatinine ratio (ACR) in a spot urine sample between 30 to 300 mg/g. Retina was examined determined by direct fundoscopic examination in dilated pupil. Data was collected in questionnaire including laboratory investigation reports with informed written consent of patient.***

***Results: Total 60 adult patients were selected according to inclusion and exclusion criteria. The age group of 40 to 60 years constituted the highest proportion (48.3%) of the respondents. Among the study subjects 36.7% were hypertensive, 20% had dyslipidemia, 8.3% had ischemic heart disease and 3.3% had history of stroke and 31.7% had no co-morbidity. This study found that 76.7% of patients were suffering from diabetic retinopathy. Among those NPDR was found in 38.3%, PDR 3.3%, Pre proliferative retinopathy 13.3%, and Maculopathy 21.7%. The incidence of retinopathy among male and female patients was 60.0% and 40.0%, respectively. This study found statistically significant association of diabetic retinopathy with glycemic status and duration of diabetes.***

***Conclusion: Diabetic retinopathy is common in diabetic patients having microalbuminuria. Glycemic status and duration of diabetes are strongly associated with the development of diabetic retinopathy.***

***Key words: Diabetic retinopathy, Type 2 diabetic patient, Microalbuminuria***

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**Introduction:**

Diabetes Mellitus is a syndrome of chronic hyperglycemia due to relative insulin deficiency, insulin resistance or both. The global prevalence of diabetes mellitus has been reported to be 8.3% for the year 2011 and projected to rise to 9.9% in the year 2030. Number of people with diabetes has been estimated to be 366.2 millions in the year 2010 and has been projected to rise to 551.9 million in 2030.[1] The chronic complications of Diabetes Mellitus occur due to microvascular and macrovascular damage. Small blood vessels throughout the body are affected but the disease process is of particular danger in three sites: retina, renal glomerulus and nerve sheaths.[2]

One of the most dreadful complication of diabetes is nephropathy which is characterized by progressive increase in urinary albumin excretion accompanied by rising blood pressure relentless decrease in glomerular filtration rate culminating eventually in end stage renal failure.[3] The cumulative incidence of diabetic nephropathy in type 1 and 2 diabetes is approximately 30-35%. In the kidney, these changes may lead to increased trafficking of

1. Dr. Kazi Nazmul Hossain, Registrar, Department of Endocrinology, BIRDEM General Hospital.
2. Dr. Jamal Uddin Ahmed, Assistant Professor, Department of Medicine, BIRDEM General Hospital.
3. Prof. Dr. Khwaja Nazim Uddin, Professor, Department of Medicine, BIRDEM General Hospital.

**Address of Correspondence:** Dr. Kazi Nazmul Hossain, Registrar, Department of Endocrinology, BIRDEM General Hospital. E-mail: remon20k59@yahoo.com

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plasma proteins across the glomerular membrane and to the appearance of protein in the urine. The presence of urinary protein not only heralds the onset of diabetic kidney disease, but it may contribute to the glomerular and tubulointerstitial damage that ultimately leads to diabetic glomerulosclerosis. The strong relationship between proteinuria and a constellation of other diabetic complications supports the view that elevated urinary protein excretion reflects a generalized vascular disturbance that affects many organs, including the eyes, heart, and nervous system.[2]

Retinopathy is another important chronic complication of diabetes. Both CKD and retinopathy results from micro vascular damage inflicted by metabolic disturbances from diabetes. So the presence of one of these conditions may predict the presence of the other one. Indeed, there are several studies that found significant association between these two conditions.[4,5,6] Unfortunately there is little data regarding the association of nephropathy and retinopathy in Bangladeshi population. In this context, this study was carried out to identify the frequency of retinopathy in type 2 diabetic patient with microalbuminuria, attending BIRDEM General Hospital.

**Methods:**

This hospital based descriptive cross sectional study was carried out in BIRDEM (Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders) from July 2013 to December 2013 on type-2 diabetic patients having microalbuminuria. Patients meeting this criteria who came over the study period in endocrinology unit of BIRDEM General Hospital were included by purposive sampling. The patients of type-2 diabetes mellitus with microalbuminuria and normal serum creatinine were included in the study. Those with type-1 diabetes, overt proteinuria, urinary tract infection, high serum creatinine, glaucoma, mature cataract, gestational diabetes mallitus and patients who have received treatment for retinopathy were excluded. Microalbuminuria was defined as an urine albumin-creatinine ratio between 30 to 300 mg/g, measured in a spot urine sample.[7] Fundus was examined by direct ophthalmoscopy in dilated pupil. Data was collected in a pre-formed standard printed data collection form after taking written informed consent of the patient. Ethical clearance was taken from the Ethical Review Committee, Bangladesh Diabetic Association.

**Results:**

Among the 60 study subjects, the youngest respondent was 34 years old and the oldest aged 70 years. The age group of 40 to 60 years constituted the highest proportion (48.3%) of the respondents (Table-I). Sixty percent of the respondents were male, and 40% female. Regarding presence of co-morbidities, more than two third (36.7%) of the study subjects were hypertensive, 20.0% had dyslipidemia, 8.3% ischemic heart disease, 3.3% had stroke & 31.7% had no known co-morbidity (Figure-1).

**Table-I**

Distribution of the respondents by age (N=60)

| Age | n | % |
|---|---|---|
| ≤40 years | 12 | 20.0 |
| 40 - 60 years | 29 | 48.3 |
| > 60 years | 19 | 31.7 |
| Total | 60 | 100.0 |

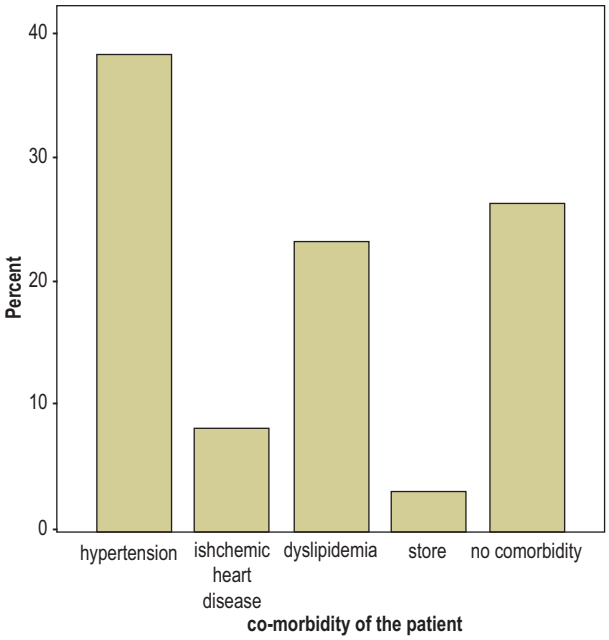


**Fig.-1:** *Presence of different co-morbidities among the respondents (N=60)*

Most of the patients (76.7%) had diabetic retinopathy on fundus examination, with only 23.3% having no retinopathy (Figure-2). Among the respondents with retinopathy, 38.3% had nonproliferative retinopathy, 21.7% had maculopathy, 13.3% had preproliferative retinopathy and 3.3% had proliferative retinopathy (Figure-3). When distribution of retinopathy was analysed among different age groups, it was found that in the age group of below 40 years, frequency of diabetic retinopathy was 23.91% , while in 40 to 60 years age group it was 47.83% and above 60

years, it was 28.26% (Figure-4). Male patients suffered more from retinopathy, with 69.6% of the male patients having retinopathy, while it was only 30.4% in females (Table-II).

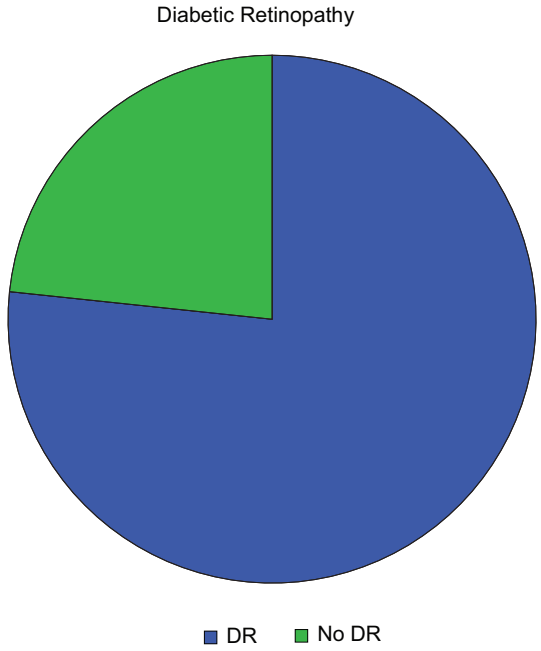


**Fig.-2:** *Frequency of diabetic retinopathy among the study subjects (N=60)*

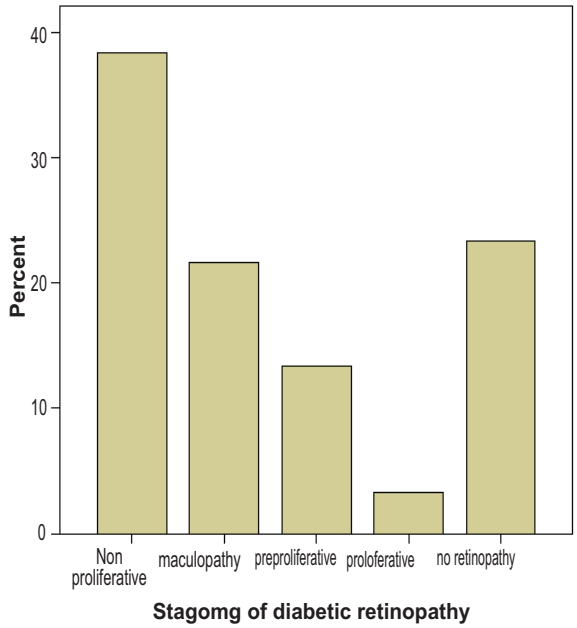


**Fig.-3:** *Types of diabetic retinopathy among the study subjects (N=60)*

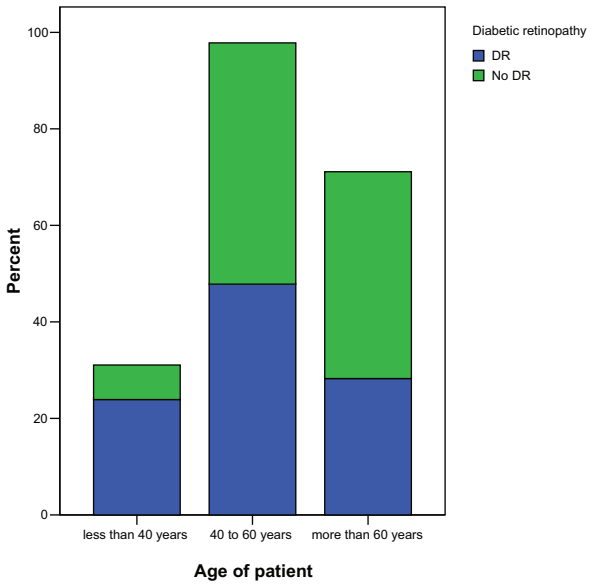


**Fig.-4:** *Distribution of diabetic retinopathy among different age groups (N=60)*

**Table-II**

*Distribution of diabetic retinopathy according to sex (N=60)*

| | Diabetic Retinopathy | No Diabetic Retinopathy |
|---|---|---|
| Male | 32 (69.6%) | 4 (28.6%) |
| Female | 14 (30.4%) | 10 (71.4%) |
| Total | 46 | 14 |

Among the patients having diabetic retinopathy, 34.8% had concomitant hypertension, and the association of hypertension with diabetic retinopathy was not significant (P= 0.305) (Table-III). Poor glycemic status was also significantly associated with diabetic retinopathy, as 60.9 % of those having $HbA_{1c} \geq 10\%$ were suffering from this condition (P<0.004) (Table-IV). Long Duration of diabetes was also significantly associated with retinopathy, as 56.5% of patients with having diabetes for >10 years had retinopathy (Table-V).

**Table-III**

*Association of hypertension with diabetic retinopathy (N=60)*

| | Diabetic Retinopathy | No Diabetic Retinopathy | P |
|---|---|---|---|
| Hypertensive | 16 (34.8%) | 7 (50.0%) | 0.305 |
| Normotensive | 30 (65.2%) | 7 (50.0%) | |
| Total | 46 | 14 | |

**Table-IV**

*Association of diabetic retinopathy with glycemic status (N=60)*

| HbA1c | Diabetic Retinopathy | No Diabetic Retinopathy | P |
|---|---|---|---|
| **<7%** | 1 (2.2%) | 4 (28.6%) | |
| **7 to 10%** | 17 (37.0%) | 6 (42.9%) | 0.004 |
| **>10%** | 28 (60.9) | 4 (28.6%) | |
| Total | 46 | 14 | |

**Table-IV**

*Association of retinopathy with duration of diabetes (N= 60)*

| Duration of DM | Diabetic Retinopathy | No Diabetic Retinopathy | P |
|---|---|---|---|
| <5 year | 3 (6.5%) | 7 (50.0%) | |
| 5 To 10year | 17 (37.0%) | 3 (21.4%) | 0.001 |
| >10 year | 26 (56.5%) | 4 (28.6%) | |
| Total | 46 | 14 | |

**Discussion:**

The objective of this cross sectional study was to find out the frequency of diabetic retinopathy in type-2 diabetes patients having microalbuminuria. It was found that among the 60 study subjects, 76.7% were suffering from diabetic retinopathy have microalbuminuria. Among those NPDR was found in 38.3%, PDR in 3.3%, pre proliferative retinopathy in 13.3%, and maculopathy in 21.7%.

Several studies have found that microalbuminuria is a predictor of retinopathy in diabetic patients. Cruickshanks et al carried out a prospective study on 1139 diabetic patients who did not have hematuria, gross proteinuria, or a history of renal disease, to find out the association between microalbuminuria and diabetic retinopathy. After a mean follow up period of 4 years, it was found that participants with microalbuminuria were 1.7 to 3.2 times as likely to have retinopathy as those without microalbuminuria, in univariate analyses. This relationship remained after controlling for other potential confounders such as glycemia, hypertension, smoking, and duration of diabetes, although it was of marginal statistical significance in younger-onset individuals with diabetes.[8] Manaviat et al studied 590 type-2 diabetes patients for retinopathy and microalbuminuria, and found that there was significant association between them (P=0.001). Among the patients having microalbuminuria, 18.9% had mild NPDR, 16.8% had moderate NPDR, 2.8% had severe NPDR and 4.9% had PDR.[9] Sobngwi et al in their study found that among the 34 patients having microalbuminuria, 21(61.76%) had retinopathy, with 16 having background retinopathy, 4 having NPDR and one having PDR.[10] Vigstrup et al conducted a prospective cohort study on 43 patients and concluded that that even a slightly raised UAE (Urinary Albumin Excretion), far below the level of clinical proteinuria, is a strong predictor with respect to development of proliferative diabetic retinopathy, as well as nephropathy. Their study also showed that diabetic patients with a normal or nearly normal UAE have a very small risk of developing proliferative changes over the next 10 years. Their study recommends to use UAE to select those patients needing a closer control and those where control could be less frequent.[11]

Our study shows that the frequency of retinopathy is more in the age group of 40 to 60 years. That age is a risk factor for retinopathy as well as other vascular complications of diabetes is a well known fact. Manaviat et al found in their study that increasing age is significantly associated with the development of diabetic retinopathy (P= 0.014).[9] Sobngwi et al found that diabetic retinopathy is significantly associated with age (P<0.001).[10]

The present study found a male preponderance in diabetic retinopathy, although there is controversy regarding the association of diabetic retinopathy with sex. Stratton et al followed up 1919 patients with type-2 diabetes and found that the incidence of retinopathy was the same in men and women, but in the multivariate model women had lower relative risk (RR) for progression (RR=0.54, 95% CI 0.37 to 0.80).[12] However, Kohner et al found in their multicenter, randomized, controlled clinical trial on 2964 patients that retinopathy was more prevalent in men than women, although this could not be explained by the major risk factors, as women had higher blood glucose and blood pressure levels in their study.[13]

There was significant association of duration of diabetes with diabetic retinopathy in our study, but no significant association was found with hypertension. Previous studies have demonstrated that both hypertension and duration of diabetes are independent risk factors for diabetic retinopathy. Yau et al found that the prevalence of any diabetic retinopathy increased with diabetes duration (21.1 vs. 76.3%, comparing <10 with ≥20 years), $HbA_{1c}$ (18.0 vs. 51.2%, comparing levels <7.0 with ≥9.0%), and blood pressure (30.8 vs. 39.6%, comparing blood pressure <140/90 or ≥140/90).[14] Wong et al found that independent risk factors for any retinopathy were longer

diabetes duration (odds ratio [OR], 1.07; 95% CI, 1.04–1.09, per year increase), higher $HbA_{1C}$ (OR, 1.21; 95% CI, 1.10–1.33, per % increase), hypertension (OR, 1.85; 95% CI, 1.04–3.30) and older age (OR, 0.73; 95% CI, 0.57–0.93, per decade increase).[15] Cruickshanks et al in their study found that the mean duration of diabetes was 16.5 ± 9.9 years in the younger age group, 16.9 ± 7.5 years in older age group (using insulin) and 11.6 ± 6.2 years in older age patients not on insulin.[8]

Poor glycemic control was found to be an important factor associated with diabetic retinopathy in our study. Manaviat et al found that HbA1c has got significant association with the occurrence of retinopathy (P=0.01).[9] Stratton et al found that there was a highly significant positive association of HbA1c with incidence and progression of retinopathy in both univariate and multivariate analysis.[12] Wong et al also found similar results.[15]

Our study had some limitations. It was performed in a tertiary care institute on hospitalized patients, which may not be representative of the whole population. Random sampling was not applied in this study. Sample size was very small, and included only patients with type-2 diabetes. Due to time and resource constraints, follow up of the study subjects were not possible.

**Conclusion:**

From this study we can conclude that there is increased prevalence of diabetic retinopathy in type-2 diabetic patients having microalbuminuria. Therefore, diabetic patients having microalbuminuria should be monitored more closely and more frequently for the development and/or progression of diabetic retinopathy. Similarly the patients having diabetic retinopathy should be screened for microalbuminuria to detect diabetic nephropathy at an early stage, and appropriate steps should be taken to prevent or delay the progression of these complications by addressing the other modifiable risk factors, including hypertension and glycemic status.

**References:**

1. Whiting DR, Guariguata L, Weil C, Shaw J. IDF Diabetes Atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Research and Clinical Practice 2011; 94 (3): 311-321.
2. Perna A, Remuzzi G. Abnormal permeability to proteins and glomerular lesions: A meta-analysis of experimental and human studies. Am J Kidney Dis 1996; 27: 34-41.
3. Mogensen CE. Microalbuminuria predicts clinical proteinuria and early mortality in maturity-onset diabetes. N Engl J Med 1984; 310: 356-360.
4. John L, Rao PS, Kanagasabapathy AS. Prevalence of diabetic nephropathy in non-insulin dependent diabetics. Indian Journal of Medicine 1991; 94: 24-29.
5. Lee KU, Park JY, Kim SW, Lee MI, Kim GS, Park SK, Park JS. Prevalence and associated features of albuminuria in Koreans with NIDDM. Diabetes Care 1995; 18: 793-799.
6. Estacio RO, McFarling E, Biggerstaff S, Jeffers BW, Johnson D, Schrier RW. Overt albuminuria predicts diabetic retinopathy in Hispanics with NIDDM. American Journal of Kidney Disease 1998; 31: 947-953.
7. Toto RD. Microalbuminuria: Definition, Detection, and Clinical Significance. The Journal of Clinical Hypertension 2004; 6: 2–7.
8. Cruickshanks KJ, Ritter LL, Klein R, Moss SE. The Association of Microalbuminuria with Diabetic Retinopathy: The Wisconsin Epidemiologic Study of Diabetic Retinopathy. Ophthalmology 1993; 100: 862-867.
9. Manaviat MR, Afkhami M, Shoja MR. Retinopathy and microalbuminuria in type II diabetic patients. BMC Ophthalmol. 2004; 4:9.
10. Sobngwi E, Mbanya J, Moukouri EN, Ngu KB. Micro-albuminuria and retinopathy in a diabetic population of Cameroon. Diabetes Research and Clinical Practice 1999; 44: 191–196.
11. Vigstrup J, Mogensen CE. Proliferative diabetic retinopathy: at risk patients identified by early detection of microalbuminuria. Acta Ophthalmologica 1985; 63: 530-534.
12. Stratton IM, Kohner EM, Aldington SJ, Turner RC, Holman RR, Manley SE, Matthews DR. UKPDS 50: risk factors for incidence and progression of retinopathy in Type II diabetes over 6 years from diagnosis. Diabetologia 2001;44(2):156-63.
13. Kohner EM, Aldington SJ, Stratton IM, Manley SE, Holman RR, Matthews DR, Turner RC, for the United Kingdom Prospective Diabetes Study. United Kingdom Prospective Diabetes Study, 30: Diabetic Retinopathy at Diagnosis of Non–Insulin-Dependent Diabetes Mellitus and Associated Risk Factors. Arch Ophthalmol 1998;116(3):297-303.
14. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, Chen SJ, Dekker JM, Fletcher A, Grauslund J, Haffner S, Hamman RF, Ikram MK, Kayama T, Klein BE, Klein R, Krishnaiah S, Mayurasakorn K, O'Hare JP, Orchard TJ, Porta M, Rema M, Roy MS, Sharma T, Shaw J, Taylor H, Tielsch JM, Varma R, Wang JJ, Wang N, West S, Xu L, Yasuda M, Zhang X, Mitchell P, Wong TY; Meta-Analysis for Eye Disease (META-EYE) Study Group. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care 2012; 35(3):556-64.
15. Wong TY, Cheung N, Tay WT, Wang JJ, Aung T, Saw SM, Lim SC, Tai ES, Mitchell P. Prevalence and risk factors for diabetic retinopathy: the Singapore Malay Eye Study. Ophthalmology 2008;115(11):1869-75.

## ORIGINAL ARTICLE

# Gastroprotective Effect of Aqueous Extract of *Glycyrrhiza Glabra* or Licuorice (Jastimodhu) Root on Ibuprofen Induced Gastric Ulcer in Experimental Rats

HAQUE S[1], KHAN I[2], AKTAR MT[3], QUADIR R[4], AHASAN F[5] , ZABIR SM[6]

***Abstract***

***Introduction: The objective of present study is to evaluate the gastroprotective activity of aqueous extract of Glycyrrhiza Glabra or Licuorice or Jastimodhu root. The cause of ulceration in patients is mainly due to hyper secretion of gastric juice and pepsin. In traditional system of medicine a number of herbal preparations have been used for the treatment of peptic ulcer. The anti-ulcer activity of aqueous extract of Glycyrrhiza Glabra or licuorice root was investigated by ibuprofen induced ulcer in rats.***

***Methods: The study was carried out in the Department of Pharmacology of Dhaka Medical College from July 2014 to June 2015.The rats were provided with aqueous extract of Glycyrrhiza Glabra or licuorice root (500mg /kg body wt) orally by gastric tube for 5 days. Then ibuprofen (200 mg/kg body wt) were given to all group after 24 hour fasting on the 7$^{th}$ day orally by gastric tube. After 4 hour of administration of ibuprofen, all rats were sacrificed. Stomach will be dissected out and collected for morphological and histopathological examination.***

***Results: Rats pretreated with aqueous extract of Glycyrrhiza Glabra showed significant decrease in stomach damage both macroscopically and microscopically as compared to control.***

***Conclusion: This study indicates aqueous extract of Glycyrrhiza Glabra have potential gastroprotective activity.***

***Keywords: Gastroprotective, Glycyrrhiza Glabra (Jastimodhu).***

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**Introduction:**

Peptic ulcer is defined as disruption of the mucosal integrity of stomach and/or duodenum leading to a local defect or excavation due to active inflammation. Upper gastrointestinal integrity is dependent upon the delicate balance between naturally occurring protective factor as mucus or prostaglandins and damaging factor as hydrochloric acid present in the digestive juices. An imbalance causes peptic ulcer formation and destruction of gastrointestinal tract mucosal lining. The ulcer irritates surrounding nerves and causes considerable amount of pain.[1, 2]

There are three important cause of peptic ulcer disease: NSAIDS, Helicobacter pylori infection and acid hypersecretory states such as Zollinger-Ellison Syndrome. Today there are two main approaches for treating peptic ulcer .The first deals with reducing the production of gastric acid and the second with reinforcing gastric mucosal protection. Although a number of antiulcer drugs such as $H_2$ receptor antagonist, proton pump inhibitors and cytoprotectants are available, these entire drug have side effect and limitation.[3,4]

Herbal Medicine is defined as branch of science in which plant based formulations are used to alleviate the diseases.

1. Dr. Sumona Haque, Lecturer, Department of Pharmacology, Shaheed Suhrawardy Medical College, Dhaka.
2. Prof. Dr. Ismail Khan, Professor, Department of Pharmacology, Dhaka Medical College, Dhaka.
3. Dr. Muqbula Tasrin Aktar, Assistant Professor, Department of Pharmacology, Shaheed Taj Uddin Ahmad Medical College, Gazipur.
4. Dr. Rukhsana Quadir, Lecturer, Department of Pharmacology, Dhaka Medical college, Dhaka.
5. Dr. Faizul Ahasan, Department of Pharmacology, Dhaka Medical College, Dhaka.
6. Dr. Sharif Mohammad Zabir, Lecturer, Department of Pharmacology, Dhaka Medical college, Dhaka.

**Address of Correspondence**: Dr. Sumona Haque, Lecturer, Department of Pharmacology, Shaheed Suhrawardy Medical College, Dhaka, Email : safwanshadab@gmail.com

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Early in the twenty century herbal medicine was a prime health care system as antibiotics or analgesics were not available. With the development of allopathic systems of medicine, herbal medicine gradually lost its popularity among people and it was based on the fast therapeutic action of synthetic drugs. Almost a century has passed and we have witnessed limitations of allopathic systems of medicine. Lately herbal medicine has gained momentum and it is evident from the fact that certain herbal remedies peaked at part with synthetic drugs. According to a study from U.S, 60-70% patients living in rural areas are dependent on herbal medicine for their day to day diseases. Substances derived from the plants remain the basis for a large proportion of the commercial medications used today for the treatment of heart disease, high blood pressure, liver disease, pain, asthma, and other problems.[5]

Liquorice is one of the most commonly used herbs in Western herbal medicine. Liquorice has been used in medicine for more than 4000 years. The earliest record of its use in medicine is found in "code Humnubari" (2100 BC). It was also one of the important plants mentioned in Assyrian herbal (2000BC). Hippocrates (400 BC) mentioned its use as a remedy of ulcers and quenching of thirst. The drug was also mentioned by Theophrastus and Dioscorides . In traditional Siddha system of medicine, liquorice is used as a demulcent, expectorant, anti-tussive , laxative and sweetener.[6]

The present study was designed to investigate the gastroprotective effect of aqueous extract of *Glycyrrhiza Glabra* or licuorice root.

**Methods:**

The study was carried out in the Department of Pharmacology of Dhaka Medical College from July 2014 to June 2015.

**Plant material**: The plant *Glycyrrhiza Glabra* or Licuorice root were purchased from BCSIR laboratory & authenticated by National Herbarium, Mirpur, Dhaka.

**Preparation of aqueous extract:** Preparation of the aqueous extracts was performed in the department of Chemistry of Dhaka University, Dhaka.

**Procedure:** Aqueous extract of Liquorice was prepared using 80 gram of powdered plant in conical flask with 300 ml of distilled water and kept it for 3 days. After this the residue were removed by filtration using a mesh & filter funnel and found 200 ml. The filtered material then extracted by the rotator evaporator to obtain 5 gm aqueous extract.

**Animals:**

A total number of 30 healthy Wister albino rats of both sex weighting 150-200 grams were selected for study and collected from ICDDR'B Dhaka.

**Ibuprofen:**

Ibuprofen was obtained from local market as they are available as drugs. The dose of ibuprofen was calculated as 200 mg/kg body weight then calculated amounts was dissolved in distilled water and was administered orally at a volume of 1ml/40mg body wt.[7]

**Animal Experimentation:**

The experiment was divided into two parts: Experiment- I and Experiment -II.

**Experimental design-I**

This part of the experiment was carried out to demonstrate the effect of ibuprofen on gastric tissue on normal rat. It was comprised of 18 rats which were divided into 3 groups each having 6 rats. These are labeled as Group-A, Group-B and Group- C.

**Group-A:** This group served as control group was received normal diet and 1ml of distilled water (5ml/kg body wt) for 7 day orally by gastric tube.

**Group-B:** Gastric damage experimental group was received 1 ml distilled water (5ml/kg body wt) for 5 day and 200 mg/kg of ibuprofen on 7$^{th}$ day after 24 hr fasting.

**Group-C:** This group was provided with 1 ml of distilled water (5ml/kg body wt) and aqueous extract of *Glycyrrhiza Glabra* (500mg/kg body wt) orally by gastric tube for 7 day.

**Experimental design-II**

This was comprised of 12 rats. They were divided into 2 groups each containing 6 rats labeled as Group-D, Group-E. This part of experiment was carried out to demonstrate the effect of pretreatment of aqueous extract on ibuprofen induced gastric ulcer in experimental rats.

**Group-D:** Gastric damage control group was received normal diet, distilled water for 5 day.

**Group-E:** They were served with aqueous extract of *Glycyrrhiza Glabra* (500mg/kg body wt) orally by gastric tube for 5 day.

Then Ibuprofen (200 mg/kg body wt) was given to all group after 24 hour fasting on the 7$^{th}$ day orally by gastric tube.

After 4 hour, all rat were sacrificed, stomach were dissected out and collected for morphological and histopathological examination.

**Collection of the stomachs:**
Abdomen was opened by "T" incision which is a vertical incision from xiphoid process to the upper part of symphysis pubis and a transverse incision extending 2 cm laterally on each side from top to vertical line. The stomach was separated from the rest of the small intestine. The stomach was opened along the greater curvature and gently rinsed under running tap water and were spread on paraffin plate. Lesion in the glandular part of the stomach was observed with the help of dissecting microscope grossly (10x)with a square grid eye piece to access the formation of ulcer.

**Parameter studied:**
**Morphological parameter:**

1. Number of lesion per rat in each group.
2. Individual lesion length and breadth in mm for each group.
3. Individual lesion area in square mm for each group.
4. Mean ulcer index (sum of length of all lesions in each stomach) in mm for each group.
5. Percentage inhibition of licuorice extract.

**Histopathological parameter:**
Degree of damage were determined depending on the extent of involvement of lesion in stomach.

Gross & microscopic examination and measurement of the morphological lesion**:**
The mucosa were washed in running tap water. Then the whole mucosa of the stomach of each rat were examined very carefully with the help of dissecting microscope(x20) with the aid of square grid eye piece (1 mm square).The ulcer were counted with the help of hand lens (5 times magnification power) and visible big lesions were measured with the help of hand lens and mm scale. Oculomicrometer were used for examination of mucosal surface and the measurement of small lesion length, breadth & area. The graduation of oculomicrometer was standardized by comparing those with the marking of the stage micrometer following way-

**When one magnification was used:**
10 graduation of oculomicrometer = 1mm of stage micrometer

Or 1 graduation of oculomicrometer = 0.1 mm of stage micrometer

Similarly with two (x2),(x4),(x10)magnification,1 graduation of oculomicrometer was equal to 0.05,0.025 respectively. The maximum length, breadth and area of each lesion were measured and the mean lesion area and mean ulcer index per rat in each group was calculated and used in lesion index for each group.

The ulcer index or lesion index (UI) were determined as the sum of length of all gastric lesions in mm for each stomach and the inhibition percentage were expressed by the following formula

$$\text{Inhibition percentage (\%I)} = [(UI_{control} - UI_{treated}) \div UI_{control}] \times 100.$$

**Results**:

All relevant information of each rat was recorded in a predesigned data collection sheet. Collected data was tabulated and statistical analysis was done by appropriate significance test (Unpaired student's 't' test).

**Table I**

*Showing the effect of Ibuprofen on mean number of lesions, mean lesion length, mean lesions breadth, mean lesions area and lesions index in each group in experiment- I*

| Groups | Mean number of lesions | Mean lesions length | Mean lesions breadth | Mean lesions area | Lesion index |
|---|---|---|---|---|---|
| Group A N=6 | 0 | 0 | 0 | 0 | 0 |
| Group B N=6 | 5.33 ± 0.81 | 5.56± 0.61 | 1.99±0.23 | 11.07± 1.55 | 26.32 ± 3.89 |
| Group C N=6 | 0 | 0 | 0 | 0 | 0 |

**Table II**

*Showing the effect of pre-treatment of aqueous extracts of Glycyrrhiza Glabra on mean number of lesions, mean lesions length, mean lesions breadth, mean lesion area and lesions index on each group in experiment- II*

| | Group D | Group E | P value |
|---|---|---|---|
| Mean number of lesions (± SD) | 5.5 ± 1.04 | 3.66 ± 0.81 | < 0.01 |
| Mean lesion length (± SD) | 8.05 ± 2.54 | 2.93 ± 0.69 | < 0.01 |
| Mean lesion breadth (±SD) | 2.61 ± 0.51 | 0.65 ± 0.18 | < 0.001 |
| Mean lesion area (± SD) | 21.93 ± 9.97 | 1.87 ± 0.52 | < 0.001 |
| Mean lesion index (± SD) | 37.71 ± 7.47 | 9.17 ± 1.46 | < 0.001 |

**Discussion:**

The peptic ulcer results from an imbalance between aggressive factors and the maintenance of mucosal integrity through the endogenous defense mechanism.

In present study, ibuprofen was used as agent to induce stomach ulcer in rats. The Ibuprofen is what is called a nonselective cyclooxygenase inhibitor which means it inhibits all types of cyclooxygenase, not just the ones that produce inflammatory mediators especially $PGI_2$ and $PGE_2$. Ibuprofen inhibit prostaglandin involved in the blood supply to the stomach as well as blood supply to the kidney. Study Showed that oral administration of ibuprofen (200 mg/kg ) to fasted rats produced gastric mucosal damage and pretreated with *Momordica Dioica extract* could effectively and dose dependently prevent this gastric damage. Dephour *et al* showed oral administration of ibuprofen to fasted rats produced gastric damage and pretreated with oral administration of ***Glycyrrhiza Glabra*** root extract could effectively and dose-dependently prevent such damage.

Abid *et al* in another study showed that oral administration of ibuprofen produce lesion of gastric mucosa and pretreated with *Glycyrrhiza Glabra* extract before the administration of ibuprofen could effectively and dose dependently prevent the formation of such lesion.

Both PGE and PGF induce the secretion of polysaccharide material in the stomach known as mucin which acts as a protective agent against potential stomach ulceration induced by HCl acid and pepsin. Ibuprofen cause gastric ulcers by inhibiting the secretion of this cytoprotective substance. Aqueous extract of *Glycyrrhiza Glabra* stimulates gastric mucus production, enhances the rate of incorporation of various sugars into gastric mucosal glycoproteins, promotes mucosal cell proliferation, inhibits mucosal cell exfoliation, inhibits prostaglandin degradation, increases the release of PGE2 and reduces the formation of thromboxane B2 and regulates DNA and protein synthesis rates in gastric mucosa.[10,11,12.] Ibuprofen cause ulceration by generation of oxygen derived free radicals (ROS). Preventive endogenous antioxidants, such as SOD and catalase enzymes are the first line of defense against ROS. Reduced glutathione is a major scavenger of free radicals in the cytoplasm and an important inhibitor of free radical mediated lipid peroxidation. The presence of some antioxidant phytoconstituents might have protected the gastric mucosa from free radical induced damage. The root of Glycyrrhiza species is one of the richest sources of biological active compounds such as phenolic and flavanoid compounds. Licuorice flavonoids were found to have exceptionally strong antioxidant effects 100 times stronger than vitamin E. The flavonoids were found to be 2.3 mg/100 mg dry extract of aqueous extract of licorice root. Study suggests that licorice extract can be used as a potential source of natural antioxidant.[8, 9,13, 14]

Aqueous extracts of licorice have been shown to inhibit the adhesion of *H. pylori* to gastric mucosa, as well as the growth of antibiotic resistant strains, suggesting multiple mechanisms of action for its anti-ulcer benefit. Study provides hope that aqueous extract of *Glycyrrhiza Glabra* can form the basis for an alternative therapeutic agent against H. pylori.[15, 16]

**Conclusion**:

In Conclusion this study established that *Glycyrrhiza Glabra* or Licuorice (Jastimodhu) has gastroprotective ability following consumption of ibuprofen. For human consumption, further pharmacological test needs to be conducted to determine appropriate dose for human and to uncover any adverse effects which may arise from *Glycyrrhiza Glabra* (Jastimodhu).

**References:**

1. Kasper DL, Fauci AS, Longo DL, Hauser SL, Jameson JL. Harrison's Principle of Internal Medicine. 16th ed. Vol. II, McGraw Hill: Medical Publishing Division, p.1746-62.
2. Jamal A, Siddiqui A, Tajuddin, Jafri MA. A review on gastric ulcer remedies used in unani system of medicine. Nat Prod Rad 2006; 5(2):153-59.
3. Blaser, M.J. "Gastroenterology". 1987, vol.93: 317-83.
4. Soll AH, Berglindn, Physiology of isolated gastric glands and pareital cell receptor and effectors regulating function and Physiology of the gastro Intestinal Tract. 2nd edition. 1987; 883-908.
5. Gupta SK, Singhvi JI,Herebal & Hepatoprotective drugs acting on PU & Liver Disease, International journal of pharmacy & technology.ISSN:0975-766X.
6. Jatav VS, Singh SK, Sharma AK. Recent Pharmacological trends in Glycyrrhiza*glabra*. International Journal of Pharmaceutical Frontier Research 2011; 1: 170-85.
7. Kumar RA , Kumar SI, YakaiahVangoori.evaluation of atiulcer activity of ethanolic extract of Momordica Dioica on pylorous ligature induced and ibuprofen induced ulcer in albino rats a, IJMRHS.2013.
8. Ligha AE, and Fawehinmi HB. Protection by Liquorice in Alcohol Induced Gastric Mucosa Damage Pakistan Journal of Nutrition 2009; 8 (10): 1532-1536.
9. Abid Shaima, Mohammad J, Abid Haider. Effect of Liquorice and Chamomile Extract in the management of gastric ulcer in rats; Medical journal of Babylon 2012-vol.9 no-3.
10. Turpie AG, *et al*. Clinical trial of deglycyrrhizinized liquorice in gastric ulcer. 1969 Apr; 10(4):299-302.

11. Chandrasekaran CV, *et al*. Dual inhibitory effect of Glycyrrhiza glabra (GutGard™) on COX and LOX products. *Phytomedicine*. 2011 Feb 15; 18(4):278-84.

12. Morgan AG, *et al*. Comparison between cimetidine and Caved-S in the treatment of gastric ulceration and subsequent maintenance therapy. 1982 Jun; 23(6):545-51.

13. Nasir M .Pathological changes on stomach of rats treated with high dose of ethanol and protective role of Licuorice ethanolic extract .department of pathology.Iraq.

14. Suhayla KM. Antioxidant Activities of Aquous and ethanolic Extracts of Licuorice root. Pakistan journal of nutrition 2014;13(5):267-270.

15. Krausse R, Bielenberg J, Blaschek W, Ullmann U. *In vitro* anti-Helicobacter pylori activity extractum liquiritiae, glycyrrhizin and its metabolites. *J Antimicrob Chemother* 2004; 54:243-246.

16. Fukai T, Marumo A, Kaitou K, Kanda T, Terada S, Nomura T. Anti-Helicobacter pylori flavonoids from licorice extract. *Life Sci* 2002; 71: 1449-1463.

## REVIEW ARTICLE

# Urinary Tract Infection in Children: An Update

ISLAM QR[1], KARIM AKMR[2], AKHTAR G[3], MALEK A[4], PAUL SK[5].

***Abstract***

***Urinary tract infection (UTI) is one of the most common bacterial infections seen in children. It is a major problem that is frequently encountered by pediatric health care providers at all levels. UTI is a significant cause of morbidity in infants and children, though infrequently associated with mortality. Most children have a single episode and recover promptly, but it may be recurrent which is more common in girls than boys. UTI in children may lead to development of renal scarring, hypertension and renal impairment, even end-stage renal disease (ESRD). If there is abnormality of urinary tract, the risk of recurrent UTI and its consequences are further increased. Signs and symptoms of UTI vary depending on the child's age and the part of the urinary tract infected. Though fever, abdominal pain and dysuria are the common features; establishing the diagnosis is difficult in early childhood due to the lack of specific urinary symptoms, difficulty in urine collection and contamination of samples. Occurrences of a first-time symptomatic UTI are highest in boys and girls during the first year of life and markedly decreased thereafter. Febrile infants younger than 2 months constitute an important subset of children who may present with fever without a localizing source. The workup of fever in these infants should always include evaluation of UTI. A young child with a high fever and no other symptoms, has a 1 in 20 (05%) chance of having UTI. This review article aims at highlighting the update of epidemiology, etiology, pathogenesis, diagnosis and treatment of such a devastating problem.***

***Key Words: Urinary tract infection, simple UTI, complicated UTI, treatment, prevention, children.***

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**Introduction:**

Urinary tract infection implies presence of actively multiplying organisms in the urinary tract along with symptoms of infection.[1] It is responsible for 3% of all infections among the pediatric population.[2] Population based studies show that 2% of boys and 7% of girls had at least one UTI by 7 years of age. Large prospective studies estimate UTI incidence of 7% in febrile infants and young children.[3] According to National Institute for Health and Clinical Excellence (NICE) guideline 2007, UTI affects at least 3.6% of boys and 11% of girls.[4] Children of 1-5 years are more vulnerable to be affected by UTI; and majority of the patients suffer from fever, abdominal pain, dysuria, decreased appetite, foul smelling urine and failure to thrive (FTT).[5] UTI is mainly due to the ascending infection from the urethra, but the diagnosis of UTI in young children is especially important as it may be the marker of urinary tract abnormalities.[5] Febrile infants younger than 2 months constitute an important subset of children who may present with fever without localizing source and work up of fever in these infants should always include evaluation of UTI.[6] A young child with high fever and no other symptoms, has a 1 in 20 (05%) chance of having a UTI.[7]

The common pathogens causing UTI are gram-negative bacteria; such as Escherichia coli (E.coli), Klebsiella spp, Proteus spp and Pseudomonas. Staphylococcus saprophyticus and Streptococcus fecalis are occasionally observed. Of these, E. coli is the most common cause of UTI accounting 85% of community acquired and 50% of hospital infection. About 90% of first symptomatic UTI

1. Dr. Qauzi Rakibul Islam, Associate Professor and Head, Department of Pediatrics, Green life Medical College, Dhaka
2. Dr. A. K. M. Rushdul Karim, Associate Professor, Pediatric Nephrology Unit, Department of Pediatrics, Mymensingh Medical College, Mymensingh
3. Dr. Gulshan Akhtar, Associate Professor, Department of Pediatrics, Green life Medical College, Dhaka
4. Dr. Abdul Malek, Assistant Professor, Department of Pediatrics, Green life Medical College, Dhaka
5. Professor Dr. Shanjoy Kumar Paul, Head, Department of Pediatric Nephrology, Sir Salimullah Medical College, Dhaka

**Correspondence:** Dr. Qauzi Rakibul Islam, Associate Professor and Head, Department of Pediatrics, Green life Medical College, Dhaka-1205. E-mail: qrislambd@yahoo.com

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and 70% of recurrent UTI are due to E. coli.[3,8,10] In recent years, wide and indiscriminate use of antibiotics have resulted an increasing incidence of resistant pathogens of UTI all over the world. These increasing occurrence of resistance of micro organisms to antimicrobial agents, especially in hospitalized patients, require rapid identification of pathogens.[2,9] Furthermore, large number of children with UTI are also seen in the community by general practitioners, but there is frequently delay in treatment and not all are referred for further investigations, even in presence of clear indication.[10] So, it is important to optimize diagnostic and management strategies of this preventable cause of renal damage by preserving the renal function of growing kidney.

**Epidemiology**

The first symptomatic UTI usually occurs in the first year of life, particularly in boys. In neonates, the incidence of UTI is 01% in term and 03% in preterm babies.[3] In infancy, especially in first 3 months of life UTI is seen more commonly in boys (3.7%) than in girls (2%).[11] Beyond 1-2 years, it occurs more commonly in girls with a male : female ratio of 1:10. In male, UTI is much more common in uncircumcised boys.[12] Girls suffer from first UTI usually by the age of 5 years, with peaks during infancy and the time of toilet training.[12] Obstructive lesion may be found in 5-10% of boys investigated for UTI and 30% of patients show the presence of vesico-ureteric reflux (VUR).[3] In studies from India[9,11] and Nepal[1] culture positive UTI was found in 16.37- 45% of cases of clinically suspected UTI. UTI may be more frequent in girls suffering from sexual abuse and their diagnosis should not be overlooked during assessment.[10] In a study from India, renal scarring was noted in 33 (47.8%) children out of 69 cases with culture positive UTI, who were enrolled for dimercaptosuccinic acid (DMSA) scan.[11]

**Etiology**

Colonic bacteria are primarily responsible for UTI in children. Elimination of normal periurethral protective flora by broad spectrum antibiotics or colonization with uropathogenic enteric organisms predisposes to UTI.[3] About 85-90 percent of first UTI in boys and girls,[3,10] and 70 percent of recurrent infection are due to E. coli.[3] The predominance of E. coli as the causative pathogen of UTI are also found in some other studies.[1,2,5,6] Other common bacteria causing UTI are Klebsiella spp., Proteus spp., Pseudomonas spp., Enterococcus spp., and Staphylococcus.[5,10] Less virulent organisms such as Pseudomonas and Staphylococcus aureus can cause UTI in children with abnormal urinary tract.[10] In some series of reports, Proteus have been found as common pathogen as E. coli, particularly in boys older than 1 year of age.[12] Other than bacteria, UTI may be due to Candida albicans and fungi, particularly in preterm infants and immune compromised children.[3] Adenovirus and some other viruses also may cause UTI, especially in the form of cystitis with gross hematuria. Acute hemorrhagic cystitis may often be due to E. coli or adenovirus.[12] The peak age of UTI is bimodal, with one peak in infancy and other peak between age of 2-4 years ( at the time of toilet training for any child).[13]

**Pathogenesis**

Urine in the proximal urethra, urinary bladder and upper part of urinary tract are normally sterile. Mechanism that maintain the sterility of the urinary tract include urine acidity, free flow of urine, a normal emptying mechanism, intact uretero-vesical and urethral sphincters, and immunologic and mucosal barriers.[13] After birth, the periurethral area and the distal urethra become colonized with microorganisms that functions as defense of urinary tract and acts as a barrier against colonization by uropathogens. Hence, in early childhood enterobacter and enterococci are part of normal periurethral flora.[14] So, abnormality of these defense mechanisms predisposes and leads to pathogenesis of UTI, which with predisposing factors also depends on bacterial virulence. UTIs are caused by bacteria that get entry into the urinary tract by the skin around the genitalia and rectum, or by the blood stream from other parts of the body.[15] In neonatal period, hematogenic (bacteremia) spread is the main way of entry of microorganism in urinary tract to cause renal infection. Beyond the neonatal period, ascending infection is the main way to develop UTI. Extension of infection also may occur directly from vagina or intestine to the urinary tract through fistula.[3] Marked female preponderance beyond infancy are contributed by shorter female urethra and male circumcision.[13] Incidence of UTI in infants who are breastfeed is lower than those who are feed with formula and particularly for first 6 months of life.[3,12] Constipation with fecal impaction and sexual activity in girls leads to incomplete bladder emptying, and stasis of urine in bladder make them prone to UTI.[12]

Pathogenesis of UTI also depend on the capability of adhesion of the organisms to epithelial cells, a pre-requisite for their multiplication and induction of inflammation. This adhesion is mediated by the presence of bacterial pili or fimbriae on the bacterial surface. Bacteria having pili can adhere effectively to uroepitheliun and ascend. Some virulent bacteria may also produce a hemolysin causing

damage to the uroepitheliun.[3] There are two types of pili, type-1 and type-2. Type-1 is found on most of the strain of E. coli but type-2 only on certain strain of E. coli which are mostly responsible for pyelonephritis, as 76% to 94% of pyelonephritogenic strain of E. coli possess this.[12] There may have genetic basis that play role in the progression of simple cystitis to pyelonephritis. So, identification of some genetic components help to predict genetic recurrences in their offspring. HSPA1B, CXCR1, CXCR2, TLR4 and TGFâ1 are the genes supposed to be associated with recurrence of UTIs in the generation.[16] UTI in children are a marker of possible anatomical, and physiological factors, such as vesicoureteric reflux (VUR). VUR leads to repeated infections which may develop chronic pyelonephritis and renal scarring with risk of developing chronic kidney disease and end stage renal disease (ESRD).[11,13] This association is likely due to two factors that VUR predisposes to UTI and recurrent UTIs can worsen VUR.[13] In children with high-grade VUR (grade 4 & 5), long-term scarring is detected at 4 - 6 fold greater rate than children with low-grade (grade 1 to 3) VUR; and an 8 to 10 fold greater rate than child with no VUR.[13] However, controversy continues regarding the association of VUR with the pathogenesis of renal scarring, reflux nephropathy and pyelonephritis.[14] In one study, finding showed that scarring was present in 40% of refluxing kidneys and 43% of non-refluxing kidneys.[18]

**Classification of UTIs and some terminologies**

UTI may be **symptomatic** or **asymptomatic** and it may be **uncomplicated** or **complicated**.[10] The three basic types of UTIs are **pyelonephritis**, **cystitis** and **asymptomatic bacteriuria**.[12,14] When UTI occurs involving the renal parenchyma is termed as **pyelonephritis**. If it involves only pelvis without parenchymal involvement is termed as **pyelitis**. Pyelonephritis is the most common serious bacterial infection in infants younger than 24 months of age who have fever without an obvious focus.[12] When UTI involves the bladder only, it is called **cystitis**, and sometimes it may be associated with hemorrhage termed as **hemorrhagic cystitis**.[12] UTI in the form of cystitis is more common among girls after two years of age.[14] Children with a positive urine culture without any manifestation of infection is termed as **asymptomatic bacteriuria**.[14] It is more common in girls with an incidence of <01% in preschool age, but is rare in boys.[12] UTI involving the kidney and/or ureters is called **upper UTI** and when it involves urinary bladder and/or urethra is termed as **lower UTI**.[14,19]

**Recurrent UTI**

It is termed when the attacks of UTI fits with any of the following three situations-

- 2 or more episodes of UTI with acute pyelonephritis / upper UTI, or
- 1 episode of UTI with acute pyelonephritis / upper UTI plus 1 or more episodes of UTI with cystitis / lower UTI, or
- 3 or more episodes of UTI with cystitis / lower UTI.[20]

Recurrence after the first UTI is observed in 30% to 50% of children. Of these, in a majority it occur within three months of the initial episode; and E. coli is the most common organism causing recurrence. School age girls are the main sufferers and rarely occur in boys without underlying complicating factors.[3]

**Complicated (Atypical) UTI**

UTIs are termed as atypical or complicated when there is UTI with serious illness, poor urine flow, abdominal or bladder mass, raised serum creatinine, septicemia, failure to respond to treatment with suitable antibiotics within 48 hours, or infection with non-E. coli organism.[20]

**Risk factors related to urinary tract infection**

During diagnosis of UTIs, attempts should be taken to identify presence of risk factor if any. The following factors are considered to be responsible in the development of UTIs - age <1 year, female gender, white child, uncircumcised boys (particularly in first year of life), previous UTI, poor urine flow, voiding dysfunction (frequency, urgency, withholding maneuvers), constipation, VUR and sexual activity.[20,22] In young children malformations and obstructions of the urinary tract, prematurity, indwelling urinary catheters, constipation and in boys lack of circumcision are particularly important; whereas in older children diabetes, trauma, and in females sexual intercourse have particular importance as risk factors.[13]

**Clinical Features**

The presence of UTI should be considered on the basis of clinical presentations, the age of the child and the severity of the disease. Unexplained fever is the most important and may be the only symptom of pediatric UTI, especially in infants. The clinical presentations observed in infants are fever, vomiting, lethargy, irritability, poor feeding, not gaining weight properly / failure to thrive (FTT), abdominal pain, cloudy or offensive / malodorous urine, diarrhea, hematuria and prolonged jaundice (in very young children, i.e. infants younger than 3 months).[15,19,20,22,23] Fever as a

sole presentation in young infants may be the important marker of renal parenchymal involvement.[22] In older children fever, abdominal / flank pain, dysuria, urinary frequency, urgency, foul smelling urine, new-onset urinary incontinence, suprapubic discomfort, malaise, vomiting, chills, tiredness, hematuria, bedwetting and wetting underwear (in toilet trained child) are the usual presentations.[15,19-23] A critical review concluded that although individual symptom and sign were helpful in the diagnosis of UTI, no individual symptom / sign or any combination of them were sufficient enough to identify children with UTI.[22]

**Differentiation between acute pyelonephritis / upper UTI and cystitis / lower UTI**

Differentiation of an upper from a lower UTI is difficult, but clinical features with urinalysis can help. Infant and children who have bacteriuria and fever of 38˚C or higher should be considered to have acute pyelonephritis or upper UTI. Infants and children presented with fever <38°C with loin pain / tenderness and bacteriuria should also be considered to have pyelonephritis or upper UTI. All other infants and children who have bacteriuria but no systemic symptoms or signs should be considered as a case of cystitis / lower UTI.[20]

**Diagnosis**

Diagnosis of UTI in children are different from adults and require special consideration. Recently, many guidelines such as American Academic of Pediatrics (AAP 2011 & 2016), National Institute for Health and Care Excellence (NICE 2007 & 2017) of London, Canadian Pediatric Society (CPS 2014), European Association of Urology (EAU) / European Society for Pediatric Urology (ESPU)-2015, and Asian Guidelines for UTI in Children 2016 : by Urological Association of Asia (UAA) / Asian Association of UTI and STI (AAUS) have tried to settle several debates in diagnosis of pediatric UTI but many questions remains.[22,25] Investigation for UTI starts by examining the urine, which include urine analysis and culture. A reliable diagnosis of UTI requires the presence of positive urinalysis and significant bacteriuria on culture in properly collected urine, before giving antimicrobial therapy.[13,22,25] But a diagnosis of probable UTI is made by the presence of pyuria on urine analysis, while culture result is pending.[13] For infants <2 months of age with a febrile illness, bacterial sepsis must be considered, and needs a different approach of investigation.[26] Another important part for diagnosis of UTI is the collection and preservation (if required) of urine. There was a big controversy, but now reached near to consensus about collection of urine sample for an accurate diagnosis.[22,24,25]

**Urine Collection**

Mode of urine collection depends on the patient‘s age, status of toilet training and severity of illness. A clean catch midstream urine sample is the recommended method of urine collection. Where it is not possible or practical (in non-toilet trained child or up to 24 months of age and severely ill patients) supra pubic aspiration (SPA) or catheter sample should be used.[20,22] To avoid contamination of perineal flora SPA is considered as the standard method in young children, but catheter sample is associated with higher success rate and less painful than SPA with high sensitivity (95%) and specificity (99%).[13] Either one of the methods is recommended by CPS, AAP, WHO and NICE guideline.[20,22,24] NICE guideline permits collection of urine sample from urine collection bag in young infants,[20] but as up to 85% of positive culture obtain from this sample is false positive, most of the guidelines including APA doesn’t recommend it; rather it is reliable only when it is negative, to exclude UTI.[22,25]

**Urine Preservation**

Urine examination should be performed from any freshly voided specimen at room temperature (<1 hour after voiding) or a refrigerated (at 4°C) specimen <4 hours after voiding.[3,13,22] If not possible, it may be preserved up to 12 to 24 hours at 4°C (not frozen) in refrigerator or with boric acid, following the instruction of the company to avoid potential toxicity against bacteria in the specimen.[10,20]

**Urinalysis**

Urinalysis include the rapid dipstick method for the presence of leukocyte esterase and nitrites; and urine microscopic examination for pyuria (white blood cells) and bacteriuria. The nitrite dipstick test representing the conversion of dietary nitrate normally present in urine to nitrites by gram-negative bacteria, and the test of leukocyte esterase detecting the presence of this enzyme that is released from white blood cell (WBC) in the urine; and these are typically done together.[13] The sensitivity and specificity of leukocyte esterase test (LET) is 73-96 and 78-92 percent respectively, when done alone. But sensitivity and specificity of nitrite test (NT) is 41-57 and 96-99 respectively. If both tests are positive, diagnostic

sensitivity of UTI reaches to 93-97 percent with specificity of 98 percent.[13,22] When both tests are positive, it is highly predictive for positive urine culture, but when both are negative the likelihood of UTI is very low.[24] The major limitations of LET is it's false positive (by external contamination and infection causing leukocytosis) and false negative (in febrile neutropenic child) results. On the other hand, the limitations of NT is it's false negative results when the bladder is emptied frequently or if the underlying pathogen is gram-positive.[22] Therefore, most of the guidelines disagree with dipstick test for the young children.[24,25] NICE guideline suggests dipstick test for infants and children 3 months or older but younger than 3 years with suspected UTI, because when LET and NT are done together diagnostically it become useful as urine microscopy and culture.[20]

**Microscopic Examination of Urine**

It is performed by many physicians to treat the case of UTI with antibiotic while the culture results are pending. Preliminary result of urine culture are not available before 24 hours and conclusive result with microbial susceptibilities are not possible before 48-72 hours. On the other hand, dipstick testing and cultures are not available in many of the health facilities in our country like some other developing countries. Thus, there is a need for more rapid determination of probability of the presence of a UTI to guide the clinician in the decision to treat empirically, signifying the rationality of the test though not a definitive test for UTI.[13,24] Presence of pyuria i.e. >10 leukocytes/$mm^3$ in an uncentrifused specimen or >5 leukocytes/high power field (HPF) in a centrifused specimen is significant, and the presence of white cells casts in urine indicate renal parenchymal involvement.[3] Bacteriuria on urine analysis of spun or unspun fresh urine is very useful urine microscopic examination; and gram-staining of the urine to detect presence of bacteria will increase its sensitivity and specificity for predicting a positive urine culture.[3,13] If microscopy is done with uncentrifused urine the sensitivity and specificity of the test is 75-94% and 93-96% respectively; but when it is done with gram-stained sample the sensitivity and specificity rises to 80-96% and 92-98% respectively.[22]

Another method of microscopic examination is an 'enhanced' urinalysis, which consist of the detection of the number of leukocytes ( ed 10/$mm^3$ ) from a fresh uncentrifused urine by a Neubauer hemocytometer, and the presence of any bacteria in a gram-stained smear.[22,24] The sensitivity and specificity of this test is 95% (94-96%) and 89% (84-93%) respectively .[22] Pyuria is the hallmark of UTI and it helps to distinguish UTI and asymptomatic bacteriuria. The key to distinguish true UTI from asymptomatic bacteriuria is the presence of pyuria in urine specimen.[22]

**Urine Culture**

Urine culture is considered as the **gold standard** for diagnosis of UTI. The rate of contamination of the obtained urine sample for culture depends on the technique of obtaining urine and thus it will influence the interpretation of culture result, based on colony counts.[13] A significant colony count depends on the methods of urine collection and clinical presentation. So, diagnosis of UTI requires adequate collection of uncontaminated urine sample for culture. Therefore, cutoffs of positive culture result are operational and not absolute.[22,24] A colony count of ed$10^5$ CFU/mL of single species of bacteria from a clean catch midstream urine sample is considered significant, but culture yielding <$10^3$ CFU/mL represent contamination and those with $10^4$ – $10^5$ is suspicious and should be repeated. If urine is obtained by catheterization ed5ã$10^5$ CFU/mL is commonly defined as UTI, and in case of SPA sample a low bacterial count of <$10^4$ CFU/mL, even presence of any number may be significant.[3,13,22,25]

**Table-I**

*Guidance on the interpretation of microscopic results.*[20]

| Microscopic results | Pyuria positive | Pyuria negative |
|---|---|---|
| Bacteriuria positive | The infant or child should be regarded as having UTI. | The infant or child should be regarded as having UTI. |
| Bacteriuria negative | Antibiotic treatment should be started if clinically UTI. | The infant or child should be regarded as not having UTI. |

**Table-II**

*Diagnosis of UTI on results of urine culture.*[3]

| Methods of collection | Colony count (CFU/mL) | Probability of infection |
|---|---|---|
| Suprapubic aspiration | Any number | 99% |
| Urethral catheterization | >5 ã$10^4$ | 95% |
| | $10^4$ – $10^5$ | Very likely |
| | $10^3$-$10^4$ | Suspicious, repeat |
| Midstream clean catch | >$10^4$ | Very likely |
| Boys | >$10^5$ | 90-95% |
| Girls | $10^4$ - $10^5$ | Suspicious, repeat |

Occasionally, UTI may be present despite colony counts lower than the described guidelines; possibly because of prior antibiotic therapy, very dilute urine, obstruction to the flow of grossly infected urine or frequent voiding (in infants).[3,13]

**Non Specific Tests for Diagnosis**

These includes complete blood count (CBC) and tests for inflammation (e.g. ESR, C-reactive protein and procalcitonin).[13,20,22] Blood culture may be done in infants with UTI and for children >1 to 2 years who are toxic.[13] C-reactive protein (CRP) alone is not sufficient to diagnose pyelonephritis or upper UTI, but CRP have high negative predictive value to exclude acute upper UTI.[20,29] On the other hand, procalcitonin is best useful parameter to predict the presence of pyelonephritis and late renal scarring from it.[22]

**Urinary Tract Imaging**

Imaging of the urinary tract as further diagnostic modalities in the evaluation of UTI in children remain as the most controversial issue. Even then, to identify abnormalities of the kidney and urinary tract that are associated with UTI, imaging studies should be done, where indicated. Main objective of imaging is to identify congenital abnormalities of kidneys and urinary tract (CAKUT), and mainly for VUR, as it will make the child more susceptible to recurrent UTI and further risk of renal scarring.[3,25] The most commonly employed imaging modalities are ultrasonography (US) of abdomen, micturating / voiding cystourethrography (MCUG/VCUG) and radionuclide imaging.[3,13,14,25]

**Renal and Urinary Bladder Ultrasonogrphy** It is the most valuable, least invasive, and relatively inexpensive diagnostic tool in evaluating a child with UTI. It is done as the primary imaging study in all children with first UTI. It can detect hydronephrosis, hydroureter, bladder wall abnormalities and acute complication of UTI (e.g. renal or perirenal abscess).[25] A high post-voidal residue (PVR) can be detected by US, which is suggestive of bladder dysfunction.[3] US is usually done within a week of diagnosing UTI in infants, but within 48 hours if the infant don't respond quickly to antimicrobials or if their illness is unusually severe. Beyond infancy, it may be delayed for few weeks.[13]

**Micturating or Voiding Cystourethrogram (MCUG/ VCUG)**

This investigation is required to detect VUR with it's grading, and to evaluate the bladder and urethra.[3] There is risk of radiation exposure and inducing UTI. It is costly and create discomfort for the patient. So, it is not done routinely, especially if US is normal. VCUG is reserved for children with the following situations.[13,14]

- Ultrasonographic abnormalities (e.g. hydronephrosis, high PVR)
- Complex UTI (persistent high fever, organism other than E. coli)
- In all patients with recurrent febrile UTIs.

It is done at the earliest convenient time after clinical response, typically towards the end of the therapy. Antibiotic prophylaxis is recommended to minimize risk of inducing infection from catheterization.

**Dimercapto Succinic Acid Scan (DMSA scan)**

This procedure is done using technetium-99m-labeled dimercapto succinic acid (DMSA) for imaging of renal parenchyma. It is not a routine test and used mainly to defect renal parenchymal scarring.[13] DMSA scan is reliable in detecting both acute and late renal parenchymal scarring and in this respect it is superior to US and intravenous urography (IVU).[14,25] It is also useful in neonates and patients with poor renal function.[14] This should be performed 3-6 months after UTI with VUR of grade 3-5, and when there is high risk for development of renal scarring.[25]

**Direct Radionuclide Cystourethrogram or Radionuclide Cystography (DRCG or RNC)**

Here instead of radiocontrast agent, a radionuclide is introduced into the bladder. It can be used to detect VUR, but can not see the grading. Due to less radiation

exposure this technology may be used for follow up studies.[3,13]

**Evaluation of UTI, VUR and Renal Scarring**

Urologic evaluation following first or recurrent UTI is required to detect underlying structural or functional abnormalities and identifying the children having high risk of renal damage. Children under 02 years are at greatest risk and should be evaluated giving especial emphasis to them.[26,27] MCUG/VCUG is usually carried out 2-3 wks after UTI has been treated and DMSA scan should be performed 3-6 months after treatment of UTI. Recurrent UTIs are common among child who have first UTI at age younger than 6 months, voiding and congenital anomalies of urinary tract, so demands evaluation.[3] Child having VUR (particularly of high grade) are prone to recurrent UTI, and about 20% to 30% of infants and children of age 12 to 36 months with UTI have VUR. VUR (specially of high grade) predisposes to UTI and recurrent UTI can worsen VUR.[13,14] But till now controversies are there about association of VUR and recurrent UTI. In some studies it has been shown that risk of VUR in children with UTI is similar to the rest of the population at around 30%. On the other hand, mild to moderate VUR does not increase the risk of recurrent UTI or renal scarring. So, MCUG/VCUG is not recommended as a routine investigation for first UTI in children, but recommended for diagnosis and grading of VUR (Table-3). At first a routine ultrasonogram of KUB is to be done and MCUG/VCUG should be performed in children with abnormal US, recurrent UTI or with other risk factors.[25,26,27]

**Table-III**

*Grades of vesicoureteral reflux[13]**

| Grade | Characteristics |
|---|---|
| **01** | Only the ureters are involved, but not the renal pelvis |
| **02** | Reflux reaches the renal pelvis, but the calyces are not dilated |
| **03** | The ureter and renal pelvis are dilated, with minimal or no blunting of calyces |
| **04** | Dilation increases, and the sharp angel of the calyceal fornices are obliterated |
| **05** | The ureter, pelvis and calyces are grossly dilated Papillary impressions frequently are absent |

*As defined by International Reflux Study Committee

**Treatment**

The goals of the treatment of an UTI are to eradicate the infection, prevent urosepsis and reduce the likelihood of renal damage. Initial therapy for treatment of patient with UTI depends on the child‘s symptoms, age and general health. It will also depend on how severe the condition is and presence of structural abnormalities.[14] Treatment includes antibiotic medication, medicines to relieve pain (where required), drinking plenty of water and follow up with or without prophylactic medication.[23] There is no difference in efficacy between oral and parental treatment of UTI. So, majority of the children can be treated with oral medication and parental antibiotics are required only when the child is not able to take orally or he/she is very ill otherwise. The choice of antibiotics should be made based on locally developed current resistance pattern of urinary pathogens.[20,25] According to a Cochrane review analysis of different guidelines of UTI management, lower UTI can be treated by short-course of oral antibiotic for 2 to 4 days; and it is as effective as the traditional 7 days course of treatment. On the other hand, acute pyelonephritis/ upper UTI can also be treated by a 7 to 10 days course of oral antibiotic or a short-course (2 to 4 days) of parental therapy followed by oral therapy depending on the patient‘s age, severity and other associated illness.[14,20,24,27]

Treatment should be initiated with empiric antibiotic and should be continued or replaced by another drugs depending on the clinical response 24 to 72 hours after initiation of treatment or depending on the result of urine culture and sensitivity reports.[14,20,27,28] Whether the patient should be treated in outpatient department (OPD) or indoor depends on the clinical situation. Very young infants, those with toxic appearance, severe dehydration, vomiting or intolerance to oral medication should be considered for hospitalization.[28] According to NICE guideline, infants younger than 3 months with UTI should be treated with parentral antibiotic, and the child 3 months or older with upper UTI may be treated with parentral or oral medication depending on the patients clinical presentation. The children 3 months or older with lower UTI are easily be treated by oral antibiotics as OPD patient. But a child with asymptomatic bacteriuria need not be treated with antibiotic.[20] Antibiotics commonly used for oral medication are trimethoprim/sulfamethoxazole (TMP/ SMX), cephalexin, amoxicillin/clavulanic acid, cefixime, cefpodoxime, nitrofurantoin and ciprofloxacin (Table-IV).

**Table-IV**

*Dosing of antibiotics commonly used for oral treatment of UTIs in children*[3,13,14,20,28]

| Antimicrobial agent | Dosing (mg/kg/day) | Remarks |
|---|---|---|
| TMP/SMX (cotrimoxazole) | TMP 8-10, bid | Avoid in infants <6 weeks and G6PD deficiency |
| amoxicillin/clavulanic acid | 30-40, 2-3 divided doses | |
| Cephalexin | 30-50, qid | |
| Cefixime | 8-10, bid | |
| Cefpodoxime | 10, bid | |
| Ciprofloxacin* | 10-20, bid | Avoid in <3 months and G6PD deficiency |
| Nitrofurantoin** | 5-7, qid | |

*Ciprofloxacin should not be used as a first-line agent to treat UTI in children, because of potential concerns about injury to developing joints. But useful in children when UTI is complicated or caused by multidrug-resistance pathogens for which there is no safe and effective alternative.[13,27,28]

**Nitrofurantoin may be used to treat lower UTIs, but not in pyelonephritis as it will not reach the therapeutic concentration in blood due to it's limited tissue penetration.[14,25]

Antimicrobial agents commonly used for parenteral treatment of UTIs are aminoglycosides (gentamicin, amikacin), ceftriaxone, cefotaxime, cephalexin, , and ciprofloxacin(Table-V).[13,14,20,28]

**Table-V**

*Doses of antibiotics used for parenteral treatment of UTIs*[a]

| Drugs | Dose and route (mg/kg/day-IV/IM) | Remarks |
|---|---|---|
| Gentamicin | 7.5, 8h or 5, once | If therapy is continued more than 48 hours, monitor blood level and kidney function. |
| Amikacin | 10-15, 12 h | |
| Ceftriaxone | 75-100, once or 12 h | May increase jaundice in neonates as displace bilirubin from albumin |
| Cefotaxime | 100-150, 8-12 h | Safe to use in neonates. |
| Ampicillin | 100, 6-8 h | In combination with aminoglycoside. |

a. Doses may be required to adjust in renal failure

**Prophylaxis**

Prophylactic therapy for a UTI is aimed at sterilizing the urine to reduce the risk of recurrent UTI in order to prevent renal damage and scarring. In otherwise healthy children with a first UTI, low grade VUR, antibiotic prophylaxis is not recommended in general. In this case it may not be associated with a reduced risk of recurrent UTI, rather will increase the risk of treatment-resistant pathogens.[25,27] But a clear benefit of long-term antibiotic prophylaxis to prevent recurrence in boys with VUR of grade 1 to 3 have been observed in different studies.[25,29] Benefit of prophylactic therapy with antibiotics have been documented in children with a history of recurrent UTI, severe VUR, immunosuppression, or partial urinary obstruction.[24,28] Even then, there is controversy about the risk-benefit ratio demanding further evaluation of long-term antibiotic prophylaxis.[25,27,29,30] Drugs commonly used for prophylaxis are TMP/SMX, cephalexin, nitrofurantoin, amoxicillin, ampicillin, cefixime, cefaclor (Table-VI)

**Table-VI**

*Drugs with doses commonly used to prevent reinfection*[13,14,28,31]

| Agent | Dosing (mg/kg/dose-bed time at night) | Remarks |
|---|---|---|
| Trimithoprim | 1-2, once or 5, twice per week | Ensure fluid intake |
| Cephalexin | 10, once | Prefered in young infants when TMP and nitro-furantoin is restricted |
| Nitrofurantoin | 1-2, once | |
| Amoxicillin | 10, once | |
| Ampicillin | 20, once | |
| Cefixime | 2, once | |
| Cefaclor | 5-10, once | |

The prophylactic dose is one-fourth to one-half of the therapeutic dose of acute infection. Antibiotics used to treat infants and neonates for their first UTI should not be used for prophylaxis.[28] If an infant or child develops infection during the period of prophylactic medication, treatment should be with different antibiotic, not a higher dose of same antibiotic.[20]

Recently, in some studies it have been shown that use of antibiotic when combined with probiotic (Lactobacillus acidophilus and Bifidobacterium) reduces the incidence of febrile UTIs in children by preventing colonization of uropathogenic bacteria. It is safe and more effective in comparison to prophylactic antibiotic alone.[32,33] Trials are continuing for a replacement of antibiotic by probiotic, cranberry juice, glycosaminoglycan and sodium pentosanpolysulfate as there is risk of break through infections, adverse drug reactions and also risk of developing antibiotic resistance with use of antibiotic as long-term prophylaxis. But they do not provide so far a definitive effective answer to use as a suitable alternatives to long-term oral antibiotic prophylaxis.[33]

**Prevention**

It is not possible to prevent all childhood UTIs; but exclusive breast feeding up to 6 months, avoidance of constipation, drinking plenty of fluids, emptying of bladder fully when urinating, encouraging girls to wipe their bottom from front to back after going to the toilet, avoiding nylon and other synthetic underwear, avoidance of using scented soap or bubble bath, circumcision, prophylactic use of antibiotics where recommended (to reduce recurrence) can reduce the incidence of UTIs.[14,19,20,23,27,33] Recently in some studies the role of routine circumcision in boys to reduce the incidence of UTIs has become questionable, as it does not reduce the risk of UTI enough to signify the surgical complication. But it is helpful particularly for children with low grade VUR and antenatal hydronephrosis.[27,33] In some studies it is claimed that drinking cranberry juice or taking cranberry supplements can reduce the recurrences and have better compliance without significant side effect than oral antibiotics, though it's regular use needs more evaluation.[19,33]

**Follow up**

Infants and children who do not require imaging investigation should not routinely be followed up. Where imaging studies are normal, a routine follow up in OPD is not necessary. But if there is abnormal imaging result or if there is recurrent UTI, the infant or child should be assessed further. This includes measurement of height, weight, blood pressure and routine testing for proteinuria. If the infant or child has a minor, unilateral renal parenchymal defect, no need for long-term follow up. But who have bilateral renal abnormalities, impaired renal function, raised blood pressure and / or proteinuria should go under meticulous follow up by a pediatric nephrologist, to reduce the progression of chronic kidney disease (CKD).[20]

**References:**

1. Singh SD, Madhup SK, Clinical Profile and Antibiotics Sensitivity in childhood Urinary Tract Infection at Dhulikhet Hospital. Kathmandu Univ Med J 2013;44(4):319-324.
2. Kalal BS, Patel RB. Microbiological and Antimicrobial Profile of Urinary Tract Infection in Children from A teaching Hospital in South India. J Pediatr 2017;11:i19-i22.
3. Hari P, Srivastava RN, Urinary Tract Infections. Pediatric Nephrology. Srivastava RN, Bagga A, 6th Edition,2016;268-289. Gaypee Brother Medical Publishers (P) Ltd.
4. Guidelines : Diagnosis and management of urinary tract infection in children : summary of NICE guidance. BMJ Publishing group Ltd 2007. https://www.ncbi.nlm.nih.gov/pmc/articles/pmc1952472/.
5. Sharma A, Shrestha S, Upadhyay S, Rijal P. Clinical and Bacteriological profile of urinary tract infection in children at Nepal Medical College Teaching Hospital. Nepal Med Coll J 2011;13(1):24-26.
6. Fisher DJ, Steele RW. Pediatric Urinary Tract Infection. Updated 2017. https://emedicine.medscape.cpm/article/969643-overview.
7. Detecting Urinary Tract Infections – Healthy Children. Org. https://www.healthychildren.org/English/health-issues/
8. Balasubramanyam V, Sharma NL. Clinical profile and gram-negative bacterial profile of urinary tract infection in children attending a tertiary care hospital of Tamilnadu, India. International Journal of Contemporary Pediatrics 2017;4(1):231-233.
9. Umesh, Bisht P, Tamta S. Microbiological Profile in Urinary Tract Infection among Children in a Tertiary Care Centre in Kumaun region, India. Int. J. Curr. Microbial. App. Sci 2016;5(4):101-108.
10. L Heather, C Malcolm. The child with UTI. In Clinical Pediatric Nephrology by Nicholas Webb and Robert Postlehbwite. 3rd Edi. Oxford Medical Publications; 2003: 197-221.
11. Gupta P, Mandal J, Krishnamurthy S, Barathi D, Pandit N. Profile of urinary tract infections in pediatric patients. Indian Journal of Medical Research 2015;141(4):473-477.
12. S Jack, Elden. Urinary Tract Infections. In Kliegman RM, Stanton BF, Geme III JWS, Schor NF, Behrman RE. Editors. Nelson Textbook of Pediatrics, 20th edition. New Delhi: Elsevier; 2016: 2556-2562.
13. Weinberg GA. Urinary Tract Infection (UTI) in Children – Pediatrics – MSD Manual Professional Edition 2018. https://www.msdmanuals.com/professional/pediatrics/urinary-tract-infection-uti-in-children.

14. Hamid F, Islam MR, Paul N, Nusrat N, Parveen R. Urinary Tract Infection in Children : A Review. Delta Med Col J 2013;1(2):51-57.
15. Moreno MA. Urinary Tract Infections in Children and Adolescents. JAMA pediatr 2016;170(9):916.doi:10:1001/jamapediatrics.2016.2163.
16. Zaffanello M, Malerba G, Cataldi L, Antoniazzi F, Franchini M, Monti E et al. Genetic risk for recurrent urinary tract infections in humans: a systemic review. J Biomed Biotechnol. 2010;2010:32102.
17. Lin DS, Huang SH, Lin CC, Tung YC, Huang TT, Chin NC et al. Urinary tract infection in febrile infants younger than eight weeks of age. Pediatrics 2000;105 (2) : E20.
18. Mahant S, Friedman J, Mac A C. Renal Ultrasound findings and vesicouretral reflux in children hospitalized with urinary tract infection. Areh. Dis. Child.2002;86:419-20.
19. Urinary tract infection in children-NHS. UK. https://www.nhs.uk/conditions/urinary-tract-infections-utis-in-children/.
20. Urinary tract infection in under 16s:diagnosis and management. NICE guideline: UTI in children and young people 2017. https://www.guidelines.co.uk/pediatrics/nice-guideline-uti-in-children-and-young-people/453701.article.
21. Urinary tract infections in children-symptoms, diagnosis and treatment/BMJ Best Practice. https://www.bestpractice.bmj.com/topics/en-us/789#referencePop1.
22. Tsai JD, Lin CC, Yang SS. Diagnosis of pediatric urinary tract infections. Urological Science 2016;27(3):131-134.
23. Urinary Tract Infection (UTI) in children – Health Encyclopedia – University of Rochester Medical Center. https://www.urmc.rochester.edu/encyclopedia/content.aspx. Content Type ID = 90 & Content ID = P03117.
24. Quigley, Raymond. Diagnosis of urinary tract infections in children. Current Opinion in Pediatrics 2009;21(2):194-198.
25. Napierala MO, Wasilewska A, Kuchar E. Urinary tract infection in children: Diagnosis, treatment, imaging – Comparison of current guidelines. Journal of Pediatric Urology 2017;13(6):567-573.
26. Robinson JL, Finlay JC, Lang ME, Bortolussi R. Urinary tract infection in infants and children: Diagnosis and management. Paediatr Child Health 2014;19(6):315-19.
27. White B. Diagnosis and Treatment of Urinary Tract Infections in children. Am Fam Physician 2011;83(4):409-415.
28. Nguyen SG, Whitehill J. Treatment of Urinary Tract Infections in Children. US Pharm.2011;36(3):HS2-HS7.
29. Keslen GR, Gadjos V, Idres N, Horen B, Lchay L, Leclair MD et al. Antibiotic Prophylaxis for the Prevention of Recurrent Urinary Tract Infection in Children With Low Grade Vesicouretral Reflux: Results From a Prospective Randomized Study. The Journal of Urology 2008;179(2):674-679.
30. Williams G, Lee A, Craig J. Antibiotics for the prevention of urinary tract infection in children: A systemic review of randomized controlled trials. The journal of Pediatrics 2001; 138(6):868-874.
31. Craig JC, Simpson JM, Williams GJ, Lowe A, Reynolds G, McTaggart SJ et al. Antibiotic Prophylaxis and Recurrent Urinary Tract Infection in children. N Eng J Med 2009; 361:1748-59.
32. Mohseni MJ, Aryan Z, Fard SE, Paydary K, Mofid V, Joudaki H et al. Combination of Probiotics and Antibiotics in the prevention or Recurrent Urinary Tract Infection in children. Iranian Journal of Pediatrics 2013;23(4):430-438.
33. Tewary K, Narchi H. Recurrent urinary tract infections in children: Preventive interventions other than prophylactic antibiotics. World Journal of Methodlology 2015;5(2): 13-19.

## CASE SERIES

# Ectopic Pregnancy: A Case Series

ROY JS[1], BEGUM A[2], SHAMPA L[3], AHMED Q[4], AKHTER K[5], NAHAR K[6]

*Abstract*

***Ectopic pregnancy occurs when a fertilized egg implants on tissue other than the lining of the uterus. The incidence of ectopic pregnancy has increased over the past decade due to increased risk factors and early diagnosis. Diagnosis of ectopic pregnancy is almost always being a challenging task as the condition is complicated by a bizarre spectrum of clinical presentation ranging from asymptomatic case to acute abdomen to hemodynamic shock. Judicious approach with combination of clinical history, Transvaginal Sonogram (TVS) and S.-βhCG can be helpful for confirmation and management of ectopic pregnancy as seen in the cases mentioned in our study. Here, we discuss cases of ectopic pregnancy with various clinical presentation. The cases were managed accordingly using expectant, medical and surgical methods.***

*Key words:* ***Ectopic pregnancy, Transvaginal sonogram, S.-βhCG***

***Journal of Green Life Med. Col. 2018; 3(2): 105-107***

**Introduction:**

Ectopic pregnancy is one of the most life threatening emergencies in each pregnancy. By definition, ectopic pregnancy is one in which the fertilized egg becomes implanted at sites other than normal lining of the uterine cavity.[1] It not only leads to fetal wastage but also to increased maternal morbidity and mortality and in many cases significantly compromises the future fertility of the patients.[2] Etiology of ectopic pregnancy most of the times remain uncertain although multiple risk factors have been attributed for its occurrence. It is observed that the frequency of ectopic pregnancy has been on an upstroke during last few decades owing to the increased incidence of venereal disease, increased usages of contraceptives, short birth spacing and increased usages of assisted reproductive technique.[3]

Diagnosis of ectopic pregnancy is almost always being a challenging task as the condition is complicated by a bizarre spectrum of clinical presentations ranging from asymptomatic case to acute abdomen to hemodynamic shock.[4]

Modern diagnostic technique and anesthesia, blood transfusion facilities, transport facilities, immediate resuscitation as well as adequate and proper surgery are the keystone of success in reducing the maternal morbidity and further successful obstetric outcome.

Here we discuss a spectrum of cases with varied clinical presentation and their management by all possible means (Medical, expectant and surgical).

**Case -1: Ruptured Ectopic Pregnancy**

A 29 years old lady 3rd gravida, para-1, abortion-1 with history of previous cesarean section and D&C presented in emergency ward in a state of shock. On enquiry from attendance, we got history of amenorrhea for 6 weeks 3 days with urinary pregnancy test positive, per-vaginal spotting for last two days with history of severe lower abdominal pain for few hours followed by sudden collapse, while she brought to hospital for management. On examination, her blood pressure was 90/40 mm of Hg, pulse – very feeble and rapid, severe anemia with sweating, her abdomen was distended and tense no palpable mass was felt. Per-vaginal examination revealed, cervix was closed,

1. Dr. Joya Sree Roy, Professor, Department of Obstetrics & Gynaecology, Green Life Medical College.
2. Dr. Afrina Begum, Associate Professor, Department of Obstetrics & Gynaecology, Dhaka Medical College.
3. Dr. Lima Shampa, Associate Professor, Department of Obstetrics & Gynaecology, Green Life Medical College.
4. Dr. Qumrunnessa Ahmed, Assistant Professor, Department of Obstetrics & Gynaecology, Green Life Medical College.
5. Dr. Kazi Foyeza Akther, Assistant Professor, Department of Obstetrics & Gynaecology, Green Life Medical College.
6. Dr. Kamrunnahar, Professor & Head, Department of Obstetrics & Gynaecology, Green Life Medical College.

**Address of Correspondence:** Prof. Dr. Joya Sree Roy, Professor, Department of Obstetrics & Gynecology, Green life Medical College Hospital, 32 Bir Uttam K.M. Shafiullah Sarak (Green Road), Dhaka-1205, Email: joyasreeroy1956@gmail.com

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and altered blood was present with fullness of all fornixes. Immediately ultra-sonogram of abdomen was done in emergency room, it was seen that there was huge amount of haemoperitoneum with a left adnexal mass of 6×5cm. Uterine cavity showed pseudo decidual reaction. Urgent resuscitation and exploratory laparotomy was done. There was haemoperitonium of about 2 liter of both clotted and fresh blood. There was Left sided ruptured fallopian tube on ampullary region. Left sided salpingectomy with peritoneal toileting of about 2.5 litre of blood was done. Peroperatively 2 units of blood were transfused.

Recovery of the patient was uneventful. After removal of drain tube and checking of hemoglobin level the patient was discharged on 5th post-operative day.

**Case-2: Unruptured Tubal Pregnancy**

A 23 year lady 2nd gravida, para-1, presented with amenorrhea of 5 weeks 5 days, occasional right sided lower abdominal pain for two days with urinary pregnancy test positive. On examination she was haemodynimically stable but her pulse rate was 100 per minute. Immediately transvaginal ultrasonography was done which showed right sided adnexal mass of 3.22×3 cm in size with a gestational sac without any cardiac pulsation. Uterine cavity showed pseudo decidual reaction without any collection in pouch of douglas, suggesting of right sided unruptured tubal pregnancy. Her S.-βhCG was 3,200 mIU/mL. the patient was advised for hospitalization. Inj. Methotrexates 50mg I/M was given and kept monitoring for 48 hours. She was advised for S-βhCG estimation on day 4 and day 7. On 7th day her βhCG became 120 mIU/mL. And then she was advised for weekly estimation of βhCG till it became negative. Subsequently, it took about one month to become normal. This patient was treated by medical management.

**Case-3: Chronic Ruptured Ectopic Pregnancy**

A 32 years multiparous lady para-3, history of two caesarian section presented with history per vaginal spotting for last 2 months, lower abdominal pain for 2 months, with dyspareunia and weakness. On query she mentioned that 2 months back, on her 25th day of cycle she suddenly felt severe lower abdominal pain, and had asyncopal attack from which she recovered on her own. Since then she visited many doctors for lower abdominal pain per, vaginal occasional bleeding and weakness and she was prescribed antibiotic, OCP, tranaxemic acid etc. When we got the patient she was very pale and sick looking. On examination BP: 110/60, pulse 100/min Anemia ++, P/A examination - diffuse tenderness of lower abdomen, P/V examination - an illdefined mass was felt through right fornix which was about 8 & 7 cm, very tender, cervical motion test was strongly positive. altered blood discharge present. USG show – a mass measuring 7.4×6.5 cm in right tubo-ovarian region with moderate collection of blood in abdominal peritoneal cavity. Her Hb was 7.6 gm/dl. S.-βhCG was 280mIU/mL. Discission for laparotomy was taken keeping two fresh bloods in hand. On exploration, it was found that the hemorrhagic mass about 8 to 9 cm occupying the right tubo ovarian region with omental adhesion. The mass was grossly friable and edematous. Ovarian separation was difficult due to extreme friability and oozing. So right sided salpingoophrectomy and left sided tubal ligation was done. After toileting abdomen was closed in layers keeping drain tube in situ. Gradually the patient improved and discharged from hospital on 8thpost operative day.

**Case-4: Ectopic Pregnancy Managed With Expectant Management**

A 19 years old newly married lady presented with overdue of her menstruation for 9 days. Her urinary pregnancy test was positive, but was associated with per vaginal spotting, so she came for consultation. Her menstrual cycle was irregular and as contraceptive measures she took emergency pill twice in her last cycle.

On examination, she was haemodynamically stable; no significant tenderness was present in abdomen. Her βhCG was 356 mIU/mL. USG showed a mass measuring 2.4×2cm in right tubal region. Uterine cavity was empty and there was no fluid in pouch of douglas, suggestive of unruptured ectopic pregnancy.

This patient was managed with expectant management and advised to assay S.-βhCG and TVS after one week. After weekly S.-βhCG assay which became normal by 1 month.

**Case-5:** Live Intrauterine Pregnancy with Simultaneous Tubal Ectopic Pregnancy (heterogenous pregnancy)

A 28 years old lady, had history of 5-years subfertility got pregnancy with ovulation inducing drugs, presented at her 7 weeks of pregnancy with shock. Her husband gave history that her urinary pregnancy test was positive; she had pervaginal spotting for last 2 – 3 days. Since morning she experienced severe abdominal pain and became unconscious.

Immediately resuscitation and investigation was started. S.-βhCG was 30,000 mIU/mL. USG showed – huge haemoperitoneum with a right sided adnexal mass of 6.5×6 cm with a small fetal pole within the gestational sac. Uterine cavity showed another alive pregnancy of 7 weeks

duration. It was a case of heterogeneous pregnancy. Decision for laparotomy was taken keeping two unit of fresh blood in hand. Uterus was enlarged, soft. With precaution and minimum handling right sided salpingectomy was done. Post operatively the patient was monitored closely and progesterone support was given duly. Fortunately the patient recovered uneventfully and continued her pregnancy with proper antenatal care. Finally she delivered a healthy male baby of term pregnancy by caesarian section. Thus she became a mother even with rare findings of heterotopic pregnancy.

**Case-6: Delayed management of Ectopic Pregnancy may cause death**

A 19 years of unmarried girl admitted in the medicine department with severe abdominal pain for last 5 days associated with vomiting. She was getting conservative management of acute abdomen. Lastly, we were called when her pregnancy test result showed positive. On per abdominal examination abdomen was hugely distended (suspected haemoperitonium) with extreme paper white paleness. Ultrasonogram report showed huge collection in peritoneum about 3-4 liter of old and fresh blood; a lump was present on left adnexal region, suggestive of ruptured tubal pregnancy. Unfortunately at that time she was in septicemic shock with acute renal failure. Emergency laparotomy was done. But we failed to save the life of this poor girl.

**Discussion:**

Early diagnosis and early treatment of ectopic pregnancy is essential to prevent maternal morbidity and mortality. Early diagnosis is possible by clinical suspicion, early recognition of sonographic findings together with S.-βhCG estimation. Several modalities of treatments are available for the management of ectopic pregnancy.

In our cases according to presentation, clinical findings and investigations guided us to manage the cases.

Medical Management with Inj. Methotrexate was given where patient was stable, gestational sac size is <3.5 cm with showing no fetal cardiac pulsation.[5] A falling S.-βhCG level is the most common indicator used for successful medical management. Medical management can be single or multiple dose of Methotrexate depending on S.-βhCG level.

Ectopic Pregnancy can be managed expectantly if S.βhCG. level is low and it resolves by itself in a large number of patients where initial S.-βhCG <2000 mIU/mL as seen in Case-4.[6]

Surgical management is done by laparotomy or laparoscopy depending on expertise and general conditions of patients. In our cases we did salpingectomy and salpingoophrectomy. Removal of ovary was only done in one case because it was matted with hemorrhagic mass so densely, separation caused excessive bleeding. Otherwise salpingectomy is the preferred surgery, though salopingostomy carries a risk of persistent pregnancy and there by requiring weekly follow up with S.-βhCG.

A high index of suspicion should be maintained in reproductive age females with each of the following symptoms: amenorrhea, abdominal pain, adnexal mass, peritoneal irritation (as with features of acute abdomen). In our case-6 due to wrong and delayed diagnosis the, unfortunate girl was robbed of her chance of spontaneous cure.

**Conclusion:**

Ectopic pregnancy still remains the most lethal gynecological emergency and a very high index of suspicions' in women with risk factors will reduce ectopic pregnancy related morbidity and mortality. The choice of therapy should be guided after detailed discussion of risk, benefits, outcome and monitoring facilities of all approaches. Hence ectopic pregnancy should be highly anticipated as an emergency basis in a woman of reproductive age group. To prevent misdiagnosis and to reduce the associated morbidity and mortality awareness of this condition by gynecologist, surgeons, general practitioner and radiologists are highly necessary.

**References:**

1. Walker JJ.Ectopic pregnancy.ClinObstetGynecol 2007; 50: 89-99.
2. Panti A, Ikechukwu NE, Luckman OO, Yakubu A, Egondu SC, Tanko BA. Ectopic pregnancy at UsmanuDanfodiyo University Teaching Hospital Sokoto: a tenyear review. Ann Niger Med. 2012;6(2):87-91.
3. John A. Rock, Howard W. Jones III, TeLinde's Operative Gynecology.10th edition. Lippincott, Williams & Wilkins, a Wolters Kluwer business. USA. 2008. P798.
4. F, Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, John C. Hauth, Dwight J. Rouse, Catherine Y. Spong. Williams Obstetrics.23rd edition.MeGraw-Hill Companies. USA. 2010 p238.
5. Korhonen J, Stenman UH, Ylotalo P. Serum human chorionic gonadotropin dynamics during sponataneous resolution of ectopic pregnancy.FertilSteril 1994: 61:632-636
6. Gracia CR, Brown HA, Barnhart KT. Prophylactic Methotrexate after liner salpingostomy: a decision analysis. FertilSteril 2001; 76:1191-1195.

# COLLEGE NEWS

*Journal of Green Life Med. Col. 2018; 3(2): 108*

**Honorary PhD degree:**

Prof. Dr. Shamsuddin Ahmed, member governing body, Green Life Medical College, awarded with honorary PhD degree by BSMMU in its 3rd convocation for his outstanding contribution in orthopedics.

| Date | Topics | Department |
|---|---|---|
| 03.01.18 | AIDs | Department of Dermatology |
| 07.01.18 | Biochemical aspect of cholesterol | Department of Biochemistry |
| 09.01.18 | Steps of developing a research proposal | Department of Community Medicine |
| 17.01.18 | Steps of developing a research proposal (continuation) | Department of Community Medicine |
| 21.01.18 | Medical Ethics | Department of Forensic Medicine |
| 24.01.18 | Recurrent abortion | Department of Gynae and Obs |
| 31.01.18 | FNAC | Department of Pathology |
| 04.02.18 | Fatty liver | Department of Medicine |
| 07.02.18 | World Cancer day | Department of Medicine |
| 14.02.18 | Anatomy of the Brachial plexus | Department of Anatomy |
| 28.02.18 | Glaucoma | Department of Ophthalmology |
| 04.03.18 | Evaluation of combination of antibiotics for MDR-Acinetobacter baumannii | Department of Microbiology |
| 07.03.18 | Ethics in medical research | Department of Pharmacology |
| 14.03.18 | Fever with convulsion | Department of Paediatrics |
| 18.03.18 | Adenoid with delayed speech | Department of ENT |
| 21.03.18 | Medico-legal aspects of wounds | Department of Forensic Medicine |
| 28.03.18 | Imaging in surgical practice | Department of Surgery |
| 01.04.18 | World Health Day ( universal health coverage) | Department of Community Medicine |
| 04.04.18 | Arsenicosis – A serious public health problem | Department of Community Medicine |
| 11.04.18 | Pregnancy with epilepsy | Department of Gynae and Obs |
| 18.04.18 | Schizophrenia | Department of Psychiatry |
| 25.04.18 | World Autism Day | Department of Otolaryngology, Head and Neck Surgery (Prof. Pran Gopal Dutta) |
| 06.05.18 | Diabetes and Ramadan | Department of Medicine |
| 09.05.18 | Interpretation of nail | Department of Dermatology |
| 16.05.18 | Cardiac changes during exercise | Department of Physiology |
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# GREEN LIFE MEDICAL COLLEGE JOURNAL

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