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ABOUT THE 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).

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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.

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 32, 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

Superbug: An Emerging Global Ferocity in Medicine

Scientists and public health officials have been warning for decades that overuse of antibiotics would inevitably lead to a rise of bacteria that have adapted to the drugs and developed a resistance to them. Old standby antibiotic treatments have lost the fight against some diseases and new strains of antibiotic-resistant bacteria are emerging with terrible frequency.

Superbug is a term used to describe the newly evolved bacterial species resistant to antibiotics. This resistance to antibiotics by Superbugs causes economic losses by increasing the duration of infection, treatment cost and decreasing the success of treatments due to hospital acquired infections.[1] Due to rapid globalization of human population by travel these resistant strains spread easily between developed and developing countries making it a global threat.

Staphylococcus aureus was the first resistant bug discovered in 1943 against Penicillin. In 1967, Streptococcus pneumoniae and after that the Enterococcus spp was found resistant to Penicillin. After that, Methicillin was the target antibiotic and the first Methicilin- resistant S. aureus (MRSA) was found in 1961 in UK and became a major bug worldwide in 1980s.[2]

Resistant gram-negative bugs emerged simultaneously with gram-positive strains. Multidrug resistance was first seen in enteric bacteria like Escherichia coli, Shigella and Salmonella in late 1950s-1960s. Extended-spectrum beta-lactamase containing bugs prevailed in Europe and then worldwide. After that Carbapenemase-producing gram-negative bugs like extensively drug-resistant Acinetobacter spp. and Enterobacteriacae were emerged. In 21st century many multidrug resistant bugs prevailed like Pseudomonas spp, M. tuberculosis strains resistant to four and more line of drugs specific for TB called as extensively drug resistant (XDR) strains and totally drug resistant (TDR) strains.[3]

The prolonged administration or indiscriminate use of antimicrobials resulted in selection pressure which favors the evolution of resistant strains and subsequently their transmission causes spread of the resistant strains in the environment. The spread of resistance traits occurs among different ecological groups and taxonomical groups by the presence of mobile genetic elements like bacteriophage, plasmids, naked DNA, transposons.[4] Due to the selection and mutation of genes these resistant strains hamper the easy passage of drugs through the cell wall, change their targets and inactivate them by producing enzymes.

In November 2015, *mcr* -1—a gene that can make bacteria resistant to colistin, an old antibiotic that is the last-resort drug for some multidrug-resistant infections was reported in China.[5] The gene has the potential to quickly spread to other bacteria and raises the possibility that bacteria already resistant to major antibiotics could become resistant to colistin as well.

Most of the infections spread occur from the contact of infected persons and lack of hygienic practices. Proper sanitation and hygiene maintenance in food and other things can reduce the spread of superbugs. Some policies and regulations should be practiced in both developing and developed countries to check the unnecessary drug promotions. Antibiotics are used vividly in food animals like chicken, cattle, pigs, agricultural fields and fish farming methods. These uses establish a direct link for the appearance of resistance in humans.[6]

It can be inferred that a successful counter attack will involve multiple strategies, by regulating and promoting awareness campaigns especially for physicians on the dangers of prescribing antibiotics for viral flus and other common infections.

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Shahanara Begum
Professor, Department of Microbiology
Green Life Medical College

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ORIGINAL ARTICLE

Pregnancy Outcome in Women with Hypothyroidism Receiving Levothyroxine Replacement: A Longitudinal Study in A Specialized Hospital of Bangladesh

HOSSAIN T[1], MAHMUD K[2], PARVEEN S[3]

Abstract

Introduction: *Maternal hypothyroidism is associated with increased risks of adverse pregnancy outcomes. The common maternal complications seen with hypothyroidism in pregnancy are gestational hypertension, preeclampsia, pregnancy loss and post partum hemorrhage. The fetal complications that commonly occur are fetal distress, low birth weight, prematurity, intra uterine and neonatal death. This study was conducted to see the pregnancy outcomes after Levothyroxine dose adjustment to maintain TSH level below 2.5 mU/L in a specialized hospital of Bangladesh.*

Methods: *Total 52 pregnant women with hypothyroidism were monitored throughout the pregnancy in the year 2014-2015. Thyroid function tests were done at the first visit and thereafter at 4 to 6 weeks interval. The dose of Levothyroxine was adjusted according to TSH report to maintain TSH level below 2.5 mU/L. The pregnancy outcome was noted at the end.*

Results: *Among the 52 pregnancies studied, there were 15 full term births (28.8%), 28 pre term delivery (53.8%), 4 Intra uterine deaths (7.7%) and 5 abortions (9.6%). Maternal complications seen in 29 pregnancies (56%) among which gestational diabetes mellitus (48%) and gestational hypertension (27%) were the commonest. Fetal complications occurred in 40% cases, among which fetal distress (21.2%) and low birth weight (19.2%) were most common.*

Conclusion: *Adverse pregnancy outcomes are commonly seen even after Levothyroxine dose adjustment to maintain TSH value within 2.5 mU/L. The pregnancy specific reference ranges for TSH should be established in each population setting.*

Key words: *Pregnancy, Hypothyroidism, TSH, Levothyroxine*

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Introduction:

Hypothyroidism in pregnancy is associated with increased risk of adverse pregnancy outcome and also has adverse effect on development of fetus.[1] The common adverse outcomes seen in pregnant women with hypothyroidism include anemia, gestational hypertension, preeclampsia, placental abruption and postpartum hemorrhage. The common fetal complications include prematurity, low-birth weight (LBW), fetal distress in labor, fetal death and perinatal death.[2] Abalovich et al. demonstrated that women with hypothyroidism have an estimated 60% risk of fetal loss if not adequately treated. [3] Leung et al. demonstrated a 22% risk of gestational hypertension in pregnant women with overt hypothyroidism.[4] Allan et al. described an increased risk of fetal death among pregnant women with hypothyroidism.[5] Recent reports suggest an increased risk for gestational diabetes in patients with primary hypothyroidism.[6] Another study demonstrated that high TSH and thyroid autoimmunity in early pregnancy were

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associated with a 4 fold increased risk for gestational diabetes and a 3 fold increased risk for low birth weight neonates.[7] Together, with some differences, previous studies overall indicate an increased risk of pregnancy specific complications, in relation to elevated maternal TSH concentration. Upon the evidences, in 2011 American Thyroid Association (ATA) guideline, the upper reference limit for serum TSH concentration was defined as 2.5 mU/L in first trimester and 3 mU/L in second and third trimester. The ATA guideline also suggested that it is reasonable to target TSH in the lower half of the trimester specific pregnancy range. If it is not available, it is reasonable to target maternal TSH level below 2.5 mU/L.[8] On the other hand, 2014 European Thyroid Association guideline suggested that if TSH trimester specific reference ranges are not available, the following reference range upper limits are recommended: first trimester, 2.5 mU/L; second trimetster,3.0 mU/L and third trimester, 3.5 mU/L.[9] The guidelines also suggested that in women with hypothyroidism already treated with Levothyroxine, TSH values should be checked every 4-6 weeks during the first trimester and once during second and third trimesters; and the Levothyroxine dose should be adjusted to maintain TSH level below 2.5 mU/L or within the trimester specific reference range.

Methods:

This was a longitudinal study conducted in BIRDEM General Hospital 2, Dhaka, Bangladesh during 2014-2015. The pregnant women with hypothyroidism receiving Levothyroxine referred to Endocrinology Outpatient Department were enrolled. The inclusion criteria was age 18-45 years, known hypothyroidism with confirmed pregnancy, with no history of thyroid malignancy, thyroid surgery or radioactive iodine therapy. The cases were selected by simple random sampling method. Free T4 and TSH level was done at the first visit by CMIA method and the dose of Levothyroxine was adjusted according to the report to maintain TSH level below 2.5 microIU/ml. A questionnaire consisting data about the subject's age, parity, obstetric history, Thyroid autoimmunity status, Levothyroxine dose before conception were filled. Weight and blood pressure were measured. The subjects were followed up at 6 to 8 weeks interval with repeat FT4 and TSH reports. Each time Levothyroxine dose was adjusted according to report and weight, blood pressure recorded. At the end, the pregnancy outcome was recorded from Department of Gynaecology and Obstetrics.

Results:

In this study total 52 women with hypothyroidism were followed during pregnancy. Majority of women were aged between 23-37 years. Among the subjects, 21 (40.4%) had history of abortion and 4 (7.7%) had history of Intrauterine death before.

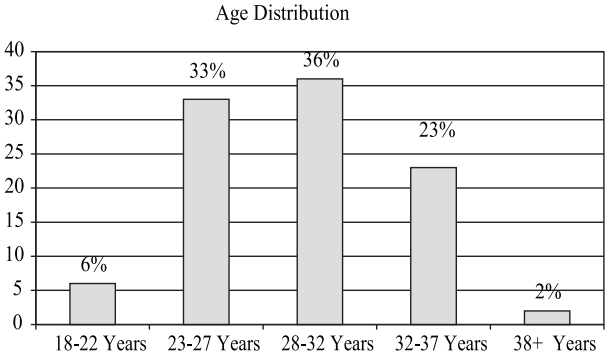

Fig.-1: *Age distribution of the samples*

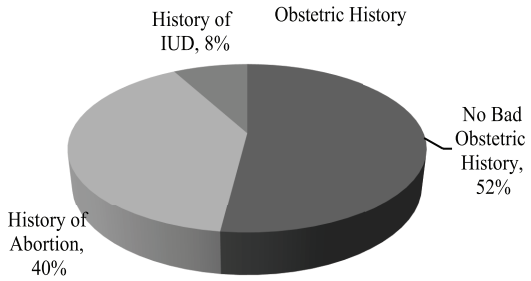

Fig.-2: *Obstetric History of samples*

Regarding thyroid autoimmunity status, 31 (59.6%) women were thyroid antibody positive. At the end there were 15 full term births (28.8%), 28 pre term delivery (53.8%), 4 Intra uterine deaths (7.7%) and 5 abortions (9.6%). (Table 1).

Table-I

Distribution of pregnancy outcome

Pregnancy Outcome	Frequency	Percentage (%)
Full term Delivery	15	28.8
Pre term Delivery	28	53.8
Intra Uterine Death	4	7.7
Abortion	5	9.6
Total	52	100

There are 56% of samples had maternal complications, among them two third (66%) had single complications and 34% had multiple complications. (Table 2). The commonest maternal complications were gestational diabetes mellitus (48%) and Pregnancy induced hypertension (27%). (Table 3)

Table-II
Distribution of Maternal Complications

Maternal Complications	Percent (n)		
Present	56% (29)	Single Complications	66% (16)
		Multiple complicatioms	34% (10)
Absent	42% (22)		
Data Missing	2% (1)		

Table-III
Types of Maternal Complications

Maternal Complications	Frequency	Percentage	Comments
GDM	25	48	10 mothers had multiple complications
PIH	14	27	
PPH	50	96	

*GDM= Gestational diabetes mellitus, PIH= Pregnancy induced hypertension, PPH=Post partum hemorrhage

Fetal complications occurred in 21 (40%) cases, among them 16 (76%) had single complications and 5 (24%) had multiple complications. (Table 4). Regarding the types of Fetal complications fetal distress (21.2%) and low birth weight (19.2%) were most common. (Table 5)

Table-IV
Distribution of Fetal Complications

Fetal Complications	Percent (n)		
Present	40% (21)	Single Complications	76% (16)
		Multiple complicatioms	24% (5)
Absent	58% (30)		
Data Missing	2% (1)		

Table-V
Types of Fetal Complications

Fetal Complications	Frequency	Percentage	Comments
LBW	10	19.2	5 Newborns had multiple complications
Congenital Anomalies	1	1.9	
Fetal Distress	11	21.2	
IUGR	4	7.7	

*LBW= Low birth weight, IUGR= Intra uterine growth retardation

Discussion:

Hypothyroidism during pregnancy has been clearly associated with adverse events like gestational hypertension, pre eclampsia, fetal deaths and spontaneous abortions.[2] In this study, it is seen that gestational diabetes is the most common complication or association in pregnancy with hypothyroidism, being associated with 48% pregnancies. It could be partly due to the fact that 59% of the women were above 28 years of age which contributed to increased risk of gestational diabetes. The study centre is a specialized and referral hospital for diabetes and endocrine diseases and this also could be a reason behind the increased finding of gestational diabetes in the study samples. But recent studies suggest an increased risk of gestational diabetes in patients with hypothyroidism. A retrospective study in the USA analyzing the medical records of 223,512 singleton pregnancies found an increased risk for gestational diabetes in patients with primary hypothyroidism.[6] Tudela et al have shown that the higher the TSH, the higher the risk of developing gestational diabetes.[10]

The next common maternal complication seen in this study was Pregnancy induced hypertension, which was found in 27% cases. This almost corresponds to the findings of Leung et al, who demonstrated that there is 22% increased risk of gestational hypertension in pregnancy with hypothyroidism.[4]

Previously, a large study performed by Antolic et al showed that women with thyroid dysfunction had a higher incidence of very preterm delivery and threatened preterm delivery compared with controls.[11] In this study, preterm delivery is found to be a common complication occurring in 53.8% cases. This finding is higher than the findings of few recent studies in India, where the incidence of preterm

delivery with hypothyroidism and pregnancy was found to be 19.40%, 11.1% and 16.67%.[12,13,14] In the present study, the higher incidence of pre term delivery could be attributed to other associated factors like gestational diabetes or hypertension. However, a 3 fold increased rate of preterm deliveries in subclinical hypothyroid women was shown in a Chinese study of 1000 women.[15] A report of 404 women with subclinical hypothyroidism showed a doubled rate of preterm birth with respect to controls.[16]

Previous studies have suggested a relationship between higher levels of maternal TSH and pregnancy loss. Negro et al. reported a significantly higher pregnancy loss rate in TPO antibody negative women with TSH concentrations between 2.5-5.0 mU/L compared to those with TSH concentrations below 2.5 mU/L (6.1% vs. 3.6%).[17] In another prospective cohort study investigating the risk of pregnancy loss (defined as miscarriage, or fetal or neonatal death) in 2497 Dutch women, the risk of child loss was found to be increased with higher levels of maternal TSH.[18] More recently, Liu and colleagues demonstrated a graded increase in miscarriage risk as maternal TSH concentrations increased.[19] In the present study pregnancy loss occurred in total 17.3% cases (abortion 9.6% and intra uterine deaths 7.7%). In a recent study in India, 6.67% of hypothyroid pregnancies had intrauterine deaths, which is similar to the findings of present study.[12] In other study done by Allan et al demonstrated 2.9% of cases having TSH 6-9.99 mU/L had fetal deaths and 8.1% of cases having TSH>10 mU/L had fetal deaths.[20]

Recent guidelines suggested that women with subclinical hypothyroidism and those with overt hypothyroidism desiring pregnancy should take Levothyroxine in a dose to ensure a TSH level of <2.5 mU/L. TSH values should be checked every 4-6 weeks during the first trimester and once during the second and third trimesters, and the Levothyroxine dose should be adjusted as necessary to reduce TSH<2.5 mU/L or within the trimester specific pregnancy range.[9] In this study, maternal TSH was closely monitored and the dose of Levothyroxine was adjusted according to TSH report. The target was to maintain TSH level below 2.5 mU/L. The rate of adverse pregnancy outcomes was high even after the effort to maintain the TSH level within this range. This could be due to other associated adverse factors like gestational diabetes, gestational hypertension, maternal age, poor nutrition etc. Since last few years, large studies demonstrated that there are population differences in TSH reference limit during pregnancy. These differences may be attributable to iodine status, thyroid auto immunity, BMI, geography, ethnicity and TSH assays used for analysis in a particular region.[21]

It is difficult to define a universal cut off value of TSH for all pregnant women. More recent studies are suggesting considering ongoing research to redefine the limit as a scientific debate.

There is no established data on the prevalence of thyroid disorders in pregnancy or reproductive age women in Bangladesh. A study shows that prevalence of sub clinical hypothyroidism and overt hypothyroidism was 6.5% and 15% in primary and secondary infertility respectively.[22] Another study in Khulna district of Bangladesh demonstrated the overall thyroid disease was estimated to be 20.43%, among which the incidence was highest in the 11-45 years group (79.89%) and female were significantly more than male, the ratio being 25:1.[23] It indicates that there could be a large number of women of child bearing age with hypothyroidism in Bangladesh who are at risk of adverse events during pregnancy. A recent study analyzing the clinic-biochemical features of hypothyroid patients showed that the higher proportion of hypothyroid cases (68%) in Bangladesh is auto antibody positive.[24] The adverse outcomes during pregnancy are augmented by autoimmunity status, as has been shown in different studies. The findings suggest for a universal screening of thyroid function and autoimmunity status in reproductive age women to reduce adverse pregnancy outcomes in Bangladesh.

There is lack of data regarding prevalence and pattern of adverse pregnancy outcomes in hypothyroid women in Bangladesh. Sufficient evidence also lacking that can indicate what could be the safe upper limit of TSH level for pregnant women of Bangladesh. A recent study by Jahan et al analyzing the association between TSH level and first trimester pregnancy loss in Bangladesh demonstrated that odds of having miscarriage whose TSH level above 2.1 mU/L is 4 times compared to those with TSH level below 2.1 mU/L after adjusting for the effects of age and BMI.[25] Findings of the present study along with the study by Jahan et al provide interest on existing discussion on redefining the upper limit of TSH level at a local level. Results that raised the issue before include the work of Panesar et al who reported a normal range for first trimester TSH levels of 0.03-2.3 mU/L; that of Gilbert et al, who found a normal TSH range of 0.02-2.15 mU/L; and that of Stricker et al who reported a 95% confidence interval for normal TSH level to be 0.08-2.83 mU/L.[26,27,28]

As the patient selection of the study was done in a tertiary level specialized hospital of Bangladesh, it may not represent the overall population picture. The study was a hospital based one and control group was not included. For better extrapolation, a population based study should be conducted in future.

Conclusion:

Hypothyroidism during pregnancy is associated with adverse pregnancy outcomes even after close monitoring and frequent dose adjustment in a specialized hospital. Since there are substantial difference in the upper reference limit and target of TSH between different populations, each region or hospital should ideally seek their own reference ranges to avoid the adverse outcomes. Further large studies and researches are required to establish the reference range of TSH for pregnant women of Bangladesh in order to reduce adverse pregnancy outcomes.

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ORIGINAL ARTICLE

Assessment of Knowledge of Cervical Cancer Transmission and Prevention among the Mothers of Daughters Aged Below 10 Years

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Abstract

Introduction: Cervical Cancer is the second most common cancer among women worldwide. It is one of the few preventable human cancers. Maternal knowledge is required for vaccination of their adolescent girls because they are key decision makers and potentially a major source of information for their daughters. Bangladesh Government will introduce HPV vaccine under EPI program for adolescent girls aged 10 years from 2018. For this reason, it is important to assess the knowledge level of mothers of daughters aged below 10 years.

Objective: The objective of this study was to assess the knowledge of Cervical Cancer transmission, prevention and HPV vaccine among mothers of daughters aged below 10 years.

Methods: A cross sectional descriptive study was conducted among the mothers of daughters aged below 10 years, live in the Mohakhali 'Sat Tola' slum area of Dhaka city. The pre-tested questionnaire was used to collect information from the respondents by face to face interview at house-hold level. Questions were on socio-demographic characteristics, knowledge about Cervical Cancer transmission, prevention and HPV vaccination. Convenient sampling technique was used to select the sample. The sample size was 100 in number. The total no. of questions on knowledge was 22. Knowledge score was divided into 3 category: poor, average and good knowledge. Poor knowledge score was 0 to 7, average knowledge score was 8 to 14 and good knowledge score was 15 to 22. Frequency, percentage and mean was done by using SPSS version 21.

Results: About 41% respondents' age was 21 to 29 years, most (63%) of them were primary school educated, most (80%) of them were house-wife and 43% of their monthly family income was between 11,000 to 15,000 taka. Respondent's mean age at marriage was 15 years and mean age was 17 years when their first child born, (39%) had two children. More than half (55%) respondents had poor knowledge and 2% respondents had good knowledge. Almost all (98%) respondents heard about cancer, 77% respondents heard about Cervical Cancer, 8% respondents knew about sign and symptom and only 2% respondents knew the causes of Cervical Cancer, 3% respondents told prevention of Cervical Cancer is possible but 12% respondents heard about VIA test. Around 18% respondents heard about HPV vaccine but nobody knew in which age this vaccine should be administered.

Conclusion: The knowledge of Cervical Cancer transmission, prevention and HPV vaccination among mothers who live in slum of Dhaka city is poor. Providing knowledge to these mothers is essential.

Key words: Cervical Cancer, Human papilloma virus, HPV vaccine.

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Introduction:

Cervical Cancer is one of the few preventable human cancers.[1] It is the second most common cancer among women worldwide and about 86% of Cervical Cancer occur in developing countries.[2] More than half a million women are newly diagnosed with Cervical Cancer each year, with approximately 90% of Cervical Cancer-related death occurring in developing countries.[3] However, in developing countries, it remains the most common cause of cancer related deaths among women. Cervical Cancer which is one of the preventable cancers and the important public health problem worldwide and especially in developing countries.[4]

There are 13 to 15 lakh cancer patients in Bangladesh, with about 2 lakh patients newly diagnosed with cancer each year. As an overview, in women, Cervical Cancer and breast cancer are most prevalent.[5] According to World Health Organization (WHO) statistics, incidence of Cervical Cancer cases in Bangladesh has been estimated at 167 per 100,000

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populations and 6,582 women die every year in the country for this cancer. The problem of Cervical Cancer in Bangladesh is particularly acute because of poverty, early age marriage, multiple marriages, high parity and illiteracy. In developing countries, women's knowledge about risk factors of Cervical Cancer is very limited. However, it is considered one of the most preventable cancers.[6]

Despite the high prevalence of Cervical Cancer, many studies have shown that women's knowledge about HPV and Cervical Cancer is very low[1]. The incidence of Human Papilloma Virus (HPV) infection and Cervical Cancer can be reduced by increasing vaccination for HPV.[7] In Bangladesh, there is little awareness among the general population, health care professionals and policy makers about Cervical Cancer prevention. Immunization against the most prevalent HPV types affecting the country may be an efficient means to long term prevention.[8] Maternal knowledge is required for vaccination of adolescent girls, they are the key decision makers and potentially a major source of information for their daughters.[9] Therefore, improving the knowledge of the mothers who have daughters aged below 10 years regarding Cervical Cancer transmission, prevention and organism is one of the most important steps in enhancing the vaccination coverage among Bangladeshi females. The objective of this study was to obtain the knowledge of Cervical Cancer transmission, prevention and organism among the mothers of selected slum area of Dhaka city and to identify the main barrier to get information about Cervical Cancer. So that possible interventions could be taken to increase the level of knowledge of Cervical Cancer among the mothers.

Methods:

This was a cross-sectional descriptive study design. This study was done in 'Sat Tola' slum in Mohakhali, Dhaka, Bangladesh. The study was conducted from January, 2016 to December, 2016. Data collection was done for four weeks. Population was the mothers of daughters aged below 10 years, were defined as study population. The mothers were selected by using convenient sampling technique. The mothers who gave voluntary consent were taken as sample. Inclusion criteria is mothers who have daughters aged below 10 years and mothers who are willing to participate in the study. Sample size was 100. Pre-tested questionnaire was used to collect information from the respondents by face to face interview at house hold level. This study used a questionnaire, consists of 22 questions about knowledge of Cervical Cancer, Cervical Cancer transmission, prevention and HPV. Among the questions 7 questions about knowledge of Cervical Cancer and Cervical Cancer transmission, 11 questions about knowledge of Cervical Cancer prevention and 4 questions about knowledge of HPV. Each question was scored '1' point for the correct response and '0' for the wrong answer. An overall total knowledge score was calculated by adding up the correct score of each respondent across all 22 questions. Knowledge score was divided into 3 categories (poor, average and good knowledge). Statistical data analysis was done using SPSS software version 21.0.

Results:

In table I shown, 41% respondents' age was between 21-29 years, 63% were primary school educated, 80% were house-wife, 43% respondents' monthly family income was 11,000-15,000 taka, mean age at marriage was 14.62±2.673 years, mean age during first child born was 17.13±2.866 years, 39% respondent had two children, mean age of last child was 63.4±39.92 months and mean knowledge score was 7.19 out of 22.

Table- I

Distribution of respondents by socio-demographic characteristics (n=100)

Socio-demographic characteristics	Frequency (n)	Percentage (%)
A. Age of respondents in year		
<20	17	17%
21-29	41	41%
30-39	30	30%
40 and above	11	11%
Don't know	1	1%
Mean age of respondents in year±SD	29.08±9.621	
B. Educational status		
No formal education	33	33%
Primary	63	63%
Secondary and above	4	4%
C. Employment status		
House wife	80	80%
Service holder	10	10%
Business	2	2%
Maid servant	8	8%
D. Monthly house-hold income in taka		
<5000	15	15%
6,000- 10,000	38	38%
11,000- 15,000	43	43%
>15,000	4	4%
E. Age at marriage of respondents in year (mean±SD)	14.62±2.673	
F. Age during first child born in year (mean±SD)	17.13±2.866	
G. Number of children of respondents		
One	28	28%
Two	39	39%
Three	17	17%
Four	8	8%
Five or more than five	8	8%
H. Age of last child in month (mean±SD)	63.4±39.92	
I. Knowledge score (mean)	7.19 out of 22	

In table II shown, 98% respondents heard about Cancer but only 77% mothers heard about Cervical Cancer where 54.9% respondents heard from neighbor. Only 8% respondents had knowledge about sign symptom and only 2% respondents had knowledge about causes of Cervical Cancer.

Table- II

Knowledge about Cervical Cancer transmission (N=100)

Variables	Frequency (n)	Prcentage (%)
A. Heard about Cancer		
Yes	98	98%
No	2	2%
B. Heard about Cervical Cancer		
Yes	77	77%
No	23	23%
C. Sources of knowledge about Cervical Cancer (n=77)		
Health worker	14	17.1%
Television	10	12.2%
Neighbor	45	54.9%
Relatives	13	15.9%
D. Knowledge about sign symptom of Cervical Cancer (N=100)		
Yes	8	8%
No	92	92%
E. Knowledge about causes of Cervical Cancer (N=100)		
Yes	2	2%
No	92	92%

Table III

Knowledge about Cervical Cancer prevention, and organism (N=100)

Variables	Frequency (n)	Percentage (%)
A. Heard about VIA test		
Yes	12	12%
No	88	88%
B. Check up Cervix by VIA test		
Yes	3	3%
No	97	97%
C. Heard about Cervical Cancer vaccine		
Yes	18	18%
No	82	82%
D. Source of knowledge about Cervical Cancer vaccine (n=18)		
Health worker	10	55.6%
Television	1	5.6%
Neighbor	5	27.8%
Relative	2	11.1%
E. Recieve Cervical Cancer vaccine		
Yes	2	2%
No	98	98%
F. Heard about Human Papilloma Virus		
Yes	6	6%
No	94	94%
G. Knowledge about age of Cervical Cancer vaccine		
Yes	0	0%
No	100	100%

In table III shown, 12% respondents heard about VIA test, only 3% check up Cervix by VIA test, 18% respondents heard about Cervical Cancer vaccine. Among them 55.6% heard from health worker. Only 2% respondents took vaccine only 6% heard about Human Papilloma Virus and 100% respondents did not know in which age vaccine should be administered.

In fig-1 shown, 60% respondents did not know whether Cervical Cancer prevention is possible or not, 36% told prevention is possible and 4% told prevention is not possible.

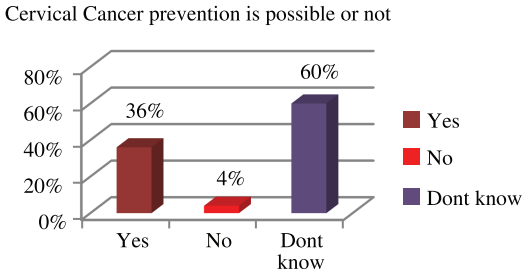

Fig-1: *Opinion about prevention of Cervical Cancer*

In fig-2 shown, 87 respondents wanted to know about Cervical Cancer from health worker, 12 respondents from hospital and 7 respondents from television.

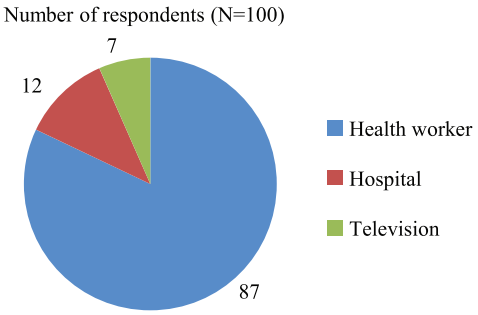

Fig-2: *Desire source of knowledge*

In fig-3 shown, 55% respondents had poor knowledge, 43% had average knowledge and only 2% had good knowledge.

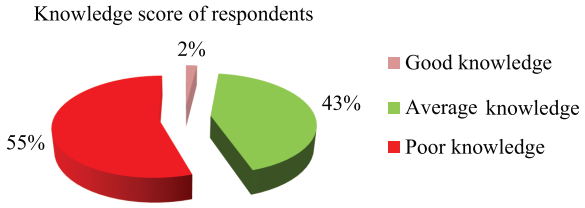

Fig-3: *Knowledge score of respondents (n=100)*

Discussion:

Knowledge on Cervical Cancer among different groups, professionals, populations and students were evaluated by survey worldwide in several studies. In Bangladesh, socio-epidemiological data on Cervical Cancer status are scarce, particularly Cervical Cancer knowledge of mothers. The mean age of the study subjects was 29.08± 9.621 years. In a study conducted by Fernandez et al. (2014), it was seen that mothers' mean age was 47.9± 5.5 years. In this study, 63% mothers had primary education, 3% mothers had secondary and 1% mothers had higher secondary education where as in a study conducted by Kose et al. (2014), 63% of the mothers were primary school, 25.7% were high school and 11.4% were university graduates. In this study, it was found that 77% mothers heard of Cervical Cancer. In a study conducted by Ahmed et al. (2013), it was seen that 66.9% of the mothers had heard of Cervical Cancer. In our study, only 2% mothers knew about causes of Cervical Cancer where as in a study, conducted at Nigeria by Ahmed et al. (2013), it was seen that 62.5% mothers knew about causes of Cervical Cancer. In our study, 12% mothers heard about VIA test and 18% mothers heard about HPV vaccine. In other studies conducted it is seen that 83.5% of the mothers[4] and 53.7% of the mothers [12] had no knowledge about HPV vaccination. Among 18 mothers who expressed that they knew about vaccination, 55.6% (n=10) stated that they learned about it from a health worker, 27.8% (n=5) of them learned it from neighbor, 11.1% (n=2) learned it from relative and 5.6% (n=1) learned it from television. In a study conducted by Kose et al. (2014), 27.1% (n=35) stated that they learned about it from a health professional, 61.2% (n=79) of them learned it from communication tools like television, radio, newspapers or internet, 11.6% (n=15) learned it from friends or relatives. In our study, only 2% (n=2) mothers took HPV vaccine, 100% (n=100) among 100 mothers did not know the age of HPV vaccine administration. In a study conducted by Kose et al. (2014), found out that a total of 0.7% mothers who had daughters were found out to be vaccinated against HPV, 83.2% of the mothers did not know age of vaccination was applied. In our study, it was seen that 94% of the mothers who have daughters aged below 10 years had never heard of HPV before. In a study conducted by Marlow et al. (2007), it was seen that HPV knowledge 72.8% of the mothers who have daughters between the ages of 8-14 had never heard of HPV before. In our study the knowledge score of Cervical Cancer showed that there was good knowledge (2%) about Cervical Cancer among the mothers, living in slum area. Study conducted by Ahmed et al. (2013), where the knowledge score of Cervical Cancer showed that there was a fair knowledge (43.5%) of Cervical Cancer among respondents living in slum area. In this study there was no significant association between mothers' education level and their knowledge score. In a similar study conducted by Ozan et al. (2011), there was no significant difference. However, in a similar study conducted by Kose et al. (2014), there was a significant association between the mothers' education level and their knowledge. According to mothers' economic conditions, there is no significant association between their knowledge about HPV and economic condition. However, there was a significant relationship between high income and the mothers' awareness of HPV was found by Sanders Thompson et al. (2011).

Conclusion:

This study showed that most of the respondents heard about Cancer and Cervical Cancer, among mothers who heard about Cervical Cancer most of them heard from neighbor. But most of the respondents did not know about sign symptoms and the causes of Cervical Cancer. Majority of the respondents did not know whether Cervical Cancer prevention is possible or not. In this study, study was done on mothers who have daughters aged below 10 years at slum area of Dhaka city where under-privileged people lived, they are deprived from health services such as home visit from female health worker from government sector that's why the mothers cannot get proper information about health, so if we want to increase the knowledge level of mothers living in a slum area of Dhaka city at first we have to provide information to increase awareness among mothers about Cervical Cancer, Cervical Cancer transmission, prevention and HPV. The mothers who had some information about Cervical Cancer stated that they learned about the subject from neighbor, health worker, relatives and television. Based on this result, it can be suggested that doctors and nurses should be informed about this situation. Despite low knowledge of Cervical Cancer, all mothers were willing to get information about this disease, where majority of them wanted to get information from health worker. We recommend improving mothers' knowledge through health education.

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ORIGINAL ARTICLE

Evaluation of Anti-Ulcer Effect of Alcoholic Extract of Nigella Sativa Seeds on Experimental Albino Rats

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Abstract

Introduction: Nigella sativa has been used as a natural remedy for many years. Recently in few studies, it has been shown that thymoquinone (TQ) component of Nigella sativa oil possess gastro protective activity. This study was done to evaluate the antiulcer effect of alcohol extracts of Nigella sativa seeds on rats.

Objective: To evaluate the anti-ulcer effect of Nigella sativa seeds extract.

Methods: Alcoholic extract of Nigella sativa was prepared with the help of Soxhlet's apparatus. Twenty four (24) albino rats (150-175gm) of either sex were divided into four groups consist of 6 rats in each group. Group-A was served as control group and provided with normal saline (2 ml/kg) & Group-B was provided with aqueous suspension of aspirin (200 mg/kg). On the other hand, Group-C was served as disease control group and provided with normal saline (2 ml/kg) & Group-D was provided with alcoholic extract of Nigella sativa (150 mg/kg) for 8 days. After 8 days of treatment, animals were fasted for 24 hours. Then administration of aqueous suspension of aspirin (200 mg/kg) and after 4 hours all rats were sacrificed and were prepared for dissection.

Results: Aspirin caused marked gastric damage in disease control group which was prevented in Nigella sativa extract treated group significantly.

Conclusion: Alcoholic extract of Nigella sativa seeds showed significant anti-ulcer effect against aspirin induced gastric ulcer in rats.

Keywords: Anti-ulcer, Nigella sativa, Aspirin.

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Introduction:

The global incidence of peptic ulcer disease has greatly increased during the last decades. The term peptic ulcer refers to an ulcer in the lower oesophagus, stomach, duodenum, in jejunum after surgical anastomosis to the stomach or rarely in ileum adjacent to a Meckel's diverticulum.[1]

Nigella sativa seeds have been in use as a natural remedy for over 4000 years in various parts of the world. These seeds are reported to benefit almost every system of the body.[2-5] Seeds of *Nigella sativa* contains >30% of a fixed oil and 0.40-0.45 w/w of a volatile oil. The volatile oil has been shown to contain 18-24% thymoquinone (TQ) and 46% monoterpenes. Recently the active principle of *Nigella sativa* oil thymoquinone (TQ) has shown to possess a gastro protective activity in rats[6] but few studies have been done to find the ulcer protective activity of alcoholic extract of the seeds of *Nigella sativa*. Therefore, the aim of this study was to evaluate the anti-ulcer effect of alcoholic extract of *Nigella sativa* seeds on experimental albino rats.

Methods:

The study was conducted in the Department of Pharmacology & Therapeutics in collaboration with

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Department of Pathology, Dhaka Medical College, from January 2010 to December 2010. Ethical clearance was taken from the ethical committee.

Experimental animals: The experiment was carried out on a total number of 24 healthy albino rats. The rats were aged between 8-10 weeks of both sexes & weighing between 150-175 gm. They were kept in medium sized metallic cages in animal house of Pharmacology Department at Dhaka Medical College, Dhaka. They were allowed to live at room temperature, fed on standard pellets of rat food & allowed to drink tap water.

Plant material: Alcoholic extract of *Nigella sativa* was made from kalojira which was bought from local market of Dhaka, Bangladesh.

Drugs & chemicals:

i) Aspirin was bought from local medicine shop, Dhaka, Bangladesh.

ii) 0.9% Sodium Chloride (normal saline) & distilled water were supplied by the Department of Pharmacology of Dhaka Medical College, Dhaka, Bangladesh.

Preparation of plant extract: 1000 gm of *Nigella sativa* (kalojira) was purchased from the local market. The seeds were dried & crushed into coarse powder which was macerated with alcohol (99%v/v) using soxhlet apparatus. The extract was evaporated by rotator evaporator at an optimum temperature of 40-50º c under vacuum. The extractive value (v/v) of alcoholic dry extract was 4.25%.

Experiment design:

The experiment was divided into 2 parts: Experiment-1 & Experiment-2.

Experiment-1:

It was comprised of 12 rats which were divided into 2 groups each having 6 rats. Groups were labelled as Group-A & Group-B.

Group-A:

This group was served as control group & they were provided with normal saline (2 ml/kg body wt) orally by gastric tube.

Group-B:

This group was provided with aqueous suspension of aspirin (200 mg/kg body wt) orally by gastric tube. After 4 hrs all rats were sacrificed by an overdose of diethyl ether & stomach was collected for gross & histological study. Experiment on these groups was carried out to evaluate the effect of aqueous suspension of aspirin in rats.

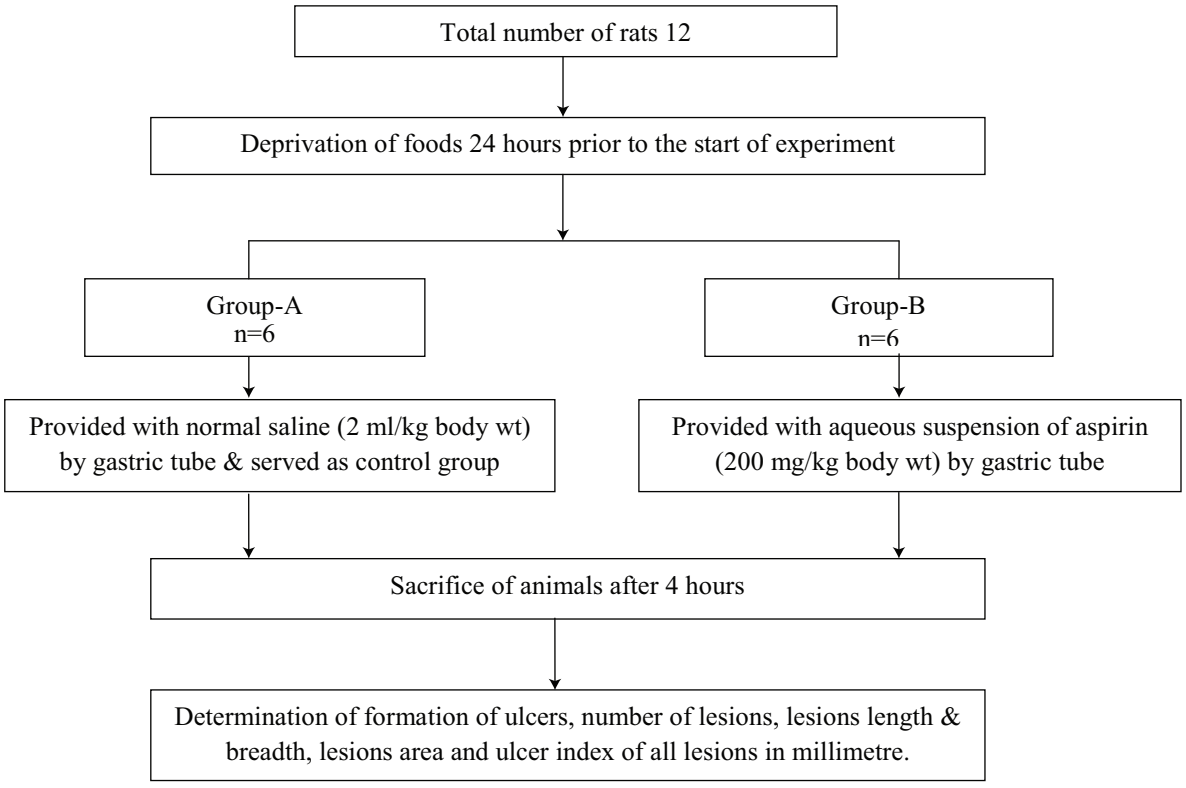

Fig 1: *Flow chart of Experiment-1*

Experiment-2:
It was comprised of 12 rats. They were divided into 2 groups each containing 6 rats labelled as Group-C & Group-D.

Group-C:
This group was served as disease control group & were provided with normal saline (2 ml/kg body wt) orally by gastric tube for 8 days.

Group-D:
They were provided with alcoholic extract of *Nigella sativa* (150 mg/kg body wt) orally by gastric tube for 8 days.

After 8 days of treatment, animals were fasted for 24 hrs. Then administration of aqueous suspension of aspirin (200 mg/kg body wt) by gastric tube & after 4 hrs, all rats were sacrificed by an overdose of diethyl ether & stomach was collected for gross & histological study. Experiment in these groups was carried out to evaluate the anti-ulcer effect of alcoholic extract of *Nigella sativa* on aspirin induced gastric ulcer in rats.

Morphological parameter studied:

i) Number of lesion (Mean ± SD) per rat in each group

ii) Individual lesion length & breadth in millimetre (Mean ± SD) for each group

iii) Individual lesion area (length × breadth) in square millimetre (Mean ± SD) for each group

iv) Mean ulcer index (sum of length of all lesions in each stomach) in millimetre for each group.

Statistical analysis: All relevant information for each rat was recorded in a redesigned data collection sheet. Collected data were screened & compiled. All data were recorded in tabulated form & the results were expressed as Mean±SD. The significance of the differences in the values was performed by paired t-test.

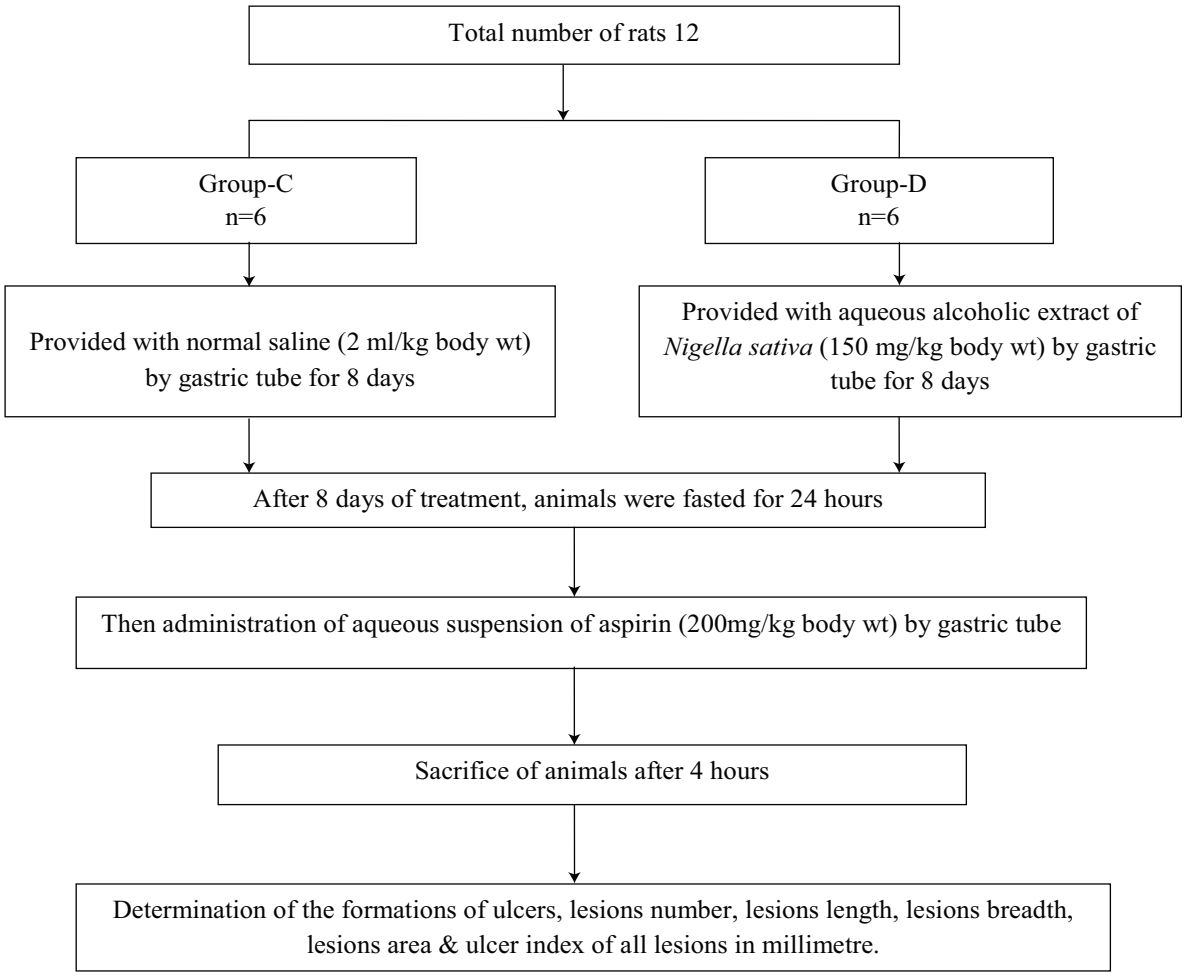

Fig 2: *Flow chart of Experiment-2*

Results:

Table I shows the effect of aqueous suspension of aspirin in rats. Group-A had no lesion in the stomach but in Group-B the (Mean ± SD) number of lesion, lesion length, lesion breadth, lesion area & lesion index were 4.83 ± 0.75, 6.52 ± 3.80, 1.63 ± 1.35, 13.58 ± 15.90 and 31.50 ± 9.60 respectively. Result showed p value < 0.001, which was highly significant. Thus, aqueous suspension of aspirin was shown to have strong ulcer producing effect in rats.

Table I

The effect of Aspirin on mean number of lesion, lesion length, lesion breadth, lesion area & lesion index in each group

Parameters	Group-A (Mean ±SD)	Group-B (Mean ± SD)
Mean number of lesion	0	4.83 ± 0.75
Mean lesion length	0	6.52 ± 3.80
Mean lesion breadth	0	1.63 ± 1.35
Mean lesion area	0	13.58 ± 15.90
Mean lesion index	0	31.50 ± 9.60

Group-A was served as control group and was provided with normal saline (2 ml/kg body wt) by gastric tube.

Group-B was provided with aqueous suspension of aspirin (200 mg/kg body wt) by gastric tube.

Table II shows the anti-ulcer effect of alcoholic extract of *Nigella sativa* in rats.

Table II

The effects of alcoholic extract of Nigella sativa on mean number of lesion, lesion length, lesion breadth, lesion area & lesion index in each group

Parameters	**Group-C** (Mean ± SD)	**Group-D** (Mean ± SD)
Mean number of lesion	5.33 ± 0.82	4.17 ± 0.75
Mean lesion length	6.75 ± 3.71	3.48 ± 2.25
Mean lesion breadth	1.63 ± 1.29	0.77 ± 0.48
Mean lesion area	13.66 ± 15.14	1.30 ± 3.55
Mean lesion index	36.00 ± 11.08	14.51 ± 2.47

Group-C was ulcer control group and they were provided with normal saline (2 ml/kg body wt) for 8 days.

Group-D was provided with alcoholic extract of *Nigella sativa* (150 mg/kg body wt) for 8 days.

Comparing Group-D with Group-C (control):

There was a significant reduction in ulcer number, ulcer length, ulcer breadth, ulcer area & ulcer index seen in Group-D which was pretreated with alcoholic extract of *Nigella sativa*. Result showed p value < 0.001, which was highly significant. Thus, alcoholic extract of *Nigella sativa* showed to have a significant anti-ulcer effect in rats.

Discussion:

Plant extracts are some of the most attractive sources of new drugs and have shown promising results in the treatment of gastric ulcers. Several folk medicinal plants and herbs have been used to treat gastrointestinal disorders or gastric ulcer.

It was found that oral administration of alcoholic extract of *Nigella sativa* seeds markedly reduced aspirin induced gastric ulcer in rats. Animals pre-treated with alcoholic extract of *Nigella sativa* seeds produced significant reduction p < 0.001 in ulcer index as established by measuring ulcer index and further by histological findings. The cytoprotective effect of Nigella sativa observed in the present study could be attributed to the endogenous generation of PG, responsible for maintaining the cellular integrity of the gastric epithelium.[7] It has been reported that plants and spices sometimes exhibit their cytoprotective action through mild irritant property. This protection is called "adaptive cytoprotection."[8] This is supported by histological findings of our study. Pre-treatment with alcoholic extract of *Nigella sativa* prevented histological changes like congestion, haemorrhage, oedema, necrosis, inflammatory & dysplastic changes, erosions & ulceration caused by the destructive stimuli of aspirin in the gastric tissue. This cytoprotective ability of *Nigella sativa* may be attributed to chemical components such as thymoquinone (TQ), a major and active constituent of *Nigella sativa*.[6] In some earlier studies, TQ has been reported to exhibit a significant protective action on gastric mucosal lesions induced by different necrotic agents.[9] Recent clinical & experimental studies have shown several therapeutic effects of *Nigella sativa* extracts including its antioxidant, hepatoprotective, immunomodulatory, anti-inflammatory and anti-tumour activities.[10] Our findings are in agreement with data reporting that an alcoholic extract of *Nigella sativa* did not only inhibit gastric secretion but also reduced the ulcer index in rats.[11] *Nigella sativa* extract was able to produce a significant reduction of the gastric mucosal damage induced by aspirin, indicating a probable local increase in PG synthesis.[12] The results of the present study establish the gastro protective role of alcoholic extract of *Nigella sativa* that

substantiates its use against gastric disorders in traditional medicine.

Conclusion:

Pre-treatment with alcoholic extract of *Nigella sativa* can partly protect the gastric mucosa against aspirin induced gastric damages in rats and promote ulcer healing. The present study has pointed out possible anti-ulcer effect of *Nigella sativa*. However, detailed chemical studies followed by pharmacological investigations and toxicity evaluations are still required to isolate the pure active principles of *Nigella sativa* and to elucidate their modes of anti-ulcer actions.

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ORIGINAL ARTICLE

Rising of Antibiotic Resistance against Urinary Pathogens

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Abstract

Introduction: Major public health threat is the emergence of antimicrobial-resistance. Urinary tract infection is a common and serious health problem worldwide. So, antibiotic resistance pattern against the common uropathogens has been rising over the years due to mismanaged therapy.

Objective: To assess the antibiotic resistance against E.coli causing urinary tract infections.

Methods: A cross-sectional study was done to observe the culture and sensitivity of 355 urine samples among patients attending the outpatient departments of International Medical College Hospital (INMCH) between December 2013 to November 2014.

Results: A total of 104 urine culture positive results were analyzed for isolation and identification of bacteria and antimicrobial resistance testing. E.coli was isolated from 83 (79%) samples followed by Enterococci (5.7%), Pseudomonas (5.7%), Acinetobacter (4.8%) and Klebsiella (3.8%). E.coli was highly resistance to Cephalexin (98.8%) followed by Levofloxacin (92.8%), Amoxycillin (89.16%) followed by Ceftriaxone and Cephradine (86.7%) while sensitive to Doxycycline (53%) followed by Ciprofloxacin (51.81%), Nitrofurantoin (49.4%).

Conclusion: E.coli reveals high rates of resistance to Cephalexin, amoxicillin and ceftriaxone in the study area. Regular monitoring of antibiotic resistance is recommended for empirical therapy.

Key words: E.coli, UTI, Antibiotic resistance

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Introduction:

Escherichia coli is one of the common pathogen causing urinary tract infections. It is concern that increasing rates of resistance of E.coli to the commonly prescribed antibiotics for UTI due to irrational use of antimicrobial agents.[1,2] Antimicrobial is emergence to resistance.[3] Resistance pattern are different in various populations and environments that also contribute.[2] Knowledge of the antimicrobial resistance patterns of E.coli causing UTI according to local epidemiology is essential for proper treatment.[4] The objective of the present study was to assess the antibiotic resistance against E.coli causing UTI.

Methods:

The study was conducted in the department of Microbiology, International Medical College Hospital (INMCH). A total of 355 urine samples were reviewed as a cross-sectional observation from the registration record of Microbiology Laboratory of IMCH. Among them, 104

culture positive results were taken for the study. Bacterial isolation and in vitro susceptibility test reports were evaluated.

Results:

Out of a total 355 urine samples, 104(29.3%) cases were culture positive. A high rate of bacterial isolation was seen among females (79%) than males (21.15%) (Table: I).

Most of the positive female cases were in the age group 16-30 years while positive male cases in 0-15 years age group (Table:I).

Table I

Age and Sex distribution of UTI cases (n=104)

Age groups	Male	Female
0-15	6	10
16-30	5	42
31-45	5	20
46-60	4	7
>60	2	3

E.coli was isolated from 83 (79%) samples followed by Enterococci (5.7%), Pseudomonas (5.7%), Acinetobacter (4.8%) and Klebsiella (3.8%) (Table: II).

Table II

Frequency of pathogens causing UTI in patients attending OPD of IMCH (n=104)

Rank Order	Organism	Isolation rate
1	E.coli	83 (79%)
2	Enterococci	6 (5.7%)
3	Pseudomonas	6 (5.7%)
4	Acinetobacter	5 (4.8%)
5	Klebsiella	4 (3.8%)

E.coli was highly resistance against Cephalexin (98.8%) followed by Levofloxacin (92.8%), Imipenem (90.4%), Amoxycillin (89.1%), Ceftriaxone (86.7%) while it is highly sensitive to Doxycycline (53%) followed by Ciprofloxacin (51.8%), Nitrofurantoin (49.4%). (Table: III)

Table III

Distribution of antibiotic resistance against bacterial isolates (n=104)

Drugs	Organism									
	E.coli (n= 83)		Enterococci (n= 06)		Pseudomonas (n=06)		Acinetobacter (n= 05)		Klebsiella (n= 04)	
	S	R	S	R	S	R	S	R	S	R
Amoxycillin	9	74	3	3	NT	NT	1	4	NT	4
Cephradine	11	72	3	3	NT	NT	2	3	1	3
Ciprofloxacin	43	40	5	1	4	2	5	-	3	1
Gentamycin	37	46	6	-	6	-	4	1	3	1
Cephalexin	01	82	2	4	2	4	1	4	1	3
Doxycycline	44	39	6	-	5	1	3	2	4	-
Ceftriaxone	11	72	4	2	2	4	3	2	3	1
Cotrimoxazole	35	48	4	2	2	4	3	2	2	2
Levofloxacin	06	77	4	2	5	1	4	1	2	2
Imipenem	08	75	5	1	5	1	5	-	4	-
Nitrofurantoin	41	42	3	3	2	4	4	1	2	2
Amikacin	31	52	5	1	6	-	5	-	3	1

(Note : S=Sensitive, R= Resistance and NT=Not Tested)

Discussion:

In the female community, Urinary tract Infection (UTI) is one of the most common bacterial infections and often associated with significant mortality and morbidity.[5,6] Factors responsible for UTI, such as short urethra contribute to the frequent microbial invasion in females.[1,7] The present study shows females have a higher infection rate (79%) as compared to the males (21.15%) which is consistent with that of other reported studies.[4,5,8] In member of Enterbacteriaceae family, especially E. coli is the major cause of UTI.[9,10,11,12] In this study, E.coli had the highest isolation rate (79%), followed by Enterococci (5.7%), Pseudomonas (5.7%), Acinetobacter (4.8%) and Klebsiella (3.8%). Similar findings were reported by Suman et al. [12]

Although diagnosis of UTIs is relatively simple, treatment is growing more complex due to emperic antimicrobial therapy and change in the resistance pattern of the urinary pathogens. There was a variation in the sensitivity pattern of E.coli to each of the antibiotics that were studied. E.coli was highly sensitive to Doxycycline (53%) followed by Ciprofloxacin (51.8%), Nitrofurantoin (49.4%). Other studies reported comparable results.[13, 14] Sensitivity to Gentamycin in the present study was 44.5% which is coincide with another study. [4]

The overall resistance of E.coli to antimicrobials was high in the present study. Among the commonly used antibiotics in UTIs, high level of resistance of E.coli was reported against Ceftriaxone (86.7%), Amikacin (62.6%) and Gentamicin (55.4%). These results are in accordance with another study.[9] Increased resistance to these antibiotics is alarming as they were considered one of the best options for UTI treatment. Extensive use is also a contributing factor for their poor activity. The Ciprofloxacin resistance in the present study was comparatively lower (48%) in contrast to other reported studies.[1, 4, 15] Being in the borderline, the drug must be used judiciously in UTIs.

Conclusion:

Increasing resistance of E. coli to commonly used antibiotics is our major concern at present. Moreover there is also variation in the antibiotic susceptibility pattern worldwide. So, a continuous evaluation of its resistance pattern in our population on a regular basis is a necessity for effective treatment and prevention of drug resistance.

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REVIEW ARTICLE

Impact of Vitamin D on Immune System

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Abstract

Historicaly Viatmin D has been thought only to have an effect on calcium metabolism and bones. Recent works has found active form of vitamin D has immunomodulatory effect on cells of immune system as well as several cytokines. Current studies linked the deficiency of Vitamin D with autoimmune disease including Type I diabetes mellitus, Multiple sclerosis, Crohn's disease, Rheumatoid Arthritis, Systemic Lupus Erythematosus and infectious disease like tuberculosis. But many studies have suggested no association between vitamin D concentration and development of immunological effect. Further research is needed in this area to understand the effect of Vitamin D in immune mediated disease. This article reviews the physiology and immunomodulatory role of vitamin D emphasizing the importance of further research.

Key words: Vitamin D, Immune system, Immunomodulatory effect

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Introduction:

Vitamin D is a fat-soluble vitamin and a steroid hormone that is unique in that it has endocrine, autocrine and paracrine effect. Vitamin D is important for the development and maintenance of bone and maintenance of normal calcium and phosphorus homeostasis.[1,2,3] Vitamin D deficiency is known for a long time mainly for its association with fracture and bone disease like rickets and osteomalacia. It was recently demonstrated that most tissues not only express the Vitamin D Receptor (VDR) but also possess 25(OH) D-1-alpha-hydroxylase activity which convert, 25-hydroxyvitamin D, to the active form, 1,25-dihydroxyvitamin D.[4] The identification of 1 alpha hydroxylase enzyme and extrarenal synthesis of 1,25 (OH)2D has provided new insights into the function of this vitamin. [5,6] Vitamin D have some effect on regulation of growth and differentiation of cells of immune system and cytokines. During the past decade association between vitamin D insufficiency and increased risk of various non-skeletal morbidities have been recognized including its role in chronic illness like autoimmune diseases.[7,8,9,10] This review attempts at revisiting the role of this important vitamin in the light of recent developments and provides a comprehensive account of the extra skeletal effects.

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Methods:

A search of the literature was done using PubMed, Google scholar, and Cochrane database using the following keywords in the search string – vitamin D extra skeletal, immune system, autoimmune diseases, rheumatoid arthritis, systemic lupus arthritis, multiple sclerosis type I diabetes mellitus, tuberculosis upto March 2017. To be included in the review, a study must have been published in English, with a case-control, cohort, or cross-sectional study design, and with the primary outcome of effect of vitamin D on immune system.

Sources of vitamin D and metabolism

Humans get vitamin D from exposure to sunlight, from their diet, and from dietary supplements.[11,12, 13] Few foods naturally contain Vitamin D, including oily fish and oils from fish, cod liver oil, Solar ultraviolet-B radiations (wavelength 290 to 315 nm) penetrate the skin and converts 7-dehydrocholesterol vitamin D3.[11] The amount of vitamin D production in the skin depends on latitude, season, time of the day, duration of sun exposure, an increase in skin pigmentation, aging, especially age >65 years and

the topical application of sunscreen and the practice of purdah.[15] Vitamin D from the skin and diet is metabolized in the liver to 25-hydroxyvitamin D. 25-hydroxyvitamin D is metabolized in the kidneys by the enzyme 25-hydroxyvitamin 1á hydroxylase (CYP27B1) to its active form, 1, 25-dihydroxyvitamin D. The renal production of 1, 25-dihydroxyvitamin D is tightly regulated by plasma parathyroid hormone levels and serum calcium and phosphorus levels.[12,13,14] Active form of vitamin D is then transported to target tissues, where it functions like a steroid, binding to the vitamin D receptor (VDR). The VDR heterodimerizes with the retinoid X receptor (RXR) and the VDR/RXR complex causes transcription of target genes. When there is a need to increase blood calcium levels 1, 25(OH) 2D3 increase calcium absorption from intestine. If this increased intestinal absorption is insufficient to re-store normal calcium levels, 1, 25(OH)2D3 works in concert with the parathyroid hormone (PTH) in the kidney to promote calcium reabsorption from the distal tube, and in the skeletal system to release calcium from bone.[12,13, 14]

Definition and Prevalence of Vitamin D Deficiency

Although there is no consensus on optimal levels of 25-hydroxyvitamin D as measured in serum, vitamin D deficiency is defined by most experts as a 25-hydroxyvitamin D level of less than 20 ng per milliliter (50 nmol per liter). A level of 25-hydroxyvitamin D of 21 to 29 ng per milliliter (52 to 72 nmol per liter) can be considered to indicate a relative insufficiency of vitamin D, and a level of 30 ng per milliliter or greater can be considered to indicate sufficient vitamin D. Vitamin D intoxication is considered when serum levels of 25-hydroxyvitamin D is greater than 150 ng per milliliter (374 nmol per liter).[16,17,18] With the use of such definitions, it has been estimated that 1 billion people worldwide have vitamin D deficiency or insufficiency.[18]

Vitamin D and the Immune System:

Autoimmune Disease and Infection

Vitamin D receptor (VDR) is present in almost all immune cells of the innate and adaptive immune compartment, including activated T cells, B cells, neutrophils, and antigen-presenting cells, such as macrophages and dendritic cells (DCs).[19,20,21] Antigen cells from the innate immune system, such as macrophages or dendritic cells (DCs) also express the vitamin D activation enzyme 1 alpha hydroxylase, also known as CYP27B1. 1, 25(OH) 2D3 has also been shown to inhibit the differentiation and survival of dendritic cells, resulting in impaired alloreactive T cell activation. The inhibition of maturation and differentiation of dendritic cells results in a decrease in IL-12 and an increase in IL-10 secretion. 1, 25 (OH)D inhibits T cells proliferation and prevents formation of gamma interferon and interleukin-2 (IL-2) by the helper T cells (TH1). It also enhances suppressor T cell (TH2) activity, thereby enhancing production of IL-4, IL-5 and IL-10. IL-17, which is involved in the pathogenesis of autoimmune inflammation. Therefore, vitamin D deficiency could theoretically increase the risk of autoimmune diseases.[22,23,24]

Observational studies in humans suggest an association between vitamin D deficiency and type I diabetes (T1D), multiple sclerosis (MS), and inflammatory bowel disease, rheumatoid arthritis, SLE, tuberculosis.[25,26]

Multiple Sclerosis

The incidence of MS is higher in more northern latitudes where there is typically less sun exposure.[27] Recent studies suggested a possible underlying mechanism to explain the linkage between vitamin D deficiency and MS. In CNS tissue samples from MS patients, both active lesions and normal appearing white matter had increased levels of VDR as well as the activating vitamin D hydroxylase compared to healthy controls.[28] In a large prospective case-control study involving over seven million Caucasian recruits with 25(OH)D levels below 20 ng/mL (50 nmol/L) had approximately a twofold increased risk for later development of MS.[29,30] Clinical trials looking at the benefits of vitamin D in MS patients unfortunately have been few and neither established the safety of supplementation nor detect any benefit.[31,32,33] A Cochrane review in 2010 supported the view that more RTCs were needed before vitamin D supplementation could be considered an evidence-based recommendation.[34]

Crohn's Disease (CD)

Inflammatory bowel disease (IBD) has higher incidences in more northern climates where there is less sun exposure and thus generally higher levels of vitamin D deficiency.[35,36] In a double-blind RCT, vitamin D administration reduced relapse rates in Crohn's disease by greater than 2-fold but failed to reach statistical significance ($P = 0.06$).[37] In a double-blind RCT, vitamin D supplementation in clinically quiescent CD patients was shown to improve fatigue, hand-grip strength, and quality of life.[38] Together, the existing body of work demonstrated that vitamin D deficiency occurs in Crohn's disease, and that supplementation can have a beneficial effect. Whether vitamin D deficiency is part of the pathogenic process of IBD remains to be determined, and larger RCTs still need to be performed to fully validate the benefit and role of vitamin D supplementation in Crohn's disease.

Type I Diabetes Mellitus

The immunomodulatory and anti inflammatory actions of vitamin D may reduce the autoimmune insulinitis of type I DM.[39,40] Vitamin D can suppress the antigen presenting capacity of macrophages, inhibit dentritic cell maturation, modulate the development of CD4 lymphocytes and inhibit the production of inferteron gamma (INNã) and interleukin-2 (IL-2) among other cytokines, which are known to activate macrophages and cytotoxic T cells leading to islet cell destruction in type I DM.[41,42,43] Several studies, mainly case-control studies, indicate that vitamin D supplementation in early infancy reduced the subsequent risk of T1D by about 30 percent.[44]

Rheumatoid Arthritis

Recent evidence demonstrates that vitamin D may correlate inversely with occurrence, development, disease activity and flare ups of RA.[45,46,47] VDR is present in monocyte, macrophage, chondrocytes and synoviocytes in Rheumatoid arthritis patients. vitamin D downregulates expression of proteins involved in T helper type 1 (Th1) cell driven autoimmunity, and participates in inhibition of antigen-presenting activity, antibody production, lymphocyte proliferation, dendritic cell differentiation and release of cytokines such as interleukin-2 (IL-2), IL-6, interferon-ã (IFN-ã) and tumor necrosis factor-á (TNF-á).[48,49,50] Several studies have confirmed that 25(OH)D3 insufficiency is common among patients with RA.[51,52,53] In a recent study, the prevalence of vitamin D deficiency (<20 ng/ml) in 4793 Japanese patients with RA was 71.8%, and severe deficiency (<10 ng/ml) was demonstrated in 11.5% of patients.[54] Some, but not all, of these studies have also found an inverse relationship between serum vitamin D levels and disease activity.[55,56,57,58,59] While the data suggests that vitamin D supplementation could reduce disease activity in RA patients, little clinical work has been done to support this hypothesis. A vitamin D analog, alphacalcidiol was found years ago in a small, open-label trial to decrease disease activity in RA patients.[60] Most of these studies therefore point to an association between low serum level of 25(OH)D3 and high disease activity, but the results are not entirely clear and unequivocal.

Systemic Lupus Erythematosus

Several studies have reported that vitamin D deficiency is more prevalent among SLE patients than the general population.[61,62] SLE patients have multiple risk factors for vitamin D deficiency.[63] Avoidance of sun exposure, use of sunscreen, renal impairment, chronic steroid use,and hydroxychlroquine in SLE patients all may result into vitamin D deficiency.[64,65,66] Low serum 25(OH)D levels was found in SLE patients in a number of studies performed in different populations from countries at variable latitudes.[67,68,69,70,71] Yet, the specific effects of vitamin D on SLE are far from clear. Four cross-sectional studies found an inverse relationship between 25(OH)D levels and lupus activity, measured by means of the SLEDAI and/or Systemic Lupus Activity Measure.[68,72,73] However, other authors have not found such an association.[69,70,71] Three largest studies with sample sizes of 378, 290 and 181 subjects, revealed strong inverse correlations between vitamin D levels and SLEDAI scores with p values of 0.018, 0.001 and 0.001, respectively.[69,71,74] In summary patients with SLE have multiple risk factor for vitamin D deficiency and lower vitamin D level may correlate with disease activity. Further well designed study is needed in this area.

Innate immunity and Tuberculosis

Exposure of monocytes and/or macrophages to bacterial infections up regulates VDR and 1á-hydroxylase expression and enhanced expression of the antibacterial proteins cathelicidin and defensin, and enhanced formation of autophagosomes.[74] Higher susceptibility to tuberculosis was seen in subjects with vitamin D deficiency including the elderly, uremic patients, and dark-skinned persons.[75,76] Some, but not all, of these studies have also found an inverse relationship between serum vitamin D levels and clinical outcome in TB patient.[77,78,79,80]

In a randomized, placebo-controlled study in which four high doses of vitamin D3 (100,000IU) at 0, 14, 28 and 42 days) were administered in a severely vitamin D–deficient TB- infected population, and again, no difference in sputum culture conversion or clinical outcome was observed.[81] So the current data is insufficient to define a role for supplementation of vitamin D in the prevention or treatment of tuberculosis.

Conclusion:

Unfortunately, the benefits of vitamin D supplementation (beyond the treatment of deficiency) in different immunological disorders remain less clear. Studies of the benefits of vitamin D face challenges unique to endogenous nutrients. Unlike many trials that compare administering a drug to a placebo where there is no drug present, vitamin D is always present in patients at some basal level. These complexities have made cross-comparison of clinical trials, with different starting and supplemented levels of circulating vitamin D, difficult, and has likely contributed to the ambiguity in the field .Unlike vitamin D deficiency and osteoporosis or rickets a causal

link between vitamin D deficiency and specific disease including autoimmune disease has not yet be proven. So administering vitamin D supplements above and beyond what is required for osteoporosis or fall prevention is not recommended yet. But as laboratory evidence and observational studies have suggested association between vitamin D concentration and development of some extraskeletal effect, the beneficial effect of vitamin D beyond bone cannot be dismissed, so large scale clinical trials are needed.

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Dengue Fever with Acute Acalculous Cholecystitis and Hepatitis: A Case Report

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Abstract

Dengue is a febrile illness caused by a flavivirus transmitted by mosquitoes. It has wide spectrum of clinical illness such as dengue fever, dengue haemorrhagic fever, dengue shock syndrome, expanded dengue syndrome. Patients with dengue fever usually present with typical symptoms such as fever, headache, retro-orbital pain, myalgia, arthralgia, nausea, vomiting, rash, leucopenia and thrombocytopenia. They can also manifest with atypical symptoms. Acute acalculous cholecystitis and acute hepatitis are atypical manifestations of dengue fever. In this report a case of 27-year-old gentleman presented with fever, abdominal pain, myalgia and vomiting. Blood culture and serological tests for hepatitis viruses were negative. Antigen (NS1), antigen for dengue was positive. Ultrasonogram showed acalculous cholecystitis and enlarged liver. Hepatic transaminase was mildly raised. He was found to have acute acalculous cholecystitis and acute hepatitis secondary to dengue fever. It is imperative that atypical presentations of dengue fever are recognized so that early diagnosis can be made thereby can reduce dengue related morbidity and mortality.

Key words: Expanded dengue syndrome, Acute acalculous cholecystitis, Hepatitis

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Introduction:

Dengue fever is an infectious disease caused by the dengue virus (DENV) of Flaviviridae family. It is endemic in the tropical and subtropical zones. The vector for the disease is the mosquito of Aedes genus. Fifty to 100 million people are affected yearly by the disease [1,2,3] and 50,000 (1%) require hospitalization.[1] Dengue infection is a disease entity that can have different clinical presentations and often demonstrates an unpredictable clinical progression and outcome. The symptoms of the disease may vary widely, the infection may be asymptomatic or it may manifest itself with fever only whereas some patients develop hemorrhagic symptoms and shock.[4] There have been increasing reports of dengue fever (DF) and dengue hemorrhagic fever (DHF) with atypical manifestations due to involvement of liver, kidneys, heart, or nervous system (expanded dengue syndrome).[4] These atypical manifestations may be potentially serious and may result in increased rates of morbidity and mortality. Therefore, clinicians should be aware of these atypical manifestations, thereby reducing morbidity and mortality resulting from dengue fever.

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Case presentation:

A 27 year old male was admitted on July 5 2017 in Green Life Medical College with the complaints of fever and myalgia for 3 days, upper abdominal pain, anorexia, nausea and frequent vomiting for 1 day. But he did not have any complaints of any arthralgia, headache or retrorbital pain.

On examination he was well nourished, anecteric, with no pallor, lymphadenopathy or any sign of active bleeding or

petichae. Tourniquet test was positive (Fig 1). His pulse was 64 beats /min, blood pressure was 120/75 mm-Hg, respiratory rate 16 breaths/min. Examination of the abdomen revealed enlarged liver, 4 cm from costal margin in midclavicular line which was tender on palpation. Murphy's sign was positive. There was no rebound tenderness, guarding, masses or any other organomegaly or ascites. Bowel sounds were present. His respiratory, cardiovascular, neurological and ear, nose and throat examinations were unremarkable.

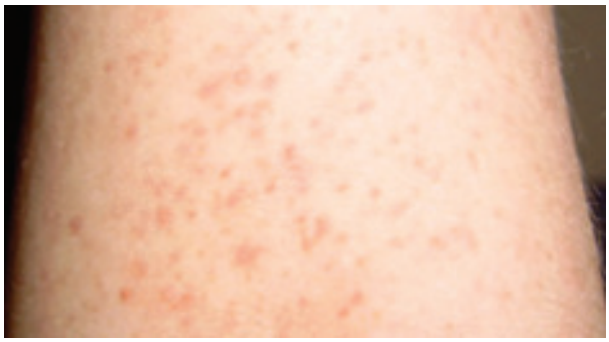

Fig.-1 : *Positive tourniquet test*

Laboratory and hematological investigations on admission were as follows: total white cell counts 2.5 x 10 9/L with 76.5% neutrophil and 13.1% lymphocytes, hemoglobin 12.0 g/dL, platelets 61x 109/L, haematocrit 48.9%. Liver function tests showed total bilirubin 1.2 mg/dL, AST 256 U/L, ALT 183 U/L, and ALP 83 U/L. Prothrombin Time and activated Partial Thromboplastin Time were within normal ranges. The ultrasound examination of his abdomen showed hepatomegaly with gall bladder wall thickening and mild pericholecystic edema (Fig 2). Serum creatinine and electrolyte panel were normal. Blood culture, peripheral blood film for malarial parasite, serology for viral hepatitis A, B and C were all negative. Chest radiography was normal. NS1 antigen for dengue was positive.

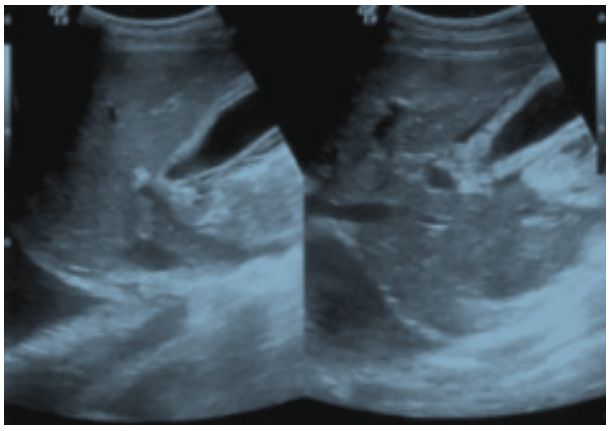

Fig. 2: *Ultrasound scan shows marked thickening of the gallbladder and pericholecystic fluid in the absence of any stones or sludge*

The presence of thrombocytopenia, increased haematocrit and positive Dengue NS1 antigen, absence of malaria parasite, negative serology for viral hepatitis, negative blood culture for enteric fever and hepatomegaly with gall bladder wall thickening and mild pericholecystic edema confirmed expanded dengue fever.

He was managed according to WHO protocol for DHF grade II initially[4]. He was started broad spectrum antibiotic. On second day of hospitalization the patient developed gum bleeding. His blood pressure reduced to 90/60 mm-Hg but there was no sign of shock, his platelet count became 43x 109/L. On third day platelet count de-creased to 20x 109/L, and on the sixth day it increased to 103x 109/L. He became afebrile on third day of admission and abdominal pain improved on sixth day. Blood pressure became normal without I/V fluid on fifth day. He was discharged on 9th day of admission. His platelet count, hematocrit, LFT and ultrasound abdomen were normal at the time of discharge.

Discussion:

Most patients with dengue fever presented with typical symptoms. However, it is important to realize that not every patient will manifest the whole range of symptoms. Clinicians should be familiar with both the typical and atypical manifestations.[5] Although atypical presentations are infrequent, and if unrecognised, may potentially lead to catastrophic illness. Acute acalculous cholecystitis (AAC) has been reported to account for approximately 10% of all cases of acute cholecystitis.[6] It is also interesting to note that this patient had manifested with two atypical manifestations, acute acalculous cholecystitis and hepatitis. Patients with AAC present with fever, right upper quadrant abdominal pain, positive Murphy's sign, and abnormal liver function tests. Ultrasonographic findings for diagnosis of AAC include thickening of the gallbladder wall over 3mm, gallbladder distention, localised tenderness, pericholecystic fluid and sludge.[7,8] A variety of clinical conditions is associated with AAC which includes certain infections. Dengue infection has been reported to be associated with AAC in up to 7.6%.[7] In dengue fever, the main pathophysiological changes of AAC could be due to increased vascular permeability, causing plasma leakage and serous effusion with high protein content, which then causes thickening of the gallbladder wall.[9] Acute acalculous cholecystitis (AAC) needs to be diagnosed early and requires prompt management, especially in critically ill patients. Management includes starting broad spectrum antibiotics after blood cultures have been obtained. Acalculous cholecystitis in the course of dengue is usually a self-limiting disease and the thickness of gallbladder wall

returns to normal after recovery. Cholecystectomy is usually not indicated in these patients due to a high risk of bleeding.[10]

Liver injury due to dengue infection is not uncommon and has been described since 1970.[11] It is attributed to direct virus infection of hepatocytes or the consequence of host immune response against virus.[12] The spectrum of hepatic involvement in dengue infection varies from mild injury with elevated aminotransferases to severe injury with hepatic failure and severe hepatic disturbances. The elevation of aminotransferases has been associated with disease severity and is a good pre-dictor of development of dengue hemorrhagic fever.[13] In Bangladesh the superimposed geographical areas for malaria, viral hepatitis, leptospirosis, enteric fever represent a challenge for identifying the etiology of acute febrile syndrome complicated by hepatitis. This case presented with fever, myalgia, abdominal pain and vomiting. The probable differential diagnosis comprises viral hepatitis, malaria, leptospirosis, and enteric fever. All the investigations for the above-mentioned differential diagnosis were negative for this patient. Excluding those differential diagnosis and presence of hepatomegaly with gall bladder wall thickening and mild pericholecystic edema the patient was diagnosed as expanded dengue fever. Expanded dengue syndrome should be considered when liver functions are deranged in a dengue endemic area because they are potential candidates for hepatic injury apart from routine hepatotropic viruses and possibilities of developing severe disease.

Conclusion:

Dengue fever may have some atypical presentations. It is imperative that atypical presentations of dengue fever are recognized so that early diagnosis can be made thereby can reduce dengue related morbidity and mortality.

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COLLEGE NEWS

Continuing Medical Education (CME) / Contining Professional Dvelopment (CPD) / Case Presentation, 2017.

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17 May, 2017
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21 June, 2017
Topics : Morbidity following caesarian section
Presenter : Dr. Mushrin Malik
Department of Gynae and Obs.

Corrigendum

In the College News of Volume 2, No. 1, January 2017 issue, the name of the presenter of "Gene Therapy" CME session was wrongly mentioned as Dr. Bakibillah. The correct name of the presenter would be Dr. Abdullah Hel Baki. Any inconvenience caused by this unintentional mistake is deeply regretted.

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Reviewer Panel

Name of the reviewers are listed according to alphabetic order not according to order of precedence.