ISSN 2313-4941

Volume 11 Number 2 July 2023

The Journal of Ad-din Women's Medical College

The Journal of Ad-din Women's Medical College

Volume 11, Number 2, July 2023

CONTENTS

An official organ of Ad-din Women's Medical College

The Journal of Ad-din Women's Medical College

ISSN 2313-4941

Volume 11, Number 2, July 2023

Published by : **Prof. Dr. Mahmuda Hassan**
Principal, Ad-din Women's Medical College
2 Bara Moghbazar, Dhaka-1217, Phone : +880-2-49362921, 49362926
Fax: 8317307, E-mail: awmc@ad-din.org, **Website: www.ad-din.org**

Printed by : **Asian Colour Printing**
130, DIT Extension Road, Fakirerpool, Dhaka, Bangladesh
Phone : 58313186, 8362258, E-mail : asianclr@gmail.com

ISN : 2313-4941

Instruction for the Authors

The Journal of Ad-din Women's Medical College (ISSN 2313-4941) is an official organ of the Ad-din Women's Medical College, Dhaka and published twice in January and July every year. This journal is recognized by the Bangladesh Medical and Dental Council (BMDC). We publish original articles, review articles, case reports and others (see page vi) including society news.

The manuscripts submitted in this journal should not have been published in any other journal before. All submitted papers are subjected to be reviewed by the board of reviewers and editorial panel before accepting any manuscripts. The unaccepted articles will not be sent back, but will be destroyed. Proof corrections by the authors are well appreciated.

Submission of manuscripts

Papers are accepted for publication with an understanding that they are submitted solely to the journal of Ad-din Women's Medical College and are subject to peer review and editorial revision. Statement and opinion expressed in the papers, communications letter herein are those of author(s) and not necessarily of the editor and/or publisher.

Papers should be submitted with three hard copies and a soft copy (CD) labeled clearly with the manuscript title, name of first author with date, designation, mobile no. and email address to the Executive Editor with a copy to Editor-in-Chief of journal of Ad-din Women's Medical College, 2 Bara Moghbazar, Dhaka-1217, Bangladesh.

Form of full papers submitted for publication

The manuscript should be prepared using MS-Word. The whole manuscript should not exceed 4000 words. The manuscript should be divided into: (title page, abstract, body/text, references), but should be submitted as one document. All parts of the manuscript should be typed or printed on only one side of the paper in double space with wide margins of at least 2.54 cm in all sides of the manuscript throughout.

While the preferred font remains Times New Roman size 12 cpi. numbering of the pages should be done consecutively, beginning from the title at the lower right hand corner of each page. Each component of the manuscript should begin on a new page in the sequence of title page, abstract, text, reference, tables and legends for illustration.

Title page

The title page should include the title of the manuscript which should be concise within 45 characters. Name of authors with their highest academic degree(s), institutional affiliations and name of the departments should be mentioned. The complete mailing address and email IDs of the first and correspondence author(s) should be included to whom the proofs and all other correspondence should be sent.

Abstract

Each manuscript requires an unstructured abstract that should include objective, methods, results, conclusion and key words in not more than 150 words for any review article or case report an 250 words for structured abstract only for original article summarizing the significant information and findings. Authors must give two to five key words identifying the most important topics covered by the manuscript. Abbreviations, diagrams, and references in the abstract should be avoided.

Body/Text:

The body of the manuscript/text should be divided into the following sections: i) Introduction, ii) Materials and Methods, iii) Results (include tables and diagrams), iv) Discussion, v) Conclusion, and vi) Acknowledgement if any (particularly on funding, study subjects and co-author).

Introduction

It includes a short yet robust background purpose and the rationale for the study (or summarized observation), including pertinent references, but data or conclusion from any work should not to be included.

Material and methods

In this section, selection of the study subjects (patient or laboratory animals, including controls) should be described clearly. The age, sex and other characteristics

of study subjects should be identified. The total methodology in details, apparatus to be used, and procedure to be followed must be given in sufficient details to allow other researcher to reproduce it, as and if required for. References should be given to establish methods including statistical lines and precise identifications should be provided for all the drugs and chemicals to be used including generic names, dosage and route of administrations. Authors(s) submitting review manuscripts are advised to include a section describing the methods used for locating selecting, extracting and synthesizing data. If data is collected from other sources (published or unpublished) then proper permission(s) should be obtained and mentioned with acknowledgement.

Results

Results should be presented in a logical sequence in the text, tables, figures and/or illustrations. The use of too many tables or diagrams in relation to the length of text may produce difficulties in the layout of pages.

Tables and Figures

Tables should be embedded in the text and numbered consecutively in the order of their first citation in the text. The title of the table should be brief yet self-explanatory. Tables should not be submitted as photograph. All figures should be included as one separate sheet or file. The title should appear above each table (short and descriptive. Please mention a clear legend and any footnotes suitably identified below, clearly. Figures should be labeled properly, fitting to necessary size of the page. Captions of all figures should be typed, double-spaced and showed on a separate sheet. All original figures should be clearly marked in pencil on the reverse side with the number, author's name.

Footnotes

Place explanatory matter in footnote, not in the heading. For uniformity of style, authors should use symbols for footnotes such as 51.7 etc.

Illustrations

Illustrations submitted (line drawings, photos, photo-micrographs, etc.) should be clean, original, or as a digital files. Digital files are recommended to use since this produces highest quality following criteria, below:

- Minimum 300 dots per inch (DPI) or higher
- Appropriate sized to fit in journal page
- Preferably in JPEG and GIF formats
- Subject/ patient face must not be identified in diagram
- Should be submitted as separate files, not embedded in text files.

Discussion

This section should present a detailed yet comprehensive analysis of findings/results to describe, compared & criticized (positively or negatively) in the light of previous relevant studies, in the country or abroad. It should emphasize the new and important aspect of the study and the conclusions that follow from them. Repetition of detailed data &/or other materials given in introduction or result section may be avoided, unless deemed essential (in rare cases).

Conclusion

In the gist, study findings should be linked with the study goals. Recommendation may be included as appropriate including implication(s) of the findings and limitations if any.

Acknowledgements

Acknowledgement may be added, but if any should be placed at the end of the body/text and should be limited within 100 words. This section may particularly be used to acknowledge those persons who do not qualify for authorships but worked significantly for this study or write up manuscripts.

Acknowledgement for funding, donated resources, or significant contributions of research materials be made as well, if author(s) wish.

References

All references should be cited in the text following Vancouver system/style in Arabic numbers, to number the texts, consecutively, following an order in which if appears first in the text using superscript (or cite within the text numbers in round brackets). If a reference is cited more than once the same number should be used each time. References cited only in tables or figure legends should be numbered in accordance with the sequence from the last number used in the text and follows the order of individual tables/figures. At the end of the paper, on a page(s) separate from the text, a references list must be added following exact Ref. No. in numerical order. References to materials available on websites should include the full internet address and the date of the version cited as: Authors' names (in normal order), document title, and date of Internet publication

or other retrieval information (date of access), text division (if applicable). Examples of references are given below.

(i) Reference from the Journals

1. Parkin DM, Clayton D, Blook RJ, Massyer E, Fried HP, Iranov E et al. Childhood leukaemia in Europe after Chernobyl: 5 years follow up. Br J Cance 1996; 73: 1006-1012
2. Paganini HA, Chao A, Ross RK, Henderson Aspirin use and chronic diseases: a cohort st of the elderly. BMJ 1989; 299: 1247-1250

Note: The name of the journal & its volume should be in Italic.

(ii) Books

1. Gyton AC, Hall JE The thyroid metabolic hormones In Textbook of Medical Physiology. 10th edn. NewTork: WB Saunders Company. 2000: 858-86

(iii) Internet

I. Harverd medical school Available https:// en.wikipedia. org/wiki/havard medical college, accessed October 2011

(iv) Thesis/Dissertations

1. Khan MAH. Lipid profile and renal function status of hypothyroid patients [MD Thesis). Dhaka Bangabandhu Skeikh Mujib Medical University:2005

(v) Scientific or technical report

1. Akutsu T. Total heart replacement device. Bethesda MD: National Institutes of Health, National Heart and Lung Institute, 1974 Apr report No. N1H-NHLI-69 2185-4 Ethical approval

The authors should mention the name of the ethical approval authority or (IRB: Institutional Review Board) for their study either separately or in materials and methods section, particularly if the study has been done on human subjects, laboratory samples or laboratory animals. However, not all surveys may not require an ethical permission, parse, in general. But it can be obtained & attached with the proposal, if the authors(s) wish.

Authorship Statement

A form must be signed by all listed authors indicating the contribution to the paper made by each. The corresponding author is responsible for obtaining signatures from all listed authors and using. A check off form, should indicate by name what each author contributed to each of the various aspects of the study: However, (e-signature are accepted except 1st & corresponding authors).

- study concept
- study design
- data collection & processing
- statistical analysis
- manuscript writing

Editorial action

Once the Board of Editors receives the manuscripts it would be examined & reviewed thoroughly for its content, quality, writing skills & if the manuscript contains any newer/novel issues, important to get it published. Rejected manuscripts will not be returned. Proofs correction by the authors will be

appreciated. Once it requires for gross errors or incompleteness. No reprint will be provided. The editors reserve the customary right to check the style and if necessary. May shorten some/few parts of the manuscripts before it can be accepted for publication and thus, to determine the priority, and time, for its publication. The editor assumes that the writings are based on honest observations. It is not the task of the editor to investigate scientific frauding paper or to check false/fake data. However, plagiarism will be checked by the reviewers; but the authors are suggested to check the plagiarism on their own, which will be prioritized for reviewing, editing & publishing the manuscripts.

Copyright

Accepted papers will be the permanent property of the Journal of Ad-din Women's Medical College. By submitting the manuscript, the authors agree that once the article is accepted for publication, copyright of their article is automatically transferred to the Ad-din Women's Medical College, Dhaka.

Further instruction for preparing paper and submission

Please read the following submission checklist that summarizes the main features for manuscripts to be submitted at the Ad-din Women's Medical Journal. Please ensure your manuscript follows the recommended number of pages, references etc. for specific articles to be accepted by the Ad-din Women's Medical Journal as shown below.

1. Type of article: **Original Article**
   No of references: 35
   Abstract: Yes, 250 words
   Max no. of printed pages: 5 (=14 msw pages*) approx. 4500 words
   Headings: Yes
   Keywords: Yes

2. Type of article: **Mini commentary focusing articles published in the journal**
   No of references: max 5
   Abstract: No
   Key notes: No
   Max no. of printed pages: 1 printed page, or Max 800 words
   Headings: No
   Keywords: No

3. Type of article: **Brief report**
   No of references: max 5
   Abstract: No
   Key notes: No
   Max no. of printed pages: 1 printed page, or max, 1000 words
   Headings: No
   Keywords: No

4. Type of article: **Editorial**
   No of references: max 10
   Abstract: No
   Key notes: No
   Max no. of printed pages: 3 pages, or max, 2000 words
   Headings: No
   Keywords: No

5. Type of article: **Clinical overview**
   No of references: 30
   Abstract: Yes, max 200 words
   Key notes: No
   Max no. of printed pages: 3 (=9 ms pages*) approx.3000 words
   Headings: No
   Keywords: Yes

6. Type of article: **Review article**
   No of references: max 60
   Abstract: Yes, max 150 words
   Key notes: No
   Max no. of printed pages: 8(= 24 ms pages*) approx. 6650 words
   Headings: Yes
   Keywords: Yes

7. Type of article: **Mini review**
   No of references: 30
   Abstract: Yes, 200
   Key notes: Yes
   Max no. of printed pages: 4(= 12 ms pages*)approx. 3500 words
   Headings: Yes
   Keywords: Yes

8. Type of article: **Case report**
   No of references: max 15
   Abstract: Yes, 200
   Key notes: Yes
   Max no. of printed pages: 4 (=12 ms pages*) approx. 3500 words
   Headings: Yes
   Keywords: Yes

9. Type of article: **Society news**
   No of references: 20
   Abstract: No
   Key notes: Yes
   Max no. of printed pages: 1 printed page, or max, 1000 words
   Headings: No
   Keywords: No

10. Type of article: **Commentary**
    No of references: max 9
    Abstract: No
    Key notes: No
    Max no. of printed pages: 1/2 printed page, or max, 500 words
    Headings: No
    Keywords: No

11. Type of article: **Perspective**
    No of references: 5
    Abstract: No
    Key notes: No
    Max no. of printed pages: 2 printed page, or max, 1000 words
    Headings: Yes
    Keywords: No

12. Type of article: **Reader's forum**
    No of references: 3
    Abstract: No
    Key notes: No
    Max no. of printed pages: 1/2 printed page, or max, 500 words
    Headings: No
    Keywords: No

13. Type of article: **Essay**
    No of references: 5
    Abstract: No
    Key notes: No
    Max no. of printed pages: 2 printed page, or max, 1000 words
    Headings: Yes
    Keywords: No

14. Type of article: **Different view**
    No of references: 10
    Abstract: No
    Key notes: No
    Max no. of printed pages: 2 printed page, or max, 1500 words
    Headings: Yes
    Keywords: No

15. Type of article: **News and views**
    No of references: No
    Abstract: No
    Key notes: No
    Max no. of printed pages: 2 printed page, or max, 500 words
    Headings: Yes
    Keywords: No

16. Type of article: **Letter to the Editor**
    No of references: 05
    Abstract: No
    Key notes: No
    Max no. of printed pages: 2 printed page, or max, 500 words
    Headings: Yes
    Keywords: No

Editorial

Value added in Teaching-Learning (T-L) Methodology of Under Graduate Medical Education in Bangladesh: Student's Benefits and Learning Outcome

Ridwana Rahman

Undergraduate medical education remains the foremost tool yet the most prudent step to add values in medical education and scientific issues. It's just like 'dream comes true' for all junior doctors (clinical, para-clinical and non-clinical).

Thus, undergraduate medical education therefore remains a crucial stage for every doctor to build their modestly, honestly but with a high responsibility-satisfying the Hippocratic oath. This is particularly important for us, the doctors serving in Low or Middle-Income Countries (LMIC), where the doctor patient ratio is very low owing to country's poverty level. However, we the junior doctors, in particular, do often face challenges- an issue which a medical undergraduate must be aware of, willingly, psychologically and socially for patient's sake following ethical grounds.

Thus, as junior faculties, we aim to delineate role of continued medical education (CME) incorporating modern T-L system- a new generation technique in Ad-din Women's Medical College after receiving hands-on training from Govt. ran CME-office in active cooperation/support by the Medical Research Unit (MRU) of Ad-din Women's Medical College (AWMC).

Past history revealed that undergraduate medical education is being restructured from time to time over the past century. Many influences, including the persuasive report of Abraham Flexner in 1910 acted to re-organize medical education in 20th century.[1] However, our modern T-L System is tailored to improve teacher's ability to assist taming undergraduate students' knowledge to boost clinical practice skill. We, the teaching staff of AWMC, thus, render relentless effort to develop medical education in increasing clinical and practical skills among students, instituting newer strategies evolving new challenges and cope up with emerging disease/pandemics to save the people.

Undergraduate medical education has been continued so far in a very traditional way and following old-fashioned methods involved in learning basic sciences but didn't help in building any interest in clinical and professional practices.

Medical teaching should be more meaningful and relevant to encourage the students towards clinical approach. Inadequate infrastructure, and lack of well-trained teachers have been identified by respondents as barriers for implementing integrated teaching learning.[2] Prolonged hours of examination, biasness, inequality among students, etc. have been persuaded us to change our views thus indulging ourselves towards a new vision towards modifying that system. These aforementioned observations have led us to decide that this method must be modified towards improving student's perception and practical skill for building up clinical practitioners and researchers.

Further, integrated teaching is an approach that aims to design teaching methods in such a way that students can gather knowledge and connect to concepts towards improving their skills so that the upcoming doctors can confidently apply those to serve the patients and thus,

Correspondence: Dr. Ridwana Rahman, Assistant Professor, Department of Physiology, Ad-din Women's Medical College, Dhaka.

Received Date : 10 July, 2023
Accepted Date : 25 August, 2023

the society. We, the CME-trained medical teachers remain aware on the application of trans-disciplinary approach and delivery of information between basic and applied sciences through different phases of undergraduate medical curriculum.

While the traditional teaching method followed a building block principle where every subject would have its own domain of time and space separately in specific targeted curriculum. Contrarily, integrated curriculum can be successful when subjects of all phases are taught by the well-trained teachers harmoniously to bring about meaningful conclusive summary to the students.[3]

Arrangement of different subjects in MBBS curriculum has also a matter of concern because it has been under sequential change for past few years. Without the knowledge of basic sciences and para-clinical subjects it is impossible gain complete clinical knowledge. Teachers always advice for the need of rearrangement regarding the sequential distribution of subjects in MBBS course of Bangladesh according to a scientific study.[4]

Undergraduate medical education is closely related to postgraduate training and professionalism as it involves knowledge and skill derived from basic and para-clinical science. Such areas are often rendered to undergo widespread restructuring to meet the expectations of the society and the health professional themselves.[5]

Basically, modern T-L systems focus to unify subjects that are frequently taught in different phases around a clinical disease, following Harden's integration ladder, comprising of 11 steps to reach the final step of transdisciplinary approach. No sooner the students will reach that stage they will be able to take more responsibility to integrate student's knowledge.

Looking at the advantages of modern T-L method, we the CME-trained teachers plan to avoid undue repetition of information and achieve effective yet practical learning and encourage the students with full of motivation. However, there are certain drawbacks too: interphase or interdepartmental planning and preparation needs much co-ordination among different phases and subjects, too. When the final step is reached individual faculty or subject may lose their identity that may also distract a student in choosing their career.

Overall, this new 'Integrated T-L system' demands well equipped training of teaching staff for the successful implementation and build a better future for our county's medical education system. But our well-trained medical teachers must rush to go for re-orientation of medical education system so as to cope up with deemed demands of our health care service delivery authorities.

Fruitful implementation of this T-L-system will help setting an example nationwide that may even play role in global medical education system, too. Eventually, we may fulfill the recommendations of worldwide leading organizations of medical education, following "Edinburgh Declaration" of World Federation for Medical Education (WFME) and our "Tomorrow's Doctors" by the UK based General Medical Council (GMC), successfully.

References:

1. Duffy TP. The Flexner Report--100 years later. Yale J Biol Med. 2011 Sep; 84(3):269-76. PMID: 21966046; PMCID: PMC3178858.
2. Deka PK. Article. Medical Education in south east Asia Current trend and Malaysia's perspective. Bangladesh Journal of Medical Science, October, 2011, Vol. 10, No. 04.
3. Tapu TT, Talukder HK, Talukder MAS, Flora TA, Ahmad KT. Current Activities to Implement Integrated Teaching Learning in Undergraduate Medical Education in Bangladesh: Students' View. Bangladesh Journal of Medical Education, January 2020; Vol.11, Issue 1.
4. Rahman MM, Talukder MHK. Views of teachers' and students' regarding the distribution of subjects in phase II and phase III of MBBS course. Bangladesh Journal of Medical Education 2019; Vol. 10, Issue 2.
5. Badhon NM, Nahar N, Jahan I, Zaman F, Hossain MI, Teachers and student's opinion regarding updated MBBS curriculum 2012 in a teaching hospital. Bangladesh Journal of Medical Education. January, 2022, Vol.-13, Issue-01.

Original Article

Vitamin D Status Among Patients With Dry Eye Syndrome Attended In Bangabandhu Sheikh Mujib Medical University (BSMMU)

Md. Adnan Islam[1], *Abir Bin Sajj[2], Tohura Sharmin[3], Md. Sharfuddin Ahmed[4], Md. Showkat Kabir[5]

Abstract

Background: Dry eye syndrome (DES) is a common ocular manifestation. Artificial tears provide relief of eye irritation in patients with aqueous tear deficiency, but do not treat the underlying inflammation in Dry eye syndrome. Aim: To assess the vitamin D status of the dry eye syndrome patients.

Methodology: This cross-sectional study was conducted in the Department of Community Ophthalmology, BSMMU, Shahbag, Dhaka, from July 2019 to June 2020. Within the period a total of 50 cases of dry eye syndrome patients that met the inclusion criteria were taken as samples after receiving their informed consent. Detailed history, physical examination and Ophthalmological examination including Tear film Breakup Time (TBUT) of each patient was performed and recorded. Eye discomfort was assessed by the Ocular Surface Disease Index (OSDI) the score of which ranges from 0 to 100. A score of 12 was used as a cutoff for normal, 13–22 for mild dry eye, 23–32 for moderate dry eye, and ≥ 33 for severe dry eye. Tear film Breakup Time (TBUT) <10 s was taken as abnormal.

Results: In this study, mean (±SD) fluorescein Tear film Breakup Time (TBUT) was 5.89±1.31 sec, Schirmer test without anesthesia was 7.45±2.31mm/5 min, Schirmer test with anesthesia was 9.06±2.06mm/5 min and Ocular Surface Disease Index (OSDI) was 34.44±5.64. Mean (±SD) serum vitamin D level ng/mL was 5.89±1.31 ng/mL. 14 (28%) cases were found as insufficient, 33 (66%) cases were deficient and only 3 (6%) cases found to have normal Vitamin D status. Vitamin D level was positively correlated with Tear Breakup Time (TBUT), Schirmer test1 and Schirmer test2 and negatively correlated with OSDI. This correlation was statistically significant for Tear film Breakup Time (TBUT), Schirmer test2 and Ocular Surface Disease Index (OSDI).

Conclusion: Vitamin-D deficiency appears to have an effect on ocular surface parameters in patients with dry eye syndrome.

Key words: Dry eye syndrome, Vitamin D, Fluorescein, Tear film Breakup Time (TBUT), Schirmer test, Ocular Surface Disease Index (OSDI).

Introduction

Dry eye syndrome (DES) is accompanied by tear instability, increased osmolarity of the tear film and ocular surface inflammation. The common symptoms of dry eye are ocular discomfort, soreness, redness, ocular fatigue, sensitivity to light and blurred vision.[1] It is a consequence of reduced tear secretion by the lacrimal glands or increased tear evaporation.[2] Hyperosmolarity of the tear due to either tear deficiency or excess evaporation may damage the corneal epithelial cells and lead to subsequent liberation of miscellaneous inflammatory cytokines and matrix metalloproteinases. This vicious cycle can further destruct the epithelium and exacerbate the dry eye.[3] Dry eye is related to a complex of localized autoimmune reactions with inflammatory properties and vitamin D is a well-known immunomodulatory and anti-inflammatory agent, which might potentially be able to reverse the processes of dry eye.[4]

Several studies found have larger amounts of vitamin D in tear fluid obtained directly from lacrimal and accessory glands compared to plasma concentration. Megalin and cubilin are vitamin D transporters. They are expressed in lacrimal and accessory glands and are responsible for producing tear fluid.[5] The vitamin D receptors are present in the corneal epithelium,

1. Indoor Medical Officer, Dept. of Community ophthalmology, Sheikh Fazilatunnesa Mujib Eye Hospital & Training Institute, Gopalgonj, Dhaka.
2. Consultant, Dept. of Cornea and Refractive Surgery, Vision Eye Hospital, Dhaka
3. Assistant Professor, Dept. of Community Medicine, Ad-Din Women's Medical Collage, Moghbazar, Dhaka
4. Vice Chancellor, Bangabandhu Sheikh Mujib Medical University, Dhaka.
5. Chairman, Dept. of Community Ophthalmology, Bangabandhu Sheikh Mujib Medical University

Correspondence: Dr. Abir Bin Sajj, Consultant, Dept. of Cornea and Refractive Surgery, Vision Eye Hospital, Dhaka. Email: abirshagata@gmail.com Phone: 01715223100

Received Date : 05 September, 2023

Accepted Date : 22 October, 2023

endothelium and retinal pigmentary epithelium. Vitamin D strengthened the corneal epithelial barrier.[2,6] Hence, vitamin D deficiency might be reasonably an important cause of dry eye.

Dry eye syndrome is prevalent among the elderly, affecting 33% of the world population.[3] Various researchers of different countries had suggested that there was a relationship between dry eye syndrome and vitamin D deficiency. [1,7] But no published data are available in our country regarding this topic. Therefore, the present study had been designed to assess the vitamin D status among the dry eye syndrome patient. The findings may be helpful as background information for better management of the patients suffering from dry eye.

Methodology

This cross-sectional study was conducted in the Department of Community Ophthalmology, BSMMU, Shahbag, Dhaka from July 2019 to June 2020. A total 50 of cases of dry eye syndrome that met the inclusion criteria were taken as samples after receiving the patient's informed consent. Ethical clearance was obtained from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU). Detailed history and physical examination of each patient were performed and recorded. Visual acuity was assessed by Snellens chart and the anterior segment of the eye was examined with slit lamp biomicroscope to know the condition of eyelid, meibomian glands, conjunctival surface and cornea. Eye discomfort was assessed by the ocular surface disease index (OSDI). The OSDI questionnaire was accustomed to quantify dry eye symptoms. Subjects were asked questions regarding the dry eye symptoms that they had experienced during a one-week recall period. The OSDI questions consisted of three subscales – ocular symptoms, vision-related functions and environmental triggers. Each answer was scored on a 4-point scale from zero (indicating no problems) to four (indicating a significant problem).

Responses to all of the questions were combined to generate a composite OSDI score that ranged from 0 to 100. A score of 12 was used as a cutoff for normal, 13–22 for mild dry eye, 23–32 for moderate dry eye, and ≥ 33 for severe dry eye. [8] Tear film evaluations were done by measurement of Tear film Breakup Time (TBUT) and Schirmers Test (SchT). A dry fluorescein strip was touched to the inferior fornix with the patient instructed to look up. The corneal surface was seen under slit lamp biomicroscope with low magnification using a cobalt blue filtered light. The patient was asked to blink once and look straight without blinking.

The time of appearance of first small black spot within blue field (dry spot) from the last blink was measured. The TBUT less than 10 seconds was taken as abnormal. Without previously instilling anesthetic drops, the chirmer strips (Tianjin Jingming New Technological Development Co., Ltd, China) were inserted into the lower conjunctival sac at the junction of the lateral and middle third, avoiding touching the cornea and the length of wetting strips in millimeters was recorded after 5 minutes for Schimer-I. 15 minutes later, strips were placed over the same point in the same person again for 5 minutes, after installation of topical anesthesia with 0.5% proparacaine hydrochloride eye drops (Alcon laboratories Inc., s.a. Alcon-Couvreur n.v.) twice at 1 minute interval and then the length of wetting was read for Schimer-II.

5ml of venous blood sample was collected from the antecubital vein and sent to the Department of Biochemistry, BSMMU for estimation of serum vitamin D levels. Serum Vitamin D level < 20 ng/ml was considered to be vitamin D deficiency, 21-29 ng/ml was considered to be insufficient and a level > 30 ng/ml was considered to be normal.[9] All the information was recorded in a prefixed questionnaire. Data was analyzed statistically by using Statistical Package for Social Science (SPSS-26). The results were expressed as frequency, percentage and mean ± SD and level of significance was calculated at $p<0.05$. Z-proportion test was performed to compare between the groups. Pearson Correlation coefficient test was performed to observe the relation between dry eye and Vitamin D level.

Results

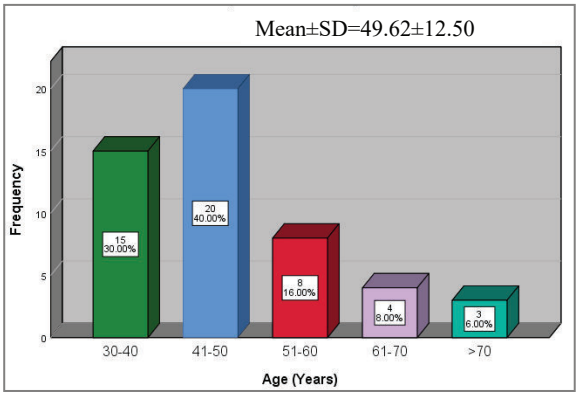


Fig 1: *Age distribution of Dry Eye Syndrome (DES) patients (n=50).*

Figure showd that mean±SD age was 49.62±12.50 years. Out of 50 patients 15 (30%) were 30-40 years of age, 20 (40%) were 41-50 years 8 (16%) were 51-60 years 4 (8%) were 61-70 years and 3 (6%) were >70 years. The youngest and the oldest patients were 30 and 91 years respectively.

Among 50 subjects, majority (62%) of the study subjects were female and only 38% were male.

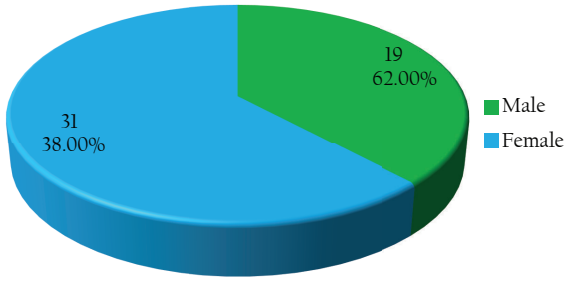


Fig 2: *Gender distribution of Dry Eye Syndrome (DES) patients (n=50).*

Table-I

Clinical characteristics of Dry Eye Syndrome (DES) patients (n=50).

Variable	Study subjects	Parameters
OSDI	34.44±5.64	Normal: 0 – 12 Mild: 13-22 Moderate: 23 -32 Severe: ≥ 33
Fluorescein TBUT (seconds)	5.89±1.31	Normal: ≥ 10 seconds Abnormal: < 10 seconds
Schirmer test 1 (mm/5 min)	7.45±2.31	Normal: 15 mm/5min Equivocal: 10 – 14 mm/5min Abnormal: < 10 mm/5min
Schirmer test 2 (mm/5 min)	9.06±2.06	Normal: 15 mm/5min Equivocal: 10 – 14 mm/5min Abnormal: < 10 mm/5min

*Data were expressed as Mean±SD.
*TBUT= Tear film Breakup Time
*Schirmer test 1= Schirmer test without anesthesia,
*Schirmer test 2= Schirmer test with anesthesia, n=study subjects.

Table I showed mean (±SD) OSDI was 34.44±5.64, fluorescein TBUT was 5.89±1.31 sec, Schirmer test without anesthesia was 7.45±2.31mm/5 min and Schirmer test with anesthesia was 9.06±2.06mm/5 min.

Table-II

Serum vitamin D status of Dry Eye Syndrome (DES) patients (n=50).

Vitamin D status (ng/mL)		Study subjects
>30	Normal	3 (6%)
20-29	Insufficiency	14 (28%)
<20	Deficiency	33 (66%)
Mean±SD		5.89±1.31

*Data were expressed as Mean±SD

Table II revealed that mean (±SD) serum vitamin D level ng/mL was 5.89±1.31 ng/mL . 14 (28%) cases were found as insufficient, 33 (66%) cases were deficient and only 3 (6%) cases found as normal in their Vitamin D status.

Table-III

Association of vitamin D status with OSDI of Dry Eye Syndrome (DES) patients (n=50).

Vitamin D status (ng/mL)		OSDI			
		Normal eye (0-12)	Mild dry eye (13-22)	Moderate dry ey (23-32)	Severe dry eye (≥33)
Normal	>30	0 (0%)	3 (6%)	0 (0%)	0 (0%)
Insufficiency	20-29	0 (0%)	1 (2%)	6 (12%)	7 (14%)
Deficiency	<20	0 (0%)	0 (0%)	0 (0%)	33 (66%)

*Data were expressed as frequency and percentage.

*OSDI-Ocular Surface Disease Index

In the severe dry eye group, 7 (14%) cases were found as insufficient and 33 (66%) deficient in their Vitamin D status. In the moderate dry eye group, only 6 (12%) cases were found as insufficient in their Vitamin D status. In the mild dry eye group, only 1 (2%) case was found as insufficient and 3 (6%) cases were found to be normal in their Vitamin D status.

Table-IV

Association of vitamin D status with TBUT of Dry Eye Syndrome (DES) patients (n=50).

Vitamin D status (ng/mL)		TBUT (sec)		p value
		< 10	>10	
Normal	>30	3 (6%)	0 (0%)	0.078ns
Insufficiency	20-29	14 (28%)	0 (0%)	<0.001s
Deficiency	<20	33 (66%)	0 (0%)	<0.001[s]

*Data were expressed as frequency and percentage
*Z-proportion test was performed to compare between the groups
*ns=not significant
*s= significant

In TBUT <10 sec group, 14 (28%) cases were found as insufficient, 33 (66%) cases were deficient and only 3 (6%) cases found as normal in their Vitamin D status. In TBUT >10 sec group, no cases were found as insufficient, deficient and normal in their Vitamin D status as all cases had dry eye. So, statistically significant differences were observed between the groups.

Table-V

Association of vitamin D status with Schirmer test 1 of Dry Eye Syndrome (DES) patients (n=50).

Vitamin D status (ng/mL)		Schirmer test 1 (mm/5 min)			
		Severe (0-4)	Moderate (5-9)	Mild (10-14)	Normal (≥15)
Normal	>30	0 (0%)	2 (4%)	1 (2%)	0 (0%)
Insufficiency	20-29	1 (2%)	9 (18%)	4 (8%)	0 (0%)
Deficiency	<20	5 (10%)	21 (42%)	7 (14%)	0 (0%)

*Data were expressed as frequency and percentage
*Schirmer test 1= Schirmer test without anesthesia

In the severe dry eye group, 1 (2%) case was found as insufficient, 5 (10%) cases were deficient in their Vitamin D status. In the moderate dry eye group, 9 (18%) cases were found as insufficient, 21 (42%) cases were deficient and only 2 (4%) cases were found as normal in their Vitamin D status. In the mild dry eye group, 4 (8%) cases were found as insufficient, 7 (14%) cases were deficient and only 1 (2%) case was found as normal in their Vitamin D status.

Table-VI

Association of vitamin D status with Schirmer test 2 of Dry Eye Syndrome (DES) patients (n=50).

Vitamin D status (ng/mL)		Schirmer test 2 (mm/5 min)			
		Severe (0-4)	Moderate (5-9)	Mild (10-14)	Normal (≥15)
Normal	>30	0 (0%)	2 (4%)	1 (2%)	0 (0%)
Insufficiency	20-29	0 (0%)	8 (16%)	6 (12%)	0 (0%)
Deficiency	<20	1 (2%)	24 (48%)	8 (16%)	0 (0%)

*Data were expressed as frequency and percentage
*Schirmer test 2= Schirmer test with anesthesia

In the severe dry eye group, 1 (2%) case was found as deficient in their Vitamin D status. In the moderate dry eye group, 8 (16%) cases were found as insufficient, 24 (48%) cases were deficient and only 2 (4%) cases were found as normal in their Vitamin D status. In the mild dry eye group, 6 (12%) cases were found as insufficient, 8 (16%) cases were deficient and only 1 (2%) case was found as normal in their Vitamin D status.

Table-VII

Correlation of vitamin D level with dry eye (n=50)

Variable		OSDI	TBUT	Schirmer test 1	Schirmer Test 2
Vitamin D	r value	-0.852	+0.479	+0.065	+0.320*
	p value	0.000s	0.000s	0.655ns	0.023s

*Pearson Correlation coefficient test was performed to observe the relation between dry eye and Vitamin D level.

In this study, dry eye was measured by OSDI, tear film breakup time (TBUT) and Schirmer test without and with anesthesia. Vitamin D level was positively correlated with TBUT, Schirmer test1 and Schirmer Test 2 and negatively correlated with OSDI. This correlation was statistically significant for TBUT, Schirmer Test 2 and OSDI.

Discussion

Vitamin D level can affect the immune system. Vitamin D strengthened the corneal epithelial barrier function through gap or tight junctions. It can control ocular surface inflammation by inhibiting Langerhans cell migration and corneal neovascularization. [6,10,11] Bae[12] reported that vitamin D supplementation is an effective and useful treatment for patients with DES. In the present study, dry eye was measured by OSDI score, tear film breakup time (TBUT), Schirmer test without and with anesthesia. OSDI score was found higher and fluorescein TBUT, Schirmer test without anesthesia and Schirmer test with anesthesia found lower score in dry eye patients. Almost similar study was found by different researchers of different countries. [2,8,13] But Jeon et al.[14] found no association between serum vitamin D levels and DES. Vitamin D level was positively correlated with TBUT, Schirmer Test 1 and Schirmer Test 2 and negatively correlated with OSDI in our study. This correlation was statistically significant for TBUT Schirmer Test 2 and OSDI. Yildirim et al. [1] and Jin et al. [2] agreed with our findings. They reported that tear break-up time (TBUT) and secretion were correlated with serum vitamin D levels. Vitamin D might be an important factor for dry eye syndrome. But Elagamy and Bawazir[15] and Arman et al. [16] demonstrated insignificant correlation with TBUT and Schirmer test.

Limitations

The limitation of our study was having small sample size and short study period in comparison to other studies. The effect of seasonal variation of vitamin D was not considered. Further study with a large sample size and longer study period is recommended.

Conclusions

After analyzing the results of the present study, it can be concluded that Vitamin-D deficiency appears to have an effect on ocular surface parameters in patients with dry eye syndrome. Therefore, vitamin D supplementation might be useful for mitigating the dry eye symptoms, including ocular discomfort, pain, redness, ocular fatigue, sensitivity to light and blurred vision.

References

1. Yildirim P, Garip Y, Karci AA, Guler T. Dry eye in vitamin D defciency: more than an incidental association. Int J Rheum Dis. 2016; 19: 49-54.
2. Jin KW, Jin Woo Ro JW, Young Joo Shin YJ, Hyon JY, Wee WR, Park SG. Correlation of vitamin D levels with tear film stability and secretion in patients with dry eye syndrome Acta Ophthalmol. 2017; 95: 230–235.
3. Shahraki K, Seif MH, Abbasi H, Amizadeh Y, Daneshtalab A, Shahraki K, Feizi S, Shojaei A. The Relation between Serum Level of Vitamin D and Dry Eye Disease. Journal of Ophthalmic and Optometric Sciences. 2017;1(5):1-6.
4. Jee D, Kang S, Yuan C, Cho E, Arroyo JG. Serum 25-Hydroxyvitamin D Levels and Dry Eye Syndrome: Differential Effects of Vitamin D on Ocular Diseases. PLoS One. 2016;11(2): e0149294.
5. Lu X, Elizondo RA, Nielsen R, Christensen EI, Yang J, Hammock BD & Watsky MA. Vitamin D in tear fluid. Invest Ophthalmol Vis Sci. 2015; 56: 5880–5887.
6. Yin Z, Pintea V, Lin Y, Hammock BD, Watsky MA. Vitamin D enhances corneal epithelial barrier function. Invest Ophthalmol Vis Sci. 2011; 52(10):7359-7364.
7. Demirci G, Erdur SK, Ozsutcu M, Eliacik M. Dry Eye assessment in patients with vitamin D deficiency. Eye & Contact Lens. 2016; 0: 1–4
8. Kurtul BE, Aydinli MS, Özer PA. The relationship between vitamin D deficiency and ocular surface clinical parameters in patients with non-sjögren dry eye. Turkiye Klinikleri J Ophthalmol. 2015; 24(1):35-40.
9. Holick MF. Vitamin D status: measurement, interpretation, and clinical application. Ann Epidemiol. 2009;19(2):73-78.
10. Elizondo RA, Yin Z, Lu X, Watsky MA. Effect of vitamin D receptor knockout on cornea epithelium wound healing and tight junctions. Invest Ophthalmol Vis Sci. 2014; 55(8):5245-5251.
11. Lu X, Watsky MA. Effects of vitamin D receptor knockout on cornea epithelium gap junctions. Invest Ophthalmol Vis Sci. 2014; 55(5):2975-2982.
12. Bae SH, Shin YJ, Kim HK, Hyon JY, Wee WR, Park SG. Vitamin D supplementation for patients with dry eye syndrome refractory to conventional treatment. Sci Rep. 2016; 6:33083.
13. Meng YF, Lu J, Xing Q, Tao JJ, Pan Xiao P. Lower Serum Vitamin D. Level was associated with risk of dry eye syndrome. Med Sci Monit. 2017; 23: 2211-2216.
14. Jeon DH, Yeom H, Yang J, Song JS, Lee HK, Kim HC. Are serum vitamin D levels associated with dry eye disease? Results from the study group for environmental eye disease. J Prev Med Public Health. 2017; 50:369-376
15. Elagamy A, Bawazir S. Dry Eye Evaluation in Saudi Patients with Vitamin D Defciency. J Ophthalmol Eye Care. 2019; 2(1): 105.
16. Arman A, Petriçli İS, Kara C, Köksal Z, Güçel F. The relationship between serum vitamin d levels and dry eye syndrome in postmenopausal women. Ann Clin Anal Med. 2020; 11(2):91-94.

Original Article

Commonly Reported Illnesses among the College Students of Birmingham, United Kingdom

*Nicolas Habib

Abstract

Introduction: Career of adolescent college students may be influenced by physical illness. However it has not been observed to characterize the common health problems and beverage intake among these students or had been studied less often so, there might have been information gaps in the knowledge in this aspects.

Aim and objectives: The aim of this study was to identify the commonly prevalent health issues among such college going adolescents students in studying the nature of taking beverages and thus to associate if any relation exist(s) between such beverage intake and prevalent illness/disease in these students.

Methodology: This observational type of cross-sectional study was conducted among the adolescents college students (of Year 12 & 13) studying at the University of Birmingham School Sixth Form, England, UK.

This study was conducted among the students of University of Birmingham School Campus for about 12 months, (from July 2022 to June 2023). All the 115 students enrolled, for the study population from which 90 samples were drawn using simple random sampling. Data were collected by employing face to face interview through a semi-structured questionnaire during my free time in between class intervals, administrating a face to face interview method.

Results: The mean age of 90-A level students was 16.74 ± 0.59 years, yielding a male predominance (83%). Most students preferred to drink artificial beverage (61%) other than any natural drink (21%). The top most common morbidity was respiratory illness (36%), the largest number among them 15% of who were suffering from upper respiratory tract illness (URTI). While assessing the commonly occurred morbidity (17%) reported to have common cold. Followed by about 1/3rd of students (33%) had been suffering from neurological diseases, it was the second most common illness and 4% had been suffering from depression and anxiety. when one tenth used to suffer from headache (14%).

Using a non-parametric test, it indicated not to yield any association between the food behaviours of beverage intake with any of the prevailing systemic illness among the students.

Conclusion: Students suffered mostly from URTI and/or common cold followed by neurological disorders/headache. The finding thus emphasizes the needs of regular health check-up of these college students, at par

Key words: *Common illness, College students, United Kingdom*

Background

Of 10.6 million children studying in school level (year 1 to 13) in the UK, 2.75 million belong to secondary school and college levels. They have a bright future. Their career may be influenced by this disease prevailing condition.[1]

Adolescent and children health is an important issue in England and the National Health Service (NHS), UK provide health care based service delivery depending on their needs, funded by the UK government since 1984. However, prevalence of Non Communicable Disease (NCD) is more (89% death) than communicable diseases. Respiratory and Neurological illnesses are more common in UK that also encompasses College and University students. [2]

Most common problems were cough and cold, asthma, hay fever etc. that were the most common respiratory illness, among the college and university students in UK. Followed by neurological disorder, headache, depression, anxiety, dizziness, insomnia, migraine remains the most common neurological illness.[2]

Student career may be influenced by the eating patterns and their diseases. Students take various type of drinking products with food or other than food. Beverage drinking is an important part of young life. It is a product of hunger reduction and entertainment also.

There are many types of drinking substances, from soft drinks to hard drinks, other than water. Choice varies

Correspondence: Year 12 student at University of Birmingham School Sixth Form, UK, Gmail- nicohabib26@gmail.com, Cell +4407404996687

Received Date : 10 August, 2023

Accepted Date : 02 September, 2023

person to person. These are made of mostly artificial ingredients. The transition of school to college campus life may be associated with increased autonomy over drink choices, or food intake and it budget, and exposure to new social groups and food cultures.

In this college campus life there is high intake of beverage drink and fast foods and low consumption of fruit and vegetables.[3] It is the shifting point of dietary behaviours track from childhood to adolescence.[4] IT is reported that transition from school to college or university life has been associated with unfavorable changes from drink to fast food intake, increases in alcohol and sugar containing drinks and snack foods, and decreases in fibrous food consumption.[5] During their college life period it has been identified that they gain body weight.[6,7] But, such weight gain may have long-term repercussions, since overweight during young adulthood has been identified as a significant predictor of obesity later in life.[8] This overweight and obesity is responsible for acute or chronic illness of minor and major varieties of Non Communicable Diseases (NCDs) and Communicable Diseases (CDs).

Common health problems and dietary pattern approach has been identified in various UK population groups.[9] However it has not been employed to characterize the common health problems and habits f beverage taking by the adolescent students. This provides an information gap for college students. This study aimed to identify common morbidities and beverage drinking patterns that exist within a UK college student population, to examine socio-demographic variables underpinning these patterns.

Based on this aforementioned literature it becomes obvious that food intake pattern remains a major determinant among the college students in many countries including UK.[10] So, this study was undertaken to study the prevailing morbidities and/or infection diseases among these adolescents college going students in Birmingham, UK, and to assess if there are associated with their food behaviour.

Methodology

Study type: Descriptive type of cross sectional study.

Duration of the study: About 12 months, from July 2022 to June 2023.

Study Population: Of all 115 students were enrolled of year 11 and 12 at university of Birmingham School sixth form.

Study Place: University of Birmingham School sixth form, about 10,000 square meter green campus with three stored buildings, located at Weoley Park Road, Selly Oak at Birmingham, UK. It was one of the first ten schools in Birmingham where about 1000 mixed gender 11 to 18 years' old student studies, belonging to 7 to 13 year for GCSE and A levels. There was 115 pupils in year 12 and 13 at the A level student.

Sample size calculation: Z^2 pq/d^2 (Z-1.96, p-50%, q-100-p, degree of precision-9, at 95% Confidence Interval, so, $(1.96)^2 \times 50 \times 50 / 9^2 = 118$ students

Sample size: Total 90 sample were collected from simple random sampling (SRS) from 115 students.

Study instrument: Data were collected using semi structured questionnaire.

Data collection procedure: Face to face interview during my free time of class intervals period.

Working Definitions:

Disease- A disease refers to specific abnormal condition or disorder that affects the body or mind and hampers normal functioning**.** [11]

Illness- It refers to the individual's personal experiences of being unwell or not feeling well due to a disease or a health condition**.** [11]

Sixth form: It is refers to the last two years of secondary education in England, Wales and Northern Ireland. They are commonly referred to as years 12 and 13 in schools, although students can attend a college and simply be in their first or second year as they have moved on from school. **GCSE**- General Certificate of Secondary Education, it is an academic qualification, generally taken in a number of subjects by pupils in secondary education in UK.

Artificial Beverage- these are made by artificial ingredients, like Coca Cola, Boost, and Sting etc. **Natural Beverage**- These contained natural ingredients, like milk, Vino, Orange juice etc. [11]

Exclusion criteria: Students who were not interested.

Inclusion criteria: All students of year 11 and 12 of University of Birmingham School sixth form.

Data analysis: All the collected yet verified/double checked data was entered into the SPSS (Statistical Package for Social Science),V. 22. Mostly, descriptive, and inferential statistics were performed with frequency table with percentage and cumulative percentage.

Results

The study involved a total of 90 teenagers, with an average age of 16.74 ± 0.59 years. They were all college-level students, with the majority (66%) falling into the 17-year-old age group, of which 83% were males. Among these students, the majority (61%) preferred artificial beverages, while a minority (7%) opted for drinks containing alcohol (Table-II).

In terms of health concerns, the most prevalent category of health issues (36%) among the participants was respiratory illnesses (Table-IV). Notably, 17% of the students suffered from common cold-like upper respiratory tract infections (Table-III). The second most common category of illnesses (33%) fell under the nervous system (Table-IV), with 14% experiencing headaches and 8% dealing with depression and anxiety (Table-III).

"The results of the non-parametric test (Table-V) indicate that there was no statistically significant relationship between the choices of beverages among students and their overall health issues.

Table-I

Comparison between age and gender of the respondent (n=99)

	Sex of respondents			
Age	Male	Female	Total	P value
16 years	26 (29%)	05 (6%)	31 (34%)	
17 years	49 (54%)	10 (11%)	59 (66%)	0.61
	75 (83%)	15 (17%)	90 (100%)	

Most students (75%) were male and 17 years old students were dominant in number (66%).

Table-II

Variability of Nature of beverage according to sex distribution (n=99)

	Sex of respondents			
Nature of drink	Male	Female	Total	P value
Natural beverage	15 (17%)	04 (4%)	19 (21%)	
Artificial beverage	47 (52%)	08 (9%)	55 (61%)	0.79
Alcohol containing beverage	04 (4%)	02 (2%)	6 (7%)	
Others	09 (10%)	01 (1%)	10 (11%)	
	75 (83%)	15 (17%)	90 (100%)	

Most students (61%) prefer artificial beverage to drink and above half of all male students (52%) were included in this group. A minor amount (7%) of them like to drink alcohol containing beverage.

Table-III

Illness status of the students (n=90)

	Variables	Frequency	Percentage
1	Common cold, cough, asthma, nose bleeding, hay fever	32	36%
2	Headache, anxiety, depression, dizziness, insomnia, migraine	30	33%
3	Back pain, joint pain	19	21%
4	Stich in abdomen, lung cancer, irregular fever and others	19	21%
	Total	90	100%

Above one third (36%) of students were suffered from respiratory illness and common cold was the top most illness (17%) of total variabilities. Second most common (14%) illness was the headache of all morbidities.

Table-IV

System specific prevalence of illness among students (n=90)

	Variable	Frequency	Percentage
1	Respiratory and immune system	32	36%
2	Neurological system	30	33%
3	Musculoskeletal system	19	21%
4	Digestive system	04	04%
5	Others	15	17%

The respiratory and immune systems emerged as the most vulnerable among all students, with 36% experiencing issues in this category. A significant proportion, specifically more than one third of the students, dealt with illnesses related to the neurological system. Musculoskeletal problems affected more than one-fifth of the participants

Table-V

Inferential study on nature of beverage intake and systemic illness (n=90)

	Variable of systemic illnesses	Type of Beverages			
		Natural drink	Artificial drink	Alcohol containing drink	Others
1	Irregular fever & Others	10	20	1	5
2	Respiratory & immune system	3	21	4	2
3	Neurological system	0	17	0	0
4	Musculoskeletal system	3	2	0	0
5	Digestive system	1	1	0	0
	Total	17	61	5	07

Fisher's Exact test Value : 20.63, df 18, P 0.29 (Non-significant)

In this non parametric test, it was indicating that there was no relationship in between nature of drinking beverage with systemic illness of the students.

Discussion

Adolescent are present a large, captive population of emerging adults who are expected to fulfil important roles in society as professionals.[12-13] The transition into adolescent period is significant as during this period emerging adults experience greater freedom to make choices regarding their health and lifestyle behaviours.[14-16] Furthermore, many students find themselves in a new environment and experience changes to support networks and social norms.[17-19]

In this study, among 90 college students, the age ranged from 16 to 17 years, where a significant portion (83%) was male (Table-I). Thus, such male predominance has also been reported in Journal of further and higher education in UK [20] and female predominance in preventive medicine journal in UK.[21]

Consequently, transition in living environment is likely to alter their drinking and eating behaviours.[22,23] As decision makers and role models, the attitudes and behaviours adopted during their college education have the potential to have further reaching impact on wider society and therefore the health and lifestyle behaviours of these students are of public health interest.[24]

College and university students are widely reported to engage in unhealthy lifestyle behaviours including unhealthy eating behaviours such as drinking, consumption of quick snacks [20], other convenient foods, and fast foods which were high consumed [14], constantly,

insufficient consumption of fruit and vegetables were reported as well. Thus, students indulging in these wrong or faulty food behaviours may have been at increased risk of weight gain-that have been reported to develop NCDs and other communicable diseases, in future.[19]

In this study, most students (61%) were seen to be preferred artificial beverage for drink while only 21% preferred natural drinks along with minor (7%) preferred to alcoholic drink (Table-III).

Findings of this study did not reveal any relation of beverage intake and systemic illnesses (Table-V). However, some of the students had reportedly been suffering from headache, depression and other neurological disorder related morbidities (Table-III).

The top most common (30%) morbidity was the respiratory illness and, among them, >17% were suffering from common cold like (the upper respiratory tract illness (Table-III). In Bangladesh, 67% children suffered from respiratory problems and among them 48% babies suffered from 48% suffered from common cold.[25]

Nearly, one fourth (33%) of these students were suffering from neurological illnesses and among them about 1/10th (14%) used to suffer from headache while another 8% of had been suffering from a degree of depression and/or anxiety (Table-III).

Published figures suggested more than a third of students consume snack food '' at least several times a week'' or 3-4 times a week or more.[14, 15, 16] The reported prevalence of fast food consumption, three or more times per week, [17] ''at least several times per week,'' and 3-4 times a week or more, is varied, ranging from 20.2% in polish university students to 46% in USA university students.[26] Of interest, using the criteria of two or more takeaway meals as a main meal per week. There was reported only 12.5% of Australian university students to meet the criteria.[27] Where as in my study I had collected only nature of beverage intake, not quantitative or other diet, which was important to compare with other studies.

In this study, physical illness and beverage drinking had not defined as qualitative or quantitatively on adolescent students. Female gender was poor in number. It was done at a single centre and prevalence study.

Conclusion

Students suffered mostly from respiratory and nervous system illnesses. Recurrent common cold and headache are the most common illnesses. Interestingly some students like to drink alcohol contain beverage.

Recommendation

It is important to further study on headache of students to determine any relation with recurrent common cold or mental stress.

References

1. School, pupils and their characteristics, academic year 2022/23 [internet]. Jun 8, 2023. Last update 13 June 2023. Available from https://explore-education-statistics.service.gov.uk
2. Final Season: Common illnesses for College Students. www.myhsn.co.uk. My HSN. 2021 Health service navigator [internet]
3. Stewart-Brown S, Evans J, Patterson J, Petersen S, Doll H, Balding J, et al. The health of students in institutes of higher education: An important and neglected public health problem. J Public Health Med 2000; 22(4): 492–9.
4. El Ansari W, Stock C, UK Student Health Group, Snelgrove S, Hu X, Parke S, et al. Feeling healthy, A survey of physical and psychological wellbeing of students from seven universities in the UK. Int J Environ Res Public Health 2011; 8(5): 1308–23.
5. Vaez M, Laflamme L. First-year university students' health status and socio-demographic determinants of their self-rated health. Work 2002; 19(1): 71–80.
6. Crump C, Rivera D, London R, Landau M, Erlendson B, Rodriguez E. Chronic health conditions and school performance among children and youth. Ann Epidemiol 2013; 23(4): 179–84.
7. Novovic Z, Mihic LJ, Tovilovic S, Jovanovic V, Biro M. Psychometric characteristics of the Beck depression inventory on a Serbian student sample. Psihologija 2011; 44: 225–43. (Serbian)
8. Klemenc-Ketis Z, Kersnik J, Eder K, Colaric D. Factors associated with health-related quality of life among university students. Srp Arh Celok Lek 2011; 139(3–4): 197–202.
9. Castren J, Huttunen T, Kunttu K. Users and non-users of web based health advice service among Finnish

university students: Chronic conditions and self-reported health status (a cross sectional study). BMC Med Inform Decis Mak 2008; 8: 8.

10. Mikolajczyk RT, Brzoska P, Maier C, Ottova V, Meier S, Dudziak U, et al. Factors associated with self-rated health status in university students: A cross-sectional study in three European countries. BMC Public Health 2008; 8: 215.
11. Stedman's Medical Dictionary. 26th edition Beltimore: Willium & Wikins; 1995, Apraxia
12. El Ansari W, Labeeb S, Moseley L, Kotb S, El-Houfy A. Physical and Psychological Well-being of University Students: Survey of Eleven Faculties in Egypt. Int J Prev Med 2013; 4(3): 293–310.
13. Lee RL, Loke AJ. Health-Promoting Behaviors and Psychosocial Well-Being of University Students in Hong Kong. Public Health Nurs 2005; 22(3): 209–20. 21. Sánchez-López MP, Cuellar-Flores I, Dresch V. The impact of gender roles on health. Women Health 2012; 52(2): 182–96
14. British Government. Participation Rates in Higher Education: Academic Years 2006/ 2007–2013/ 2014. London: British Government; 2015.
15. El AW, Stock C, John J, Deeny P, Phillips C, Snelgrove S, et al. Health promoting behaviours and lifestyle characteristics of students at seven universities in the UK. Cent Eur J Public Health. 2011;19:197–204.
16. Devine P, Lloyd K, Gray AM. University student food attitudes and behaviour survey. Belfast: University of Ulster; 2006.
17. Lake AA, Adamson AJ, Craigie AM, Rugg-Gunn AJ, Mathers JC. Tracking of dietary intake and factors associated with dietary change from early adolescence to adulthood: the ASH30 study. Obes Facts. 2009;2:157–65
18. Mikkilä V, Räsänen L, Raitakari OT, Pietinen P, Viikari J. Consistent dietary patterns identified from childhood to adulthood: the cardiovascular risk in young Finns study. Br J Nutr. 2005;93:923–31
19. Papadaki A, Hondros G, Scott J, Kapsokefalou M. Eating habits of university students living at, or away from home in Greece. Appetite. 2007;49:169–76.
20. Larson NI, Neumark-Sztainer D, Story M. Weight control behaviors and dietary intake among adolescents and young adults: longitudinal findings from project EAT. J Am Diet Assoc. 2009;109: 1869–77.
21. Woodruff SJ, Hanning RM, Lambraki I, Storey KE, McCargar L. Healthy eating index-C is compromised among adolescents with body weight concerns, weight loss dieting, and meal skipping. Body Image. 2008;5:404–8.
22. Guo SS, Huang C, Maynard LM, Demerath E, Towne B, Chumlea WC, et al. Body mass index during childhood , adolescence and young adulthood in relation to adult overweight and adiposity: the Fels longitudinal study. Int J Obes. 2000;24:1628–35.
23. Neumark-Sztainer D, Wall M, Larson N, Eisenberg M, Loth K. Dieting and disordered eating behaviors from adolescence to young adulthood: findings from a 10-year longitudinal study. J Am Diet Assoc. 2011;111:1004–11.
24. Fayet F, Petocz P, Samman S. Prevalence and correlates of dieting in college women: a cross sectional study. Int J Womens Health. 2012; 13:405–11.
25. Habib RB, ARML K, Rouf MA, Ullah MS, Hossain MN, Rahman MN, Boyan RK, Hye MA. Respiratory Morbidities among Children in a Grass Root Level Hospital in Bangladesh. Official Organ of Bangladesh Medical Association. 2019 Jan;48(1):1.
26. Tanton J, Dodd LJ, Woodfield L, Mabhala M. Eating behaviours of British university students: A cluster analysis on a neglected issue. Advances in preventive medicine. 2015 Sep;2015.
27. Anderson AH, Carter M, Stephenson J. Perspectives of university students with autism spectrum disorder. Journal of autism and developmental disorders. 2018 Mar;48:651-65.

Original Article

Determination of Minimum Inhibitory Concentration (MIC) of Tigecycline against Salmonella typhi

Sanjoy Saha[1*], MM Islam[2], Md. Kutub Uddin Mollick[3]

Abstract:

Introduction: Typhoid fever, caused by S. Typhi, is prevalent in developing countries, particularly the Indian subcontinent. Salmonella infections can cause enteric fever, gastroenteritis, septicemia, and non-typhoidal Salmonellae (NTS) infections, especially in immunocompromised patients.

Objective: To determine the Minimum Inhibitory Concentration (MIC) of Tigecycline against Salmonella Typhi.

Methodology: This interventional study conducted at Department of Pharmacology & Therapeutics in collaboration with Department of Microbiology at Ad-din Sakina Women's Medical College, Jashore during March 2023 to April 2023.MIC of Tigecycline was determined by Broth Dilution Technique against standard strain of Salmonella typhi ATCC 24683.

Result: The MIC of Tigecycline against Salmonella typhi was 2.0 μg/ml.

Conclusion: Tigecycline is a potential therapeutic agent for Salmonella typhi infection, and should be restricted on the basis of blood culture and in MDR and XDR cases of typhoid fever only.

Key Words: Salmonella, Tigecycline, Minimum Inhibitory Concentration

Introduction:

Typhoid fever which is caused by S. Typhi is endemic in developing countries; more so in the Indian subcontinent.[1] Infections with Salmonellae can result in various clinical presentations like enteric fever, gastroenteritis, septicemia with or without supportive lesion and carrier state. Salmonella typhi and paratyphi A, B and C cause typhoid fever and paratyphoid fever respectively, while non typhoidal Salmonellae (NTS) that has more than 2500 serotypes, causes gastroenteritis and invasive infections like meningitis and osteomyelitis in immunocompromised patients adults and children.[2] Salmonella typhi is mostly acquired directly or indirectly through human feces by fecal-oral route from the diseased person or a carrier.

1. Associate Professor, Department of Pharmacology, Ad-din Sakina Women's Medical College, Jashore.
2. Associate Professor, Department of Pharmacology, Ad-din Sakina Women's Medical College, Jashore.
2. Professor and Head, Department of Hepatology, Khulna Medical College, Khulna

***Correspondence:** Dr. Sanjoy Saha, Associate Professor, Department of Pharmacology, Ad-din Sakina Women's Medical College, Jashore. Email: dr.sanjoysahammc@ gmail.com

Received Date : 05 September, 2023

Accepted Date : 10 October, 2023

Salmonella infections, especially those involving the blood stream, have a high mortality rate (about 30%). This can be reduced to about 1% with appropriate use of antibiotics.[3, 4] However, resistance of Salmonella Typhi to chloramphenicol, cotrimoxazole and ampicillin developed in the 1980s. Threat of growing resistance to antibiotics is of grave concern to human health as it can lead to prolonged illness and more rate of complications.[5]

The World Health Organization (WHO) recommends treatment with azithromycin, ciprofloxacin, or ceftriaxone due to widespread resistance to older first-line antimicrobials. With an increasing use of fluoroquinolones against enteric fever, gradually resistance also developed ciprofloxacin. Resistance to third generation cephalosporins such as ceftriaxone is beginning to emerge as well.[6] Decades of empiric antibiotic use have resulted in the development of these MDR organisms (resistant to ampicillin, co-trimoxazole, and chloramphenicol) followed by extensively drug-resistant (XDR) S. typhi strains (resistant to chloramphenicol, ampicillin, co-trimoxazole, fluoroquinolones, and ceftriaxone).

An outbreak of MDR S. Typhi in late 1990s in Tajikistan caused more than 24,000 infections.[7] The world witnessed its first case of Extensively Drug-Resistant (XDR) Typhoid Fever in 2016 in Pakistan.[8] More recently, the World Health Organization (WHO) recorded that there were 5,274 cases of XDR typhoid fever out of a total of 8,188 cases of typhoid fever reported in Pakistan from November 2016 up to December 2018. [9]

Similar outbreaks have been documented worldwide, particularly in regions such as Southeast Asia, the Indian subcontinent, Africa, and South America [10,11]. This highlights the escalating challenge of drug-resistant typhoid infections globally. The emergence of resistance has significantly reduced the available therapeutic options for treating typhoid and other Salmonella infections. Managing outbreaks of multidrug-resistant (MDR) and extensively drug-resistant (XDR) Salmonella Typhi poses significant challenges, particularly in developing countries with limited resources. Therefore, there is an urgent need to explore new approaches for treating drug-resistant Salmonella strains.

One promising avenue in the treatment of typhoid is the antibiotic tigecycline, which is not commonly used for Salmonella infections. Tigecycline belongs to the glycylcycline class of antibiotics and shares structural similarities with tetracycline antibiotics. It exhibits a broad spectrum of activity, effectively targeting a wide range of gram-positive, gram-negative, and anaerobic bacteria. Its mechanism of action involves binding to the 30S ribosomal subunit in susceptible bacteria, ultimately hindering protein synthesis by impeding the incorporation of amino acids into peptide chains, thereby halting bacterial growth.[12]

The objective of this study was to determine the minimum inhibitory concentration (MIC) of Tigecycline against Salmonella typhi. MIC represents the lowest concentration of a drug required to prevent visible in-vitro growth of the organism. This research seeks to shed light on the effectiveness of Tigecycline as a potential treatment option against drug-resistant Salmonella typhi strains, in the face of rising antibiotic resistance.

Materials and method:

The interventional study was conducted in the Department of Pharmacology and Therapeutics in collaboration with the Department of Microbiology at Ad-din Sakina Women's Medical College, Jashore, Bangladesh during the period of March to April 2023.

Ethical Approval:

Ethical clearance was obtained from Ethical Review Committee (ERC) and Institutional Review Board (IRB) of Ad-din Sakina Women's Medical College (ASWMC), Jashore.

Collection of antibiotic Tigecycline:

Tigecycline antibiotics for this study were obtained through the purchase of Injection Tegalon vials (500 mg) from the local market. These vials were manufactured by Healthcare Pharmaceuticals LTD, Bangladesh.

Test organism:

Standard reference strain of Salmonella typhi, ATCC 24683 was collected from the Department of Microbiology of Ad-din Sakina Women's Medical College, Jashore.

Procedure of Experiment:

Determination of MIC of Tigecycline against test organisms

Technique: Broth dilution.

Preparation of stock solution of Tigecycline:

Five hundred (500) mg of Tigecycline powder was mixed well with 500 ml of sterile Distilled Water (DW) by using a sterile syringe. The prepared Tigecycline Injection had the concentration of 500 mg in 500 ml. So, 1 ml solution contain 1 mg Tigecycline (Stock Tigecycline solution-I). Then 1 ml of stock Tigycycline solution-I was mixed with 99 ml of sterile D/W. This 1:100 dilution of stock Tigycycline solution-I had the concentration of 10 μg/ml. This solution was marked as Stock Tigecycline Solution-II which was used as stock solution for the determination of MIC of Tigecycline.

Calculations:

Tigecycline 500 mg + 500 ml D/W.

So, 500 mg Tigecycline in 500 ml

Thus 1 ml contains 1 mg of Tigecycline (Stock Tigecycline Solution-I)

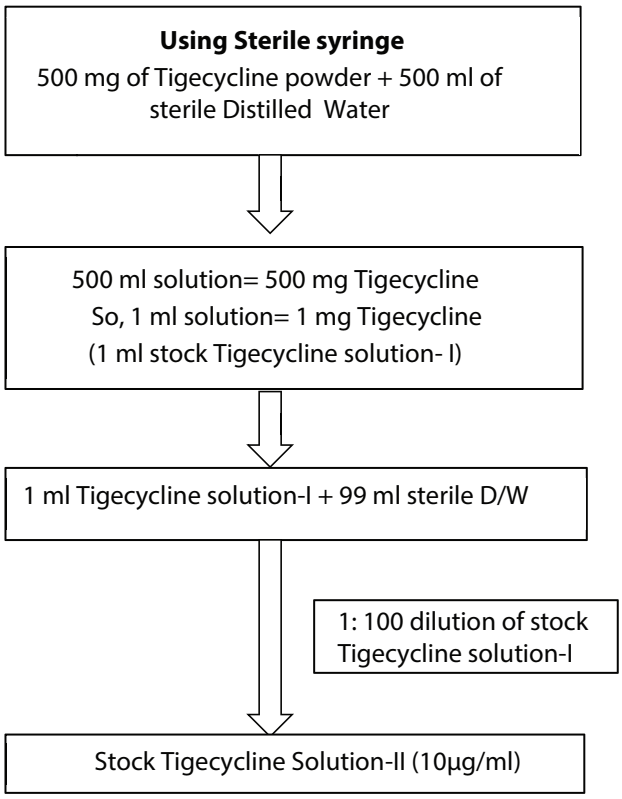
1 ml of solution + 99 ml D/W (1:100 dilution).

So, 100 ml contains 1 mg Tigecycline = 1000 μg Tigecycline

So, in 1 ml, the concentration is 1000/100 = 10 μg Tigecycline /ml (Stock Tigecycline Solution-II)

This stock Tigecycline solution-II (concentration 10 μg/ml) was used for the determination MIC of Tigecycline by broth dilution technique

Flowchart:



Preparation of different concentrations of Tigecycline solution:

Set – I: Tigecycline solution was made by adding 0.25 ml of stock Tigecycline solution-II with 9.75 ml of Trypticase soya broth medium. The concentration of Tigecycline in this dilution was 0.25 µg/ml.

Calculation:

1 ml of stock Tigecycline solution contains 10 µg of Tigecycline. (Stock Tigecycline Solution-II)

So, 0.25 ml Tigecycline solution contains 2.5 µg of Tigecycline

So 10 ml of set I preparation contains 2.5 µg of Tigecycline

And thus 1 ml of set I preparation contains 25 µg of Tigecycline

Set – II: Tigecycline solution was made by adding 0.5 ml of stock Tigecycline solution-II with 9.5 ml of Trypticase soya broth medium. The concentration of Tigecycline in this dilution was 0.5 µg/ml.

Similarly, **Set-III, IV, V and VI** of Tigecycline solution respectively were made by adding a measured amount of stock Tigecycline solution-II with the measured amount of broth medium. The concentrations of Tigecycline were 0.75 µg/ml, 1 µg/ml, 1.5 µg/ml and 2 µg/ml respectively: (Table 1).

Control – 1: was made with 10 m1 of Trypticase soya broth medium (to be inoculated with bacterial suspension) in test tubes.

Control – 2: was made with 10 m1 of Trypticase soya broth medium (no inoculation with bacterial suspension) in test tubes. (Table 1) With each 10 ml preparation except control-1 (set VII) 20 µl bacterial suspensions were added after matching its opacity with that of 0.5 McFarland Standard.

Table-I

Composition and different concentrations of working Tigecycline solutions and the controls:

No. of Sets	Stock Tigecycline solution-II (ml)	Trypticase soya Broth media (ml)	Total (ml)	Concentration of Tigecycline (µg/ ml)	Test organism (µl)
I	0.25	9.75	10	0.25	20
II	0.5	9.50	10	0.5	20
III	0.75	9.25	10	0.75	20
IV	1	9	10	1	20
V	1.5	8.5	10	1.5	20
VI	2	8	10	2	20
VII	Control-1	10	10	-	-
VIII	Control-2	10	10	-	20

Inoculation of bacterial suspension to different concentrations of stock Tigecycline in test tubes:

After matching the turbidity of bacterial suspension with 0.5 McFarland standards, 20 μl or one drop (0.02 m1) of bacterial suspension of Salmonella typhi is inoculated. These inoculums were also added to the control -2 but were not added to Control-1.

Incubation: The test tubes were marked set wise with black marker and were placed in the incubator at 37° C for 18 -24 hours.

Examinations of test organisms in different dilutions and concentrations of Tigecycline: After 18 to 24 hours of incubation at 37° C, the growth of test organisms in each preparation of Tigecycline was examined and compared against that of control by matching their turbidity. The clear preparations were considered as no growth of bacteria and turbid one as growth of bacteria. The MIC was reported as the lowest concentration of Tigecycline required to prevent the visible growth of test organisms. The observations and results of the experiment were shown in Table-II.

Subculture of materials from effective dilutions of Tigecycline in MacConkey agar media: The materials from last two sets of growth and all sets of no growth of Tigecycline preparations were subcultured in the pure MacConkey (solid) media plates (without antibiotic and antibiotic mixed media). After 18 to 24 hours of incubation at 37°C, the growth of test organisms were examined.

Observations and results:

Table-II shows visible growth of Salmonella typhi observed at Set-I to Set-V. But the organisms failed to grow at Set-VI. So the minimum inhibitory concentration (MIC) of Tigecycline against Salmonella typhi was 2.0 μg/ml.

Table-II

MIC of Tigecycline against Salmonella typhi

No of Sets	Concentration (μg/ ml)	Salmonella typhi
Set-I	0.25	Growth
Set-II	0.5	Growth
Set-III	0.75	Growth
Set-IV	1	Growth
Set-V	1.5	Growth
Set-VI	2	No Growth
Set-VII	Control-1(Trypticase soya broth + No bacteria inoculation)	No Growth
Set-VIII	Control-2 (Trypticase soya broth+ Bacterial inoculation with no antibiotic)	Growth

Table-II also showed control-1 containing Trypticase soya broth medium without any bacterial inoculum had no visible growth and control -2 containing Trypticase soya broth medium with bacterial inoculum observed their visible growth.

Result of Experiment: The MIC of Tigecycline against Salmonella typhi was 2.0 μg/ml at set VI.

Discussion:

Typhoid fever which is caused by S. Typhi is endemic in developing countries; more so in the Indian subcontinent.[1] Salmonella infections, especially those involving the blood stream, have a high mortality rate (about 30%). This can be reduced to about 1% with appropriate use of antibiotics.[3, 4] Threat of growing resistance to antibiotics is of grave concern to human health as it can lead to prolonged illness and more rate of complications.[5] Outbreaks of MDR- and XDR- Typhoid fever have been documented worldwide, particularly in regions such as Southeast Asia, the Indian subcontinent, Africa, and South America.[10, 11] The emergence of resistance has significantly reduced the available therapeutic options for treating typhoid and other Salmonella infections. Therefore, there is an urgent need to explore new approaches for treating drug-resistant Salmonella strains.

The objective of this study was to determine the minimum inhibitory concentration (MIC) of Tigecycline against Salmonella typhi.

The study was conducted during the period of March 2023 to April 2023 in the department of Pharmacology and Therapeutics with the collaboration of Department of Microbiology, Ad-din Sakina Women's Medical College, Jashore to determine the MIC of antibiotic Tigecycline against standard strain of Salmonella typhi. It was an interventional study. The MIC of antibiotic Tigecycline was determined by broth dilution technique. The stock solution of Tigecycline was made. Then the working solution of various concentrations was made by diluting the stock Tigecycline solution. The concentrations were 0.25 μg/ ml,. 5 μg/ ml, and 0.75 μ g/ml, 1 μg/ml, 1.5 μg/ml, and 2 μg/ml. The MIC of Tigecycline against Salmonella typhi was 2.0μg/ml. A near similar type of study was done at Department of Microbiology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India where the investigators found the MIC of Tigecycline against

Salmonella typhi was 2.0 μg/ml [13] which is similar to our study. Another study was done by Thomas R. Fritsche et al. in the year 2005 where the MIC of Tigecycline was determined against various species of Enterobacteriaceae including Salmonella spp where the MICs varies 2-8 μg/ml in different species.[14] From the study it is evident that the minimum inhibitory concentration of Tigecycline, **i.e.** 2.0μg/ml, is much lower than other Salmonella sensitive antibiotics like Ciprofloxacin and Azithromycin.[15]

Conclusion:

It is evident that the minimum inhibitory concentration of Tigecycline, i.e. 2.0μg/ml, is much lower than other Salmonella sensitive antibiotics like Ciprofloxacin and Azithromycin. But indiscriminate use of this antibiotic will cause antibiotic resistance. As Tigecycline is a potential therapeutic agent, its use should be restricted on the basis of blood culture and in MDR cases of typhoid fever only.

References:

1. Ochiai RL, Acosta CJ, Danovaro-Holliday MC, Baiqing D, Bhattacharya SK, Agtini MD et al. A study of typhoid fever in five Asian countries: disease burden and implications for controls. Bull World Health Organ 2008; 86(4):260-8.
2. Gordon MA, Kankwatira AM, Mwafulirwa G, Walsh AL, Hopkins MJ, Parry CM et al. Invasive non-typhoid Salmonellae establish systemic intracellular infection in HIV-infected adults: an emerging disease pathogenesis. Clin Infect Dis 2010; 50(7):953-62.
3. Mirza SH, Beeching NJ, Hart CA. The prevalence and clinical features of multi-drug resistant Salmonella Typhi infections in Baluchistan, Pakistan. Ann Trop Med Parasitol 1995; 89(5): 515-9.
4. Mermin JH, Townes JM, Gerber M, Dolan N, Mintz ED, Tauxe RV. Typhoid fever in the United States, 1985-1994: changing risks of international travel and increasing antimicrobial resistance. Arch Intern Med 1998; 158(6):633-8. Bangladesh Crit Care J September 2019; 7 (2): 102-105
5. Koul PB, Murali MV, Sharma PP, Ghai OP, Ramchandran VG, Talwar V. Multi-drug resistant Salmonella Typhi infection: clinical profile and therapy. Indian Pediatr 1991; 28(4):357-61.
6. Sah R, Donovan S, Seth-Smith HM, Bloemberg G, Wüthrich D, Stephan R, et al. A novel lineage of ceftriaxone-resistant Salmonella Typhi from India that is closely related to XDR S. typhi found in Pakistan. Clin Infect Dis. 2020;71:1327–30. .
7. Tarr PE, Kuppens L, Jones TC, Ivanoff B, Aparin PG, Heymann DL. Considerations regarding mass vaccination against typhoid fever as an adjunct to sanitation and public health measures: potential use in an epidemic in Tajikistan. Am J Trop Med Hyg 1999; 61(1):163-70.
8. Klemm EJ, Shakoor S, Page AJ, et al. Emergence of an Extensively Drug-Resistant Salmonella enterica Serovar Typhi Clone Harboring a Promiscuous Plasmid Encoding Resistance to Fluoroquinolones and Third-Generation Cephalosporins. MBio 2018;9:e00105-18. 10.1128/mBio.00105-18
9. Akram J, Khan AS, Khan HA, Gilani SA, Akram SJ, Ahmad FJ, et al Extensively drug-resistant (XDR) typhoid: evolution, prevention, and its management. Biomed Res Int. 2020;2020: 6432580. doi: 10.1155/2020/6432580.
10. Mirza SH, Beeching NJ, Hart CA. Multi-drug resistant typhoid: a global problem. J Med Microbiol 1996; 44(5):317-9.
11. Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. Typhoid fever. N Engl J Med 2002; 347(22): 1770-82.
12. Zhanel GG, Homenuik K, Nichol K, Noreddin A, Vercaigne L, Embil J, Gin A, Karlowsky JA, Hoban DJ. The glycylcyclines: a comparative review with the tetracyclines. Drugs.
13. Malini R. Capoor, Deepthi Nair, Jitendra Posti, Smita Singhal, Monorama Deb, Pushpa Aggarwal and Parukutty Pillal. Minimum inhibitory concentration of carbapenems and tigecycline against Salmonella spp. Journal of Medical Microbiology (2009), 58, 337–341.
14. Fritsche, T. R., Strabala, P. A., Sader, H. S., Dowzicky, M. J. & Jones, R. N. (2005). Activity of tigecycline tested against a global collection of Enterobacteriaceae including tetracycline-resistant isolates. Diagn Microbiol Infect Dis 52, 209–213.
15. Gao Y, Dutta S, Wang X. Serendipitous discovery of a highly active and selective resistance-modifying agent for colistin-resistant gram-negative bacteria. ACS omega. 2022 Mar 30;7(14):12442-6.

Original Article

Short Term Neurodevelopmental Outcome of Asphyxiated Term Neonates with Maintenance Phenobarbitone Therapy; Preliminary Findings of Ongoing Study in A Tertiary Care Hospital of Bangladesh

*Saha D[1], Ahmed T[2], Begum M[3], KS Anwar[4], Mistry B[5], Saha NC[6]

Abstract

Phenobarbitone (PB) is the most commonly prescribed anticonvulsant worldwide to control neonatal seizure in asphyxiated neonates. In spite of limited clinical evidence regarding the best use of drug, their dose and duration: it appears that long term maintenance use of phenobarbitone might slow psychomotor development. Aim of this study was to assess the neuro developmental morbidity in asphyxiated neonates with long term anticonvulsant.

This randomized clinical trial enrolled 79 asphyxiated neonates with HIE-II/ III, gestational age ≥ 35 completed weeks from January 2020-January 2021 where cases were categorized into three groups by lottery method. Group A and B received PHB 4mg/kg/day twice daily for 6 weeks and PHB 2mg/kg/day once daily for 2 weeks respectively while Group C didn't receive any anti-seizure medication. Neurodevelopmental assessment was done at 6 months of age in every case. Data were analyzed by Chi-square & logistic regression test to find out the outcome.

Among 79 cases mean gestational age was 37.74±0.98 weeks, M: F was 3:2 and most of them were inborn (51.4%). At 6 months 49 cases were analyzed, 19 were in group A and 15 cases from group B and 15 cases from group C. Cognitive impairment was found 5.844 times more in group A (52.63%) followed by group B (6.67%) and group C (13.33%) (p= 0.001). Group A had 5.844 times more cognitive impairment than other two groups (P= 0.039). No significant functional impairment in motor, speech, hearing and vision were found among the study groups. This study concluded that prolonged use of maintenance Phenobarbitone may impair cognitive function.

Key words: Asphyxiated neonate, Neurodevelopmental outcome, Phenobarbitone

Introduction

Perinatal asphyxia (PNA) remains the major causes of neonatal mortality and morbidity in developing countries. According to WHO 23% of neonatal deaths are due to birth asphyxia and of which approximately 840,000 live numbers develop serious squeal.[1,2]

Phenobarbitone (PB) is the most commonly prescribed first-line anti-seizure drug (ASD) for treatment of neonatal seizures. PB acts on GABA A receptor which enhance inhibition of synaptic transmission and interrupting the spread of epileptic activity.[3] Major mechanisms of PB are modifications of ionic (sodium and calcium) conductance in neuronal membranes.[4] Based on very-low-quality evidence, WHO has recommended phenobarbitone as a first-line ASD in the management guidelines for neonatal seizure.[5] The debate concerning the best drugs, their dose and duration still continues.[6]

The most frequently encountered adverse characteristics of prolonged PB use are slowed motor and psychomotor speed, poorer attention and mild memory impairment. The developmental changes in neuronal chloride gradient leads to depolarization of immature neuron

1. Associate Professor, Dept. of Pediatrics Neurology. Ad-din Women's Medical College Hospital, Dhaka.
2. Assistant Professor, Dept. of Pediatrics, Bashundhara Ad-din Medical College Hospital, Dhaka.
3. Professor and Head, Dept. of Pediatrics, Bashundhara Ad-din Medical College Hospital, Dhaka.
4. Head, Medical Research Unit, Ad-din Women's Medical College
5. Assistant Professor, Pediatric Neurology, National Institute of Neurosciences & Hospital (NINS)
6. Professor and Head, Department of Pediatric Neurology, National Institute of Neurosciences and Hospital

Correspondence: Dr. Dipa Saha, MBBS. FCPS (Pediatrics) FCPS (Pediatric Neurology and Development). Addin Women's Medical College Hospital, E-mail: dipasaha182@gmail.com Cell: 01717337891

Received Date : 20 October, 2023
Accepted Date : 25 November, 2023

after GABA A receptor activation. Thus GABAergic medication (PB) in neonate may cause a paradoxical excitatory response.[7] So the study was done to see the neuro developmental morbidity in asphyxiated neonates with long term use of PB.

Materials and methods

This randomized clinical trial was done in Special care baby unit in Bashundhara Ad-din Medical College hospital from January, 2020 -January, 2021. A total of 95 asphyxiated neonates with HIE-II/ III, gestational age ≥ 35 completed weeks who were admitted in this hospital were included in this study. Among them 16 cases were excluded due to low birth weight (LBW) (5), neonatal jaundice (2), TORCH infection (1), metabolic disorder (1), gross congenital abnormality (2), Referral (3). After exclusion 79 cases were enrolled in this study and randomization was done by lottery method and categorized into three groups. Group A and B received PB 4mg/kg/day twice daily for 6 weeks and PB 2mg/kg/day once daily for 2 weeks respectively while Group C didn't receive any anti-seizure medication after acute management.

Before enrollment, informed consent was taken from parents. Immediate resuscitation was done. Thorough history and physical examination, investigation was done. Any complications during hospital stay were managed accordingly. Follow up was given regarding physical, neurodevelopmental assessment at 6 month. Neurodevelopmental assessment was done according to developmental milestone. Inability to perform age appropriate function beyond the expected age was considered impaired development. Due to loss of follow up (24) and death (6), at 6 months 49 cases were analyzed and 19 were in group A and 15 cases from group B and 15 cases from group C.

Analysis was performed with SPSS software, versions 20.0. Continuous data that were normally distributed was summarized in mean, standard deviation, median, minimum and maximum. Skewed data was presented in the maximum, upper quartile, median, lower quartile, minimum and number of observations. Categorical or discrete data was summarized in frequency counts and percentages. For end points analysis, chi square test was used for categorical variables and an analysis of variance (one-way ANOVA Test) for continuous outcomes. The association of outcomes with treatment was estimated by computing the relative risk (RR) and 95% confidence intervals (CI) and by logistic regression. All p-values are two-sided and values lower than 0·05 were considered statistically significant CONSORT flow chart was used for summarization the number of patients screened, excluded prior to randomization by major reason and overall, thenumber of patients randomized and the number entering and completing each phase of the study. A two-sided P value of less than 0.05 was considered to indicate statistical significance.

Result

Out of the total 95 asphyxiated babies with seizures admitted in our SCBU during the study period, 79 babies fulfilled study criteria. The baseline variables were comparable among the groups. Mean age was 17.36 ± 34.08 hours (0.72.33 ± 1.42 days) and males were predominant among the study cases. Most of them had normal vaginal delivery (NVD) (81.48% in Group A, 80.76% in Group C and 76.92% in Group B) in hospital and had obstructed and prolonged labor and needed immediate resuscitation. Gestational age ranged from 37.58 ± 0.82 to 37.88 ± 1.3 weeks among the groups, mean birth weight was 2.76 ± 0.44 kg, and mean OFC was 33.81 ± 1.85 cm. All study cases had seizure after birth asphyxia (PNA with HIE II). Diminished reflexes was found more in group C (50%) followed by group A (40.74%) and group B (38.46%), there was statistical significance [Table I].

At 6 months 49 cases were analyzed, 19 were in group A and 15 cases from group B and 15 cases from group C. Mean weight (7.10 ± 0.95 kg) and OFC (41.27 ± 2.41 cm) among group B were more than Group A (weight: 6.10 ± 1.07 kg, OFC: 40.22 ± 2.84 cm) and Group C (Weight: 6.48 ± 0.60 kg, OFC: 40.13 ± 1.50 cm) at 6 month but no statistical difference were found among the groups (Figure 1). Cognitive impairment was found more in group A (52.63%) followed by group B (6.67%) and group C (13.33%) (p= 0.001). No significant functional impairment in motor, speech, hearing and vision were found among the study groups [Table II]. When cognitive function was adjusted with other covariant (Age, sex, Place of delivery, Meconium-stained liquor, Gestation age, Birth weight, Number of anticonvulsants used for seizure control) there was 5.844 time more cognitive impairment in group A then group B and C (P = 0.039) [Table III].

CONSORT flow chart

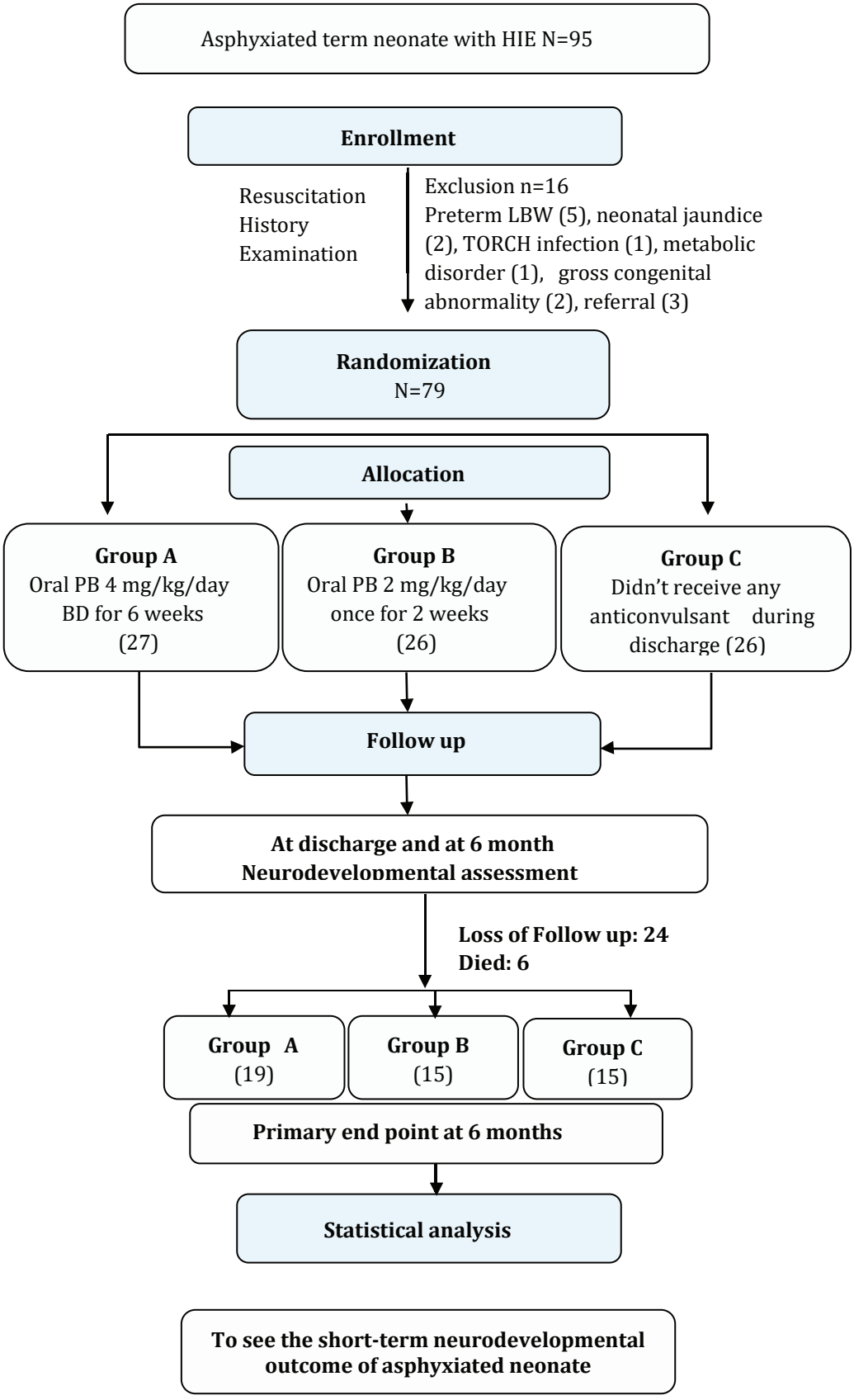


Table-I

Clinico- demographic profile among the study cases (N=79)

Variable	Group A (27)	Group B (26)	Group C (26)	P value
Age (days) mean ± SD	0.96 ± 1.77	0.66 ± 1.2	0.55 ± 1.3	0.586
Sex (M: F)	1.8:1	1.6:1	1.4:1	0.899
Place of delivery n (%)				
Home	12 (44.44%)	11 (42.30%)	6 (23.07%)	0.431
Hospital	15 (55.55%)	15 (57.69%)	20 (76.92%)	
Maternal age (Years)	25.46 ± 4.69	22.70 ± 5.4	23.46 ± 3.9	0.105
Obstructed/prolonged labor n (%)	15 (55.55%)	11 (42.30%)	18 (69.23%)	0.105
Mode of delivery n (%)				
NVD	22 (81.48%)	20 (76.92%)	21(80.76%)	0.876
LUCS	5 (18.51%)	6 (23.07%)	5 (19.23%)	
Meconium-stained liquor	5 (18.51%)	3 (11.53%)	4 (15.38%)	0.807
Needed immediate resuscitation	22 (81.48%)	20 (76.92%)	23 (88.46%)	0.782
Gestational age (Weeks)	37.80 ± 0.49	37.58 ± 0.82	37.88 ± 1.3	0.528
Birth weight (Kg)	2.87 ± 0.45	2.76 ± 0.40	2.66 ± 0.47	0.232
OFC (cm)	34.11 ± 1.99	33.93 ± 1.7	33.4 ± 1.87	0.391
Convulsion	27 (100%)	26 (100%)	26 (100%)	0.108
Diminished reflexes	11 (40.74%)	10 (38.46%)	13 (50%)	0.801

One way ANOVA test

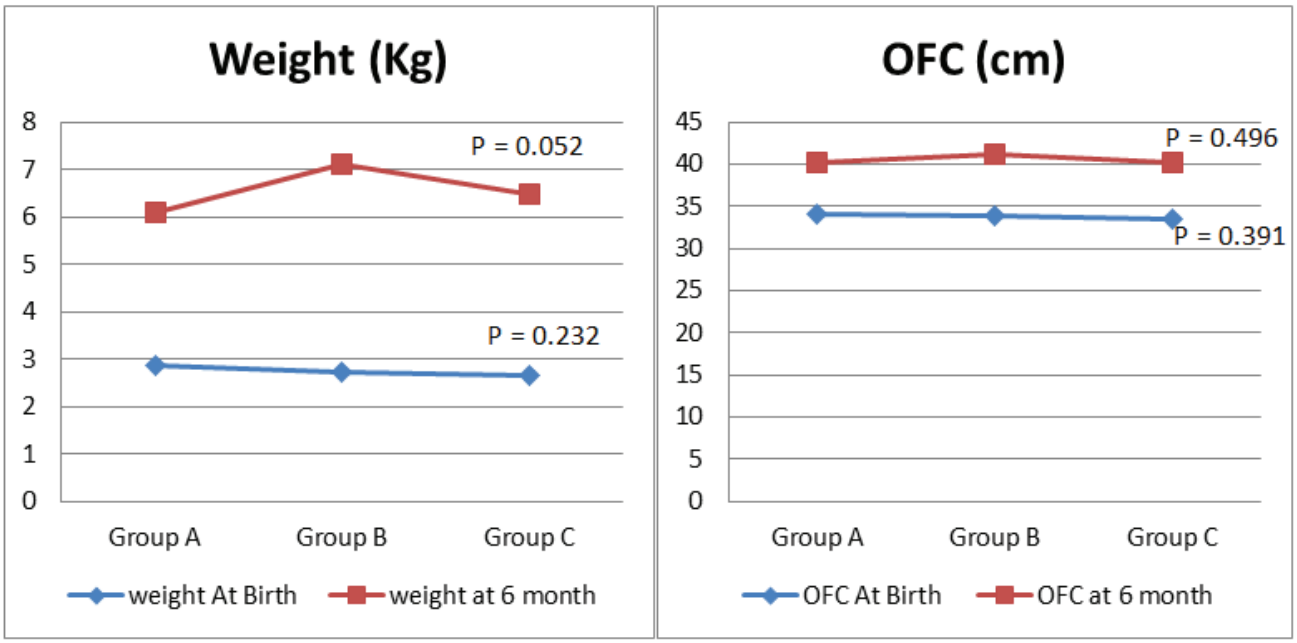


Figure 1: *Physical outcome among the study cases*

Table-II

Neurodevelopmental outcome among the study cases at 6-month n=49

Variable	Group A (19)	Group B (15)	Group C (15)	P value*
Cognitive impairment	10 (52.63%)	1 (6.67%)	2 (13.33%)	0.001
Motor delay	3 (15.78%)	3 (20%)	2 (13.33%)	0.648
Impaired speech	2 (10.52%)	2 (13.33%)	2 (13.33%)	0.955
Visual impairment	2 (10.52%)	1 (6.67%)	2 (13.33%)	0.909
Hearing impairment	2 (10.52%)	1 (6.67%)	1 (6.67%)	0.826

*Chi Square test

Table-III

Prediction of neurodevelopmental outcome in asphyxiated neonates n=49

Variable	Unadjusted OR 95% CI	P Value*	Adjusted OR 95% CI	P value**
Cognitive impairment	3.437(1.25-9.43)	0.001	5.844 (1.09-31.3)	0.039
Motor delay	0.969 (0.187-4.75)	0.64	0.464 (0.55-3.857)	0.301
Impaired speech	0.821 (0.133-5)	0.60	0.323 (0.134-4.6)	0.186
Visual impairment	1.143 (0.17-7.6)	0.62	0.389 (1.144- 3.47)	0.202
Hearing impairment	1.71 (0.217-13.5)	0.495	0.606 90.68-3.840)	0.431
Seizure	2.40 (0.473-12.1)	0.252	0.81(1.15-6.04)	0.231

*Chi square test **Logistic regression

Covariates were analyzed: Age, sex, Place of delivery, Meconium-stained liquor, Gestation age, Birth weight, Number of anticonvulsants used for seizure control

Discussion

To reduce excessive neuronal excitability associated with seizure formation, phenobarbitone reduces membrane excitability, increases postsynaptic inhibition, or changes neural network synchronization. Diminished neural excitability causes slowed motor and psychomotor speed, as well as reduced attention and slight memory impairment.[8,9] Phenobarbitone is effective anticonvulsants, but long-term use can result in clinically significant adverse effects. It can cause hyperactivity, behavioral difficulties, drowsiness, and possibly dementia as a side effect. The reported seizure cessation rates by PB vary between 33% - 40% after giving a single loading dose of 15-20 mg/kg.[10] Gilman, et al. showed rapid sequential loading with PB (up to 40 mg/kg) could improve the clinical response rate in neonates with seizures till a cumulative response rate of 77%.[11] The present study also showed that initial seizure control rate with PB was same as previous study. Maitre et al. in their study showed that increased exposure to PB was associated with significant decreasing cognitive and motor scores. They also concluded that increased exposure to PB is associated with worse neurodevelopmental outcomes.[12] This finding was consistent with present study. We found more cognitive impairment among the group who received PB twice for 6 weeks than who didn't receive PB for longer period. On a variety of developmental parameters and over a wide range of follow-up durations, studies in pediatric

populations demonstrated significant deficits owing to PB exposure after birth.[13]

We assessed all developmental domains. Few studies on pediatric neurology, particularly the effect of long term PB on cognitive function have been conducted globally- as it clearly evidences. On a 20 years literature search we failed to yield any evidence in this spectrum neither in Bangladesh and globally. Hence, it remains crucial to look deep-inside into it to determine its hidden/ unexplored issues- which globally has not been conducted so far.

PB causes neurotoxicity and poor neurodevelopmental outcomes, as has been well documented in animal models. In the developing rat brain, PB therapy at levels comparable to those used to treat seizures in humans has been proven to trigger neuronal death. [14,15] PB has also been shown to interfere with maturation of synaptic connections. [16]

Conclusion:

Significant cognitive functional impairment was found among the asphyxiated neonates who received long term maintenance Phenobarbitone. However large scale, long term follow up study may justify the statement more accurately.

Limitation of this study: It is a single center study, small sample size. We didn't use any psychometric tool for precise assessment of cognitive function.

References

1. Lincetto O. Birth asphyxia summary of the previous meeting and protocol overview. Geneva: World Health Organization. 2007.
2. State of the World's Children, UNICEF; 2009.
3. Stephen F, Amy M. Barbiturates and Primidone. In: JM Pellock, DR Nordli, R Sankar, JW Wheless. Pellock's Pediatric Epilepsy diagnosis and treatment.4t edition. New York: Demos Medical.2017: 745- 766.
4. M Pacifici G. Clinical pharmacology of phenobarbital in neonates: effects, metabolism and pharmacokinetics. Current pediatric reviews.2016; 12: 48-54.
5. Guidelines on Neonatal Seizures. Geneva, World Health Organization, 2011.
6. P Jain, N Sankhyan. Phenobarbital for Neonatal Seizures: A Time for Perusal. Indian Pediatrics.2016; 53: 381-382.
7. RA Shellhaas, HC Glass, T Chang. Neonatal Seizures. In: Swaiman, K.F, Ashwal, S, Ferrier D.M, Schor, N.F, Finkel, R.S, Gropman, A.L, Pearl, P.L. and Shevell, M. Swaiman's Pediatric Neurology: Principles and Practice.6th Edition. Elsevier Health Sciences, 2017: 129-137.
8. Volpe JJ. Neonatal seizures. Neurology of the Newborn, 5th ed. Philadelphia: WB Saunders Elsevier; 2008. P. 203-36
9. Guillet R, Kwon J. Seizure recurrence and developmental disabilities after neonatal seizures: Outcomes are unrelated to use of phenobarbitone prophylaxis. J Child Neurol. 2007;22:389-95.
10. Van Rooij LG, Hellström-Westas L, de Vries LS. Treatment of neonatal seizures. Semin Fetal Neonatal Med. 2013;18: 209-15.
11. Gilman JT, Gal P, Duchowny MS, Weaver RL, Ransom JL. Rapid sequential phenobarbital treatment of neonatal seizures. Pediatrics. 1989;83: 674-8.
12. Maitre NL, Smolinsky C, Slaughter JC, Stark AR. Adverse neurodevelopmental outcomes after exposure to phenobarbital and levetiracetam for the treatment of neonatal seizures. Journal of Perinatology. 2013; 33: 841-6.
13. Ries M. Cognitive effects of "older" anticonvulsants in children with epilepsy: a review and critique of the literature. J Pediatr Pharmacol Ther. 2003 Apr; 8(2):115–31.
14. Bittigau P, Sifringer M, Genz K, Reith E, Pospischil D, Govindarajalu S, et al. Antiepileptic drugs and apoptotic neurodegeneration in the developing brain. Proc Natl Acad Sci USA. 2002 Nov 12; 99:15089–94.
15. Kim J-S, Kondratyev A, Tomita Y, Gale K. Neurodevelopmental Impact of Antiepileptic Drugs and Seizures in the Immature Brain. Epilepsia. 2007 Sep; 48:19–26.
16. Forcelli PA, Janssen MJ, Vicini S, Gale K. Neonatal exposure to antiepileptic drugs disrupts striatal synaptic development. Ann Neurol. 2012 May 11; 72(3):363–72.

Original Article

Prevalence of Generalized Anxiety Disorder among Medical Support Staff during COVID-19 Pandemic

Faisal Ahmed[1], Jannat Ara[2], Rahat Bin Habib[3]

Abstract

Introduction: The pandemic COVID-19 not only caused grievous public health problems but also caused enormous psychological distress, especially among the medical support staff. These mental health issues leading to Generalized Anxiety Disorder (GAD). Ther is a lack of substantial data on psychological effects due to COVID pandemic on Bangladeshi medical health workers. This study aims to provide prevalence of GAD on Bangladeshi health workers

Objective: The study aimed to investigate the prevalence of generalized anxiety disorder among medical support staff (Doctors & Health Care Workers) in some hospitals during the COVID-19 pandemic swept over Bangladesh recruited from Dhaka division. Face-to-face interviews were conducted to obtain Socio-demographic data using a semi structured to learn status of the COVID-19 pandemic in those hospitals and anxiety symptoms among those Docs/HCWS.

Result: In this study of total 289 study populations majority (65.7%) were male and (34.3%) were female. With a mean age of 31.09±8.91 years. Majority of them (64.4%) used to work indoor, while 11.1% worked outdoors, 8.0% in emergency department and 16.6% in critical care unit (OT, ICU and HDU). Out of all those Docs/HCWS 51.2% use to be in direct contact with COVID-19 suspected patients feverish or infected, 48.8% did not. More than half of those Docs/HCWS participated less self-protection against COVID-19 of the (55.4%) Docs/HCWS had a little trust in infection control measures practised by the health care authority and just over half (52.2%) were worried on being infected with COVID-19. Among them, 73.4% lived with their family.

Nearly 2/3rd of the participants or persons they were living with (64.7%), didn't get infected by COVID-19. Among those who looked for COVID-19-related information, 59.6% spent at least 30 minutes daily. The majority of the respondents (58.0%) had minimal anxiety and others had variable levels of generalized anxiety disorder.

Conclusion: Measures should be taken to overcome the obstacles to improve the betterment of the working status and service.

Keywords: COVID-19, Anxiety, Healthcare, Mental health, Support staff, Pandemic

Introduction:

The COVID-19 pandemic placed an unprecedented burden on the healthcare system along with it's medical support staff (Doctor's, Nurse, Lab expert, ICU worker etc.) are facing increased demands for patient care, infection control, and emotional support. Stress and anxiety associated illness among these Health Care Workers facing such challenges can have impaired mental health that can lead to conditions like generalized anxiety disorder (GAD). GAD is a common mental disorder characterized by persistent worries about everyday events if deems excessive.[1] While previous studies have examined the prevalence of GAD among healthcare professionals. However, data on the prevalence of GAD during COVID-19 pandemic lacks, particularly in Bangladesh, Asia and Africa.

Purpose of this study was to evaluate the prevalence of GAD among COVID medical support workers during the COVID-19 pandemic to identify the potential risk factors of those coping strategies.

The COVID-19 pandemic has imposed a lot of stress and anxiety induced psychological disorder particularly in our country among the HCWs. HCWs who played an inevitable role in offering health care emergencies and routine service delivery in such high infectious environment (COVID-19). During that on-going pandemic the HCWs had to deploy a high level of intellect. Generalized anxiety sickness (GAD) is a common mental health problem that impacts humans of all ages and backgrounds. It is characterized by continual and excessive worry about a huge variety of normal occasions and sports.[2]

1. Medical Officer (CS), Civil Surgeon Office, Mymensingh
2. Assistant Surgeon, Dhulasar Union Center, Kalapara, Patuakhali
3. Assistant Professor (Paediatrics), Saheed Sayed Nazrul Islam Medical College & Hospital, Kishoreganj

Correspondence: Dr. Faisal Ahmed, Medical Officer (CS), Address: Room-204, Civil Surgeon Office, Mymensingh Sadar, Mymensingh beside Aat ani Pukur Par Mobile no: 01715458709. Email address: tusher151@gmail.com

Received Date : 10 August, 2023

Accepted Date : 25 September, 2023

Shedding light on mental health impact of the pandemic on healthcare professionals, our research can inform interventions and programs aimed at supporting their well-being.

The incidence of GAD in various stages of COVID-19 pandemic is very essential to evaluate as very few data are found on this issue from Bangladesh. Understanding the significance of GAD amongst clinical guide staff can assist healthcare businesses enhance effective interventions to aid their intellectual fitness and well-being. This study may even contribute to the existing literature on mental health issues amongst healthcare employees during pandemics, which is crucial to develop evidence-based solutions to cope with the intellectual fitness effect of any upcoming pandemics.[3]

Methodology:

This was a cross-sectional study. The study period is estimated to be 6 months from July to December, 2020. The study was conducted at Dhaka Medical College and Hospital (DMCH), Kurmitola General Hospital (KGH), Government Hospital of Kuwait Bangladesh Friendship, and Mugda Medical College and Hospital in Dhaka and Tungipara UHC from Tungipara, Gopalganj.

The study population was purposively selected from the selected area. Total 289 medical support workers (cleaner, security guard, aya, wards boy, etc.) who worked for at least one month in a dedicated department of covid and have not been diagnosed with generalized anxiety disorder were enrolled. The data were collected by face-to-face interview with the respondents during their work at their place of work without interrupting their regular work and with the permission of the authority. Data were recorded in a semi-structured questionnaire. The Generalized Anxiety Disorder-7 was the main data collection tool. Data were checked for consistency, relevance, and quality control and compiled, coded, cleaned, classified, and edited according to objectives and variables through the Statistical Package for Social Sciences (SPSS version 22).

Missing data were checked by frequency runs. Data were analysed using IBM "Statistical Package for the Social Sciences" software (version 22), Microsoft Word, and Microsoft Excel for Windows for data management and analysis. Generalized anxiety disorder was analysed using descriptive statistics and expressed in both numbers and percentages. The prevalence of GAD was measured according to the degree of severity in both numbers and percentages. The analysed data were presented in frequency distribution through suitable tables and graphs. Minimal probable analysis was performed according to the objectives as needed.

Ethical Implication:

- A written consent form in Bengali was used to obtain the respondents' consent, and translated from the original text prepared in English.
- At the beginning of the interview, respondents were informed about all the specific aims of the study, as well as its purpose.
- Respondents were also assured that their data would remain confidential.
- Finally, the risks and benefits of the study were elaborated.
- They were informed that they had the full right to participate in the study and to refuse at any time.
- No treatments or interventions were performed in this study.
- A copy of the written informed consent was provided to all respondents.
- Data were collected only from respondents who volunteered as participants.
- This study was performed in accordance with the guidelines set out in the Protocol of the Declaration of Helsinki.

Results:

Table-I

Socio-demographic characteristics of the respondents (N = 289)

Socio-demographic Characteristics	Frequency (f)	Percentage (%)
Sex		
Female	99	34.3
Male	190	65.7
Age group (in years)		
18 to 25	83	28.7
26 to 35	135	46.7
36 to 45	49	17.0
46 and above	22	7.6
Marital status		
Single	77	26.6
Married	204	70.6
Widowed or divorced	8	2.8
Educational status		
Primary	35	12.1
Junior school	73	25.3
S.S.C.	77	26.6
H.S.C.	76	26.3
Graduation or above	28	9.7

Socio-demographic characteristics of all 289 respondents, reveals male predominance (65.7%) vs. (34.3%) female. The age of the respondents ranged between 18 to 63 years with a mean age 31.09±8.91 years, though majority (46.7%) belonged to 26 to 35 years age group. While majority of the respondents (70.6%) were married, 77 were single (26.6%) and only 8 (2.8%) were widowed &/or divorced, none of those HCWS were illiterate, 12% had primary & 25% Junior School, 52.9% had SSC and HSC and only 9.7% completed graduation or post-graduation.

Table-II

Work-related characteristics of the respondents (N = 289)

Work-related characteristics	Frequency (f)	Percentage (%)
Respondents' profession		
Cleaner	90	31.1
Cook	9	3.1
Security guard	45	15.6
Aya	49	17.0
Ward boy	71	24.6
Others	25	8.7
Current work station		
Indoor	186	64.4
Outdoor	32	11.1
O.T./ICU/HDU	48	16.6
Emergency	23	8.0
Direct contact with feverish or infected patients		
Yes	148	51.2
No	141	48.8

Table II shows, the work-related characteristics of the respondents. 31.1% were cleaner, 24.6% were ward boys, and 15.6% were security guards. 17.0% were aya and the rest of them were cook and others. The majority of them (64.4%) worked indoors. 11.1% worked outdoors, 8.0% worked in emergency and 16.6% of them worked (OT, ICU, HDU). Out of 289 respondents, 51.2% of them required direct contact with feverish or infected patients and 48.8% of them didn't.

Table-III

Social characteristics of the respondents (N = 289)

Social characteristics of the respondents	Frequency (f)	Percentage (%)
Living situation of the respondents in the past 2 weeks		
Family	212	73.4
Friends	14	4.8
Colleague	63	21.8
A person her/himself or persons living with her/him got infected		
No	187	64.7
Yes	102	35.3
Psychological support from social media or news received by respondents		
Not helpful	169	58.5
Helpful	120	41.5

Table III shows, the social characteristics of the respondents. Among them, 73.4% lived with their family. The rest of them resided with their colleagues (21.8%) and friends (4.8%). Nearly two third of the participants or persons they were living with (64.7%), didn't get infected by COVID-19. Just over one-third (35.3%) of medical support staff or persons they were living with got infected. The majority of them (58.5%) found psychological support from social media or news, not helpful at all. Only 41.5% found them helpful. Respondents' average time spent on acquiring information on COVID-19 daily was 21.6 minutes though the majority of them (52.9%) didn't spend any time at all. Among those who looked for COVID-19-related information, 59.6% spent at least 30 minutes daily.

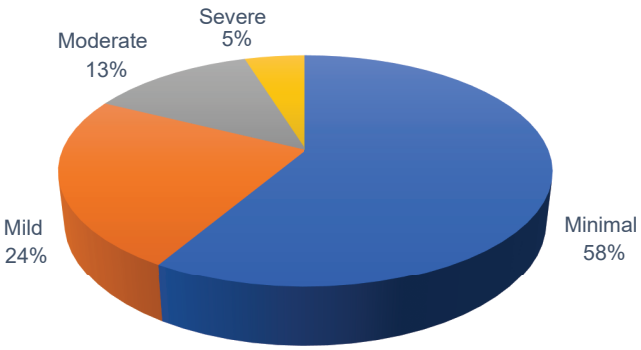


Figure 1: *Distribution of magnitude of generalized anxiety disorder among respondents (N = 289)*

Figure 1 shows the majority of the respondents (58.0%) had minimal anxiety. 24.0% of the medical support staff had mild anxiety, 13.0% had moderate anxiety and only 5.0% had severe anxiety.

Discussion:

This cross-sectional study was conducted during the COVID pandemic in Bangladesh. It was found that all the 289 medical support staff who participated voluntarily in the research were suffering from some sort of generalized anxiety disorder. Psychological interventions in the face of such epidemics are part of the health care system in public health emergencies.[4] We are educated from previous epidemics that recognition and support of the mental health issues of the health care support staff bring out good performance to control and contain the epidemic.[5] We are social by nature and isolation brings down our mental status especially when in medical emergency.[6] In a genuine sense, mental go-betweens are among the foremost basic components driving inveterate infection or declining it.[7] Partitions from family and low-income family units cause different mental well-being issues for tainted people and their family individuals.[8] From a mental viewpoint, COVID-19, as a major scourge, includes the event of mental clutters that are predominant to the patient's capacity to handle.

One of the most common outcomes about of COVID-19 is the mental brokenness of individuals who fear disease or have tainted relatives. Mental brokenness probably happens when an outside life emergency surpasses the individual's passionate reaction and adapting capacity driving to mental disappointment or lopsidedness. Owing to the deadly results of the COVID-19, lives are undermined, and there are more than 20.000 passings on 26 Walk 2020, so it is considered a worldwide well-being crisis.[9]

Governments ought to carefully consider the lessons learned from the episode of COVID-19. There ought to be tall straightforwardness of data to avoid the discharge of rumours, early travel limitations, early isolate methods, and extravagant stores on antibodies and treatment improvement. Governments and open specialists within the tainted nations have executed different control methodologies for the scourge. So also, they would be required at the show and in the close future to actualize mental intercessions for the recouped patients and those individuals who were on the cutting edge, particularly the healthcare workers.[10] Deficiently coordination among therapeutic and mental divisions that display mental mediation administrations speaks to a critical challenge. This needs for participation squanders mental well-being assets and delays the conclusion and follow-up administrations. Other than that, the deficiency of proficient therapists and experienced analysts decreases the adequacy of the mediation. Owing to the strict directions and disease evasion rules, cutting-edge healthcare laborers alone are the central staff who give mental intercession to patients in healing centers. All focus specified is considered fundamental challenges that ruin analysts and therapists in their interest of moving forward regarding mental well-being in tainted people and their families.[11] This study measured the prevalence of generalized anxiety disorder among medical support staff during the COVID-19 pandemic. In this study, it is found that 42.1% of medical support staff are suffering from various degrees of generalized anxiety disorder (GAD 7 ≥ 5) which was consistent with the study in Ethiopia[12] but inconsistent with studies in China[13] and Turkey.[14] The people who work in medicine are helping others while also being at risk of getting sick themselves. Medical staff helped fight COVID-19, even if they didn't have much training. Moreover, when the hospital was suddenly assigned to treat COVID-19 patients, they didn't have enough resources to create separate rooms for isolation. Eventually, the situation got better, but there still wasn't enough staff and resources to properly handle everything. The people who work in healthcare need to wear special clothes that cover their whole body. They have to wear this for 8 to 12 hours and it includes things like a face mask, gloves, hat, shoe covers, and special glasses. They wear these clothes when they work in units where sick people are kept away from others. To stay safe when taking off their protective gear, workers can't eat, drink or use the restroom while they work. A lot of them don't have enough water because they sweat too much, and some get bladder infections and a red, bumpy skin reaction. People who work in places where sick people are kept apart from others should always stay in touch with those who might be sick or infected. In these busy situations, people who help with medical care can feel really tired in their minds and bodies. That's why they may have trouble sleeping because they feel very stressed. People who were very anxious during the COVID-19 pandemic worried about getting sick with the virus. They didn't find much help from social media or the news, but they felt less uncertain about how to control the disease as time went on. People who trust that safety measures at work will protect them are less

worried about the pandemic, according to my research. Medical support staff's worries can make them anxious and affect their ability to sleep well.[15] During and after a disease spread, approximately one out of every six healthcare workers experienced serious stress symptoms.[16] Research has proven that getting ready for a disaster is really crucial. It helps a lot to have well-defined plans, rules, actions, and some practice runs, as these things can greatly affect a person's mental state. When people know what's going on, knowing how the medical staff is getting ready and what their jobs are can help to concentrate on important things and not feel nervous. The crisis caused confusion and changes in how things were done. This caused a lot of people to feel stressed, worried, and sad.[17]

Conclusion

This study was carried out to assess the prevalence of generalized anxiety disorder among medical support staff during covid-19 pandemic at different healthcare facilities in the Dhaka division. All the medical support staff responding to the spread of COVID-19 reported minimal to severe symptoms of generalized anxiety disorder.

Limitations of the Study:

The research was achieved in a limited variety of hospitals; therefore, the effects may not observe in all hospitals. The statistics accumulated become self-stated, which can cause a recall bias. Additionally, individuals with a record of mental disorder have been not excluded, which may bring about a relapse or growth in symptom severity at some stage in the COVID-19 period.

Recommendations:

The findings can help provide specific interventions for generalized anxiety disorder for medical support staff, especially for those who have different social and work-related risk factors.

1. Hospital administration should provide sufficient mental health education and training among medical staff.
2. To understand the problems found among the medical support staff in limited resource facilities, teleconsultation should be incorporated.
3. More studies among large-scale Bangladeshi medical support staff are warranted to confirm the finding of this study.

References:

1. Grey I, Arora T, Sanah A. Generalized Anxiety Mediates the Relationship Between Loneliness and Sleep Quality Amongst Young Adults During the COVID-19 Pandemic. Psychological Reports. 2022 Mar 26:00332941221079723.
2. Skalski SB, Konaszewski K, Büssing A, Surzykiewicz J. Resilience and mental well-being during the COVID-19 pandemic: serial mediation by persistent thinking and anxiety about coronavirus. Frontiers in Psychiatry. 2022 Jan 27;12:2603.
3. Adibi A, Golitaleb M, Farrahi-Ashtiani I, Pirani D, Yousefi K, Jamshidbeigi Y, Sahebi A. The prevalence of generalized anxiety disorder among health care workers during the COVID-19 pandemic: a systematic review and meta-analysis. Frontiers in psychiatry. 2021 May 31;12:658846.
4. Khalaf MA. Psychological consequences of COVID-19 and challenges for post-traumatic interventions. Journal of Psychology Research. 2020 Jan;10(1):24-9.
5. Xiang YT, Yang Y, Li W, Zhang L, Zhang Q, Cheung T, Ng CH. Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed. The Lancet psychiatry. 2020 Mar 1;7(3):228-9.
6. Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, Rubin GJ. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. The lancet. 2020 Mar 14;395(10227): 912-20.
7. Deter HC. Psychosocial interventions for patients with chronic disease. BioPsychoSocial Medicine. 2012 Dec;6:1-5.
8. Kun P, Han S, Chen X, Yao L. Prevalence and risk factors for posttraumatic stress disorder: a cross-sectional study among survivors of the Wenchuan 2008 earthquake in China. Depression and Anxiety. 2009 Dec;26(12):1134-40.
9. Yang Y, Li W, Zhang Q, Zhang L, Cheung T, Xiang YT. Mental health services for older adults in China during the COVID-19 outbreak. The Lancet Psychiatry. 2020 Apr 1;7(4):e19.
10. Sohrabi C, Alsafi Z, O'neill N, Khan M, Kerwan A, Al-Jabir A, Iosifidis C, Agha R. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). International journal of surgery. 2020 Apr 1;76:71-6.

11. Duan L, Zhu G. Psychological interventions for people affected by the COVID-19 epidemic. The Lancet psychiatry. 2020 Apr 1;7(4):300-2.

12. Necho M, Birkie M, Gelaye H, Beyene A, Belete A, Tsehay M. Depression, anxiety symptoms, Insomnia, and coping during the COVID-19 pandemic period among individuals living with disabilities in Ethiopia, 2020. PloS one. 2020 Dec 30;15(12):e0244530.

13. Huang Y, Wang Y, Zeng L, Yang J, Song X, Rao W, Li H, Ning Y, He H, Li T, Wu K. Prevalence and correlation of anxiety, insomnia and somatic symptoms in a Chinese population during the COVID-19 epidemic. Frontiers in psychiatry. 2020 Aug 28;11:568329.

14. Şahin MK, Aker S, Şahin G, Karabekiroğlu A. Prevalence of depression, anxiety, distress and insomnia and related factors in healthcare workers during COVID-19 pandemic in Turkey. Journal of community health. 2020 Dec;45:1168-77.

15. Styra R, Hawryluck L, Robinson S, Kasapinovic S, Fones C, Gold WL. Impact on health care workers employed in high-risk areas during the Toronto SARS outbreak. Journal of psychosomatic research. 2008 Feb 1;64(2):177-83.

16. Lu YC, Shu BC, Chang YY. The mental health of hospital workers dealing with severe acute respiratory syndrome. Psychotherapy and Psychosomatics. 2006;75(6):370-5.

17. Wong EL, Wong SY, Lee N, Cheung A, Griffiths S. Healthcare workers' duty concerns of working in the isolation ward during the novel H1N1 pandemic. Journal of clinical nursing. 2012 May;21(9-10): 1466-75.

Original Article

Fast Food Intake Frequency among Young Generation during COVID-19 Pandemic in Selected Area of Dhaka City

*Sumaiya Nowshin Monisha,[1] Priti Easmin,[2] Mishila Rahaman,[3] Samia Mahbuba,[4] Nila Akter Keya[5]

Abstract

Introduction: Fast food is energy dense food with a high amount of refined sugar, wheat, flour, trans-fat, polyunsaturated fat, salt, numerous additives and low nutrient value in terms of protein, fiber, vitamins and mineral content. The nationwide lockdown due to COVID-19 forced people to stay at home for a prolonged period associated with anxiety, and boredom caused by home confinement influenced to change in lifestyle patterns, reduction diet quality and promote overconsumption.

Objective: The study aimed to observe the frequency of junk food consumption among the young generation (15-25 years old) during the COVID-19 Pandemic and compare the change of before and during COVID-19 situation.

Methods & materials: It was a cross-sectional study conducted in different area of north and south city corporation in Dhaka city focusing on the young generation aged 15-25 years old from September 2020 to April 2021. Total sample size was 315 and the sample was selected randomly following the inclusion and exclusion criteria. The data was collected from the participant through Online Google Form due to of pandemic issue.

Data Analysis: Collected data was coded and analyzed by using SPSS for Windows, version 20 (SPSS Inc., Chicago, IL, USA). The statistical significance of difference between values was assessed by chi-square test. A probability level of 0.05 or less significant.

Result: The study had found out among the 3-age category from 19-22 years preferred fast food more (64.78%) than others during the pandemic period ($p=0.04$). Male were taking fast food more than female. Female had increased fast food consumption 12.35% than before and male had increased 15.27% than before ($p<0.01$). That significantly stated male participants were more influenced by the Pandemic towards fast food. And a significant weight gain (57.14%) was noticed among the 19-22 years age participants, 32.4% male informed to gain weight more than 4kg and 37.4% female1-2 kg during that period. The physical activity level was significantly ($p<0.01$) dropped during the Pandemic both in male and female participants.

Conclusion: The study exposed during pandemics people were taking fast food relentlessly more (13.81%) than normal period. But in spite of attempting to cut down the unhealthy habit of taking fast food, they couldn't make it totally because of their slothful life and being quarantine in a long period in the home.

Keywords: Overweight, Obesity, Pandemic, Adolescence, BMI

Introduction:

Fast food term refers to fast food which are easy to make and quick to consume was first entitled by 1972 by Michael Jacobson, Director of the Centre for Science, Washington D.C.[1] Foods like chips, chocolate, soft drinks etc. are generally taken as fast food.[2]Many Asian countries are undergoing rapid economic and social change, resulting in radical shifts in dietary patterns and lifestyle habits.[3,4] The South East Asia and Western Pacific regions are currently facing an epidemic of diseases associated with obesity diabetes and cardiovascular diseases (CVD).[4,5] India has the highest number of people with diabetes in the world and China occupies the second position.[6] The World Health Organization itself describes an escalating global epidemic of overweight and obesity-'Globesity' taking over many parts of the world.

Traditional dietary patterns are shifting towards western dietary patterns predominantly fast food. Fast food

1. Research Assistant, DiaDem Project, Center for Health Research and Implementation (BADAS-CHRI)
2. Assistant and Nutrition Supervisor, Sonocare
3. Post graduate, Dept. of Food and Nutrition, Govt. College of Applied Human Science
4. Post graduate, Dept. of Food and Nutrition, Govt. College of Applied Human Science
5. Program Officer, Bangladesh Breastfeeding Foundation, Dhaka. Current Research Officer, Medical Research Unit, Ad-Din Women's Medical College Hospital, Dhaka

Correspondence: Sumaiya Nowshin Monisha, Research Assistant, DiaDem Project, Center for Health Research and Implementation (BADAS-CHRI)

Received Date : 02 August, 2023

Accepted Date : 12 August, 2023

contains trans-fat that behaves like saturated fats which clog up the human arteries and cause plaque Contributing to Heart Disease and stroke symptom.[7] Processed meats increase the risk of type 2 diabetes and Coronary Heart Disease (CHD); red meat, high fat dairy as protein sources and sodium content are linked to high risk of CHD[3,4]. There are multifold possible mechanisms for increasing risk of cardio-metabolic outcomes associated with frequent fast-food intake may contribute to central obesity, insulin resistance and elevated blood pressure.[3,4] According to WHO Commission on Ending Childhood Obesity (the ECHO Commission), "There is unequivocal evidence that the marketing of unhealthy foods and sugar- sweetened beverages is related to childhood obesity".[8]

Lower-income countries in Asia represent an unprecedented opportunity to the manufacturers and marketers of ultra-processed foods, fast food and sugar-sweetened beverages. From 2011 to 2016, fast-food sales grew by 113% in India, 83% in Viet Nam.[8] A study in Mangalore India found out of their 300 participants 292(97.3%) were fast food users and 42(14.4%) consumed it every day. The majority of 192(64.36) them were introduced to fast foods through television commercials and 73(57%) developed this habit as they were bored with home made food. Parental consumption of fast foods were found to influence fast food consumption among children (p=0.024). [9]

A Dhaka based study on 10-16 aged school going children revealed that sedentary activities (p = 0.014), eating fast food (0.008) and cakes/biscuits (p = 0.018) were as potential determinants of overweight and obesity in the children and adolescents.[10]

A study in Bangladesh on 27 public and private universities and colleges had found out that among 475 youth, 50.6%, 43.7%, and 53.3% in overweight, pre-obese and obese-1 category whose were consuming fast food at least once in week. The rates of soft drinks consumption (4–6 times/week) were 40.5%, 59.2%, and 73.3% respectively.[11] Besides, obesity epidemic was observed among those who had not the habit of doing physical exercise. This study provides evidence of increasing trend and threat to overweight and obesity for the Bangladeshi youth.[11]

In December 2019, an outbreak of pneumonia in Wuhan City, Hubei Province in China, latterly identified in a new beta coronavirus called SARS-CoV-2.[12] The World Health Organization (WHO) declared the outbreak of the infectious disease COVID-19 (Coronavirus Disease-2019) as a pandemic.[13] To slow down the transmission of the virus, the majority of countries worldwide took strong containment measures with restrictions on daily living such as home confinement, social distancing, and temporary closing of businesses, schools, and universities, and remote working.[14] The Covid-19 has forced most hotels, restaurants and local food shops to shut down. However, Covid- 19 has not prevented people from eating their snacks especially middle -class people have found their alternative way to have those items as frozen foods or ready-to-cook foods. This new indoor food habit of people amid the Covid 19 induced period of staying home has fueled growth in the frozen food business. Different supermarkets and grocery stores in the capital have reported a surge in the demand for frozen foods especially: parata, chicken samosa, puri, chicken spring roll, singara, chicken sausage, chicken nuggets, and French fries.

According to super shop Meena Bazar, the sales of frozen food have increased 25-29% in the Covid-19 pandemic. "There has been a good demand for frozen food sales have increased because most hotels and restaurants are closed," said Shahin Khan, CEO of Meena Bazar. Golden Harvest is the largest producer of frozen food in the country which shares around 22% of the total market. Officials of the company said the demand for processed foods has almost doubled in pandemic times. Md Shahidullah, general manager (marketing) of Golden Harvest, said, "We are not able to produce enough products according to the demand it has increased suddenly because of the Covid-19 pandemic." Pran-RFL has a separate frozen food brand named Jhotpot. Kamruzzan Kamal, director of the marketing department of the company, said sales of frozen foods have increased 50-60%. The present study was conducted to determine the frequency of fast-food intake among the young generation during COVID-19 period and compare than the before pandemic.

Materials & Methods:

Study Place: The study was conducted at different place of north and south city corporation in Dhaka city.

Study Design: The study was cross-sectional.

Study Period: The study was conducted from September, 2020 to April, 2021.

Sample Size: Total sample size was 315.

Sampling Technique: Data was collected by using structured questionnaire that was converted to Online Google Form due to pandemic issue.

Inclusion Criteria:

1. 15 to 25 years aged young people.
2. Those who took junk food during COVID-19 Pandemic
3. Those who had internet access.
4. Those who were willing to participate in this study.

Exclusion Criteria:

1. Below 15 and above 25 years aged people
2. Those who were suffering from different major diseases such as; Hypothyroidism
3. Those who didn't have internet access
4. Those who were not willing to participate in this study.

Ethical Clearance:

Ethical clearance was obtained from Nutrition Foundation of Bangladesh, Bangladesh Breastfeeding Foundation.

Data Analysis Plan:

Collected data was coded and analyzed by using SPSS for Windows, version 16 (SPSS Inc., Chicago, IL, USA). The statistical significance of difference between values was assessed by chi-square test. A probability level of 0.05 or less was considered as significant.

Result:

Table-I

Attributions of study participants

Variables	Values	Frequency (%)
Age category	15-18 years	33 (10.50%)
	19-22 years	198 (62.90%)
	23-25 years	84 (26.70%)
Gender	Female	243 (77%)
	Male	72 (23%)
Participants prefer fast food	264 (83.8%)	
Age specific choice of fast food	15-18 years	29(10.98%)
	19-22 years	171(64.78%)
	23-25 years	64(24.24%)
Participants like soft drinks		224 (71.10%)
Age specific choice of soft drinks	15-18 years	30(13.08%)
	19-22 years	141(63.08%)
	23-25 years	53(23.84%)

Table-1 shows the basic attributes towards fast food according to age and gender of the study participants.

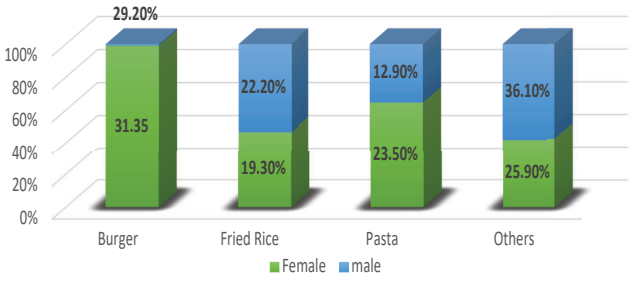


Fig-1: *Status of choice of fast food according to gender*

The figure shows that among all 31.35% female and 29.20 % male liked burger, 19.30% female and 22.20 % male liked fried rice, 23.50% female and 12.90% male liked pasta

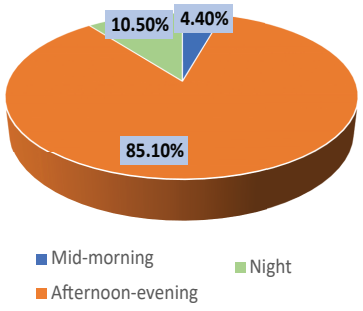


Fig-2: *Usual time of consuming fast food*

The figure shows that $^{4}/_{5}$ (85.10%) of participants usually like to intake fast food in the afternoon-evening period.

Table-II

Comparison of frequency of fast-food and gender before the pandemic

Fast food frequency before the Pandemic	Gender		Total	P value
	Female	Male		
2-3 times	152(62.55%)	42 (58.33%)	186 (59.05%)	
4-5 times	25(10.29%)	11 (15.28%)	37 (11.75%)	0.2
Not eating	66(27.16%)	19 (26.39%)	92 (29.20%)	
Total	243(100%)	72(100%)	315(100%)	

Table-II demonstrates before the pandemic situation 62.55% female and 58.34% male consumed fast food 2-3 times a week, was not significantly (p=0.20) influenced by gender.

Table-III

Comparison of consuming fast food during Pandemic between female & male participants

Fast food taking during the Pandemic	Gender		Total	P value
	Female	Male		
2-3 times	170 (70%)	44(61.12%)	214(67.94%)	<0.001
4-5 times	37 (15.2%)	20 (27.78%)	57 (18.09%)	
Not taking	36 (14.8%)	8 (11.1%)	44 (13.97%)	
Total	243(100%)	72(100%)	315 (100%)	

Table-III demonstrates, during this COVID-19 Pandemic 45.27% female and 33.33% male were taking fast food 2-3 times a week, was significantly influenced by gender.

Table-IV

Fast food consumption rate (before and during) and ordering method

Variables		Frequency (%)
Taking fast food before Pandemic		223 (70.79%)
Fast food intake by gender	Female	177(72.84%)
	Male	53(73.62%)
Taking fast food during Pandemic		271 (86.03%)
Fast food intake by gender	Female	207 (85.19%)
	Male	64 (88.89%)
Making fast food in home		184 (68%)
Ordering fast food in online		119 (43.92%)
COVID affected vs taking fast food		13(4.13%)

Table-IV shows the increased rate of consuming fast food during Pandemic than before according to their gender, ordering method and fast-food intake with COVID-19 affected rate.

Table-V

Weight Change and Physical Activity Level during Pandemic

Weight Change and PAL		Frequency
Weight increases overall		75(23.81%)
Weight increase by gender		
Male	More than 4 kg weight	23 (32.40%)
Female	1-2 kg weight	91 (37.40%)
Weight increase by age	15-18 years	13(9.78%)
	19-22 years	76(57.14%)
	23-25 years	44(33.08%)
PAL by Gender		
Female	Yes	54 (22.20%)
	No	189 (77.80%)
Male	Yes	27 (37.50%)
	No	45 (62.50%)

Table-V shows the level of weight gain and physical activity level (PAL) amid the Pandemic condition in different age group and gender.

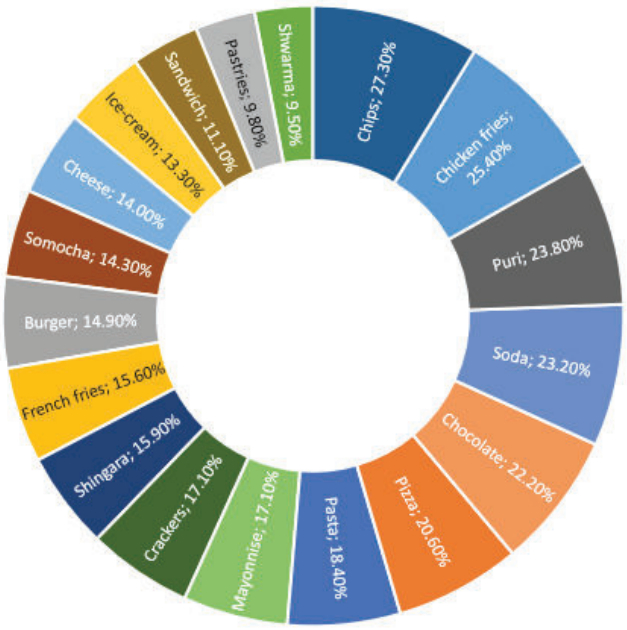


Fig-3: *Distribution of consumption fast food rate during COVID-19 Pandemic*

Discussion:

Among the total 315 participants 62.90% (198) were from 19-22 years aged group and female (77%) were participants predominantly in this study. Out of all 83.8% (264) preferred fast food and most of them (85.10%) were tend to consume it as an evening snack and 71.10% (224) liked soft drinks, burger, fried rice and pasta were the most favorite fast food to them**.** The study had showed instead of cutting down fast food from their diet for better health participants were more frequent towards it; as in male the rate was increased 15.27% and in female 12.35% ($p<0.001$) The findings were similar with a study had been done in India where unhealthy dietary pattern was observed among younger patients compared to older patients ($p = 0.001$) and increased consumption of snacks, fried or processed foods among 24.5% were reported.[15]

This could be happened because of their staying home for a long period which they usually didn't and their monotonous lifestyle at home. Among the 68% (184) were making fast food at home and 43.92% (119) were reported to order from online. There was no significant ($p=0.1$) relation between fast food taking and COVID affectation. The participants who consumed fast food during the Pandemic, 23.81% (75) had weight In the 19-22 years age category the rate of weight was increased higher 57.14% (76) than the other 2 categories and 32.40% (23) male respondents gained more than 4kg weight and 37.40% (91) female respondents were claiming to gain 1-2 kg during this period. The study also showed some similarity with the referenced survey in India. People in India were doing less physical activity during lockdown specially among men, the rate was low likewise in Dhaka City, Bangladesh during lockdown period 62.5% (45) men and 77.80% (189) women were reported to not enact any vigorous activity. The physical

activity level was reduced almost half (41.67%) than before pandemic period specifically among men.

Since individuals with obesity and associated metabolic comorbidities such as diabetes and cardio metabolic disease were more prone to getting COVID-19 infection[16,17] Similar findings were reported by a number of studies showing moderate levels of quarantine induced stress and anxiety in Indian adults with more than 80% adults preoccupied with fearful thoughts of getting coronavirus infection.[18,19] But in spite of attempting to cut down the unhealthy habit of taking fast food, they couldn't make it totally because of their slothful life and being quarantine in a long period in the home. They were increased of consuming pizza 20.60%, chocolate 22.20%, soda 23.20%, puri 23.80%, chicken fry 25.40%, and chips 27.30% more than before the Pandemic that symbolize a study done in North India where CHO consumption increased by 21%, Fat 13%, Frequency of snacking increased by 23%, increased consumption of sugar among 7%. [20]

Conclusion:

Because of the isolation period, avoiding sedentary behaviors or physical inactivity is difficult and, consequently, reduced PA and lower energy expenditure could negatively affect physical and mental health. The change in fast food consuming habit between before and after COVID are not that much significantly notable in female participants but the change is striking among male participants. They were stuck in a lethargic, monotonic life than ever before. Preparing fast food at home, ordering online, and going to a restaurant after lockdown is over symbolizes the obsession towards fast food although there was a worldwide crisis exists

Acknowledgement:

We express our sincere gratitude to Moffashara Sultana Ratna, Assistant Professor, Department of Food & Nutrition for her generous guidance & relentless encouragement through the period of this work.It is a genuine pleasure to express our deep sense of thanks & gratitude to our mentor, philosopher, supervisor Dr. S. K. Roy, Senior Scientist & Chairman, Nutrition Foundation of Bangladesh, his dedication and keen interest above all overwhelming attitude to help his students had been responsible for completing our work, an outmost gratitude to Ms. Khurshid Jahan the director of Bangladesh breast feeding Foundation (BBF) for her spontaneous support, a special thanks to the co-supervisor, Program Officer, Nila Akter Keya (BBF) for helping us unconditionally and we also extent our indebtedness to the Senior Program Officer, Ambrina Ferdaus, (BBF) for her valuable guidance in our dissertation paper.

References:

1. Baskar R, Junk food:impact on health. J Drug Deliv Ther.2012; 2(3):1-7
2. Kaushik JS, Narag M and Parakh A. Fast Food Consumption in children. Indian Pediatrics 2011; 48(2): 97-110.
3. OdegardAO,KohWP,Yaun JM, Gross MD, Pereira MA, Western-style fast food intake and cardiometabolic risk in an Eastern country. Circulation 2012; 126 (2): 182-8.
4. Pan A, Malik VS, Hu FB. Exporting diabetes mellitus to Asia: the impact of western-style fast food. Circulation 2012; 126(2): 163-5.
5. Tabassum A, Rahman T. Differences in consumer attitude towards selective fast food restaurants in Bangladesh: An implication of multiattribute attitude model. World Rev Bus Res 2012; 2(3): 12-27.
6. International Diabetes Federation. Diabetes Atlas. 4th edition. Belgium: International Diabetes Federation, 2009
7. Younis FH, Eljamay SM. Fast Food Consumption among Teenagers aged between (13to 25) years old and Their Effects on Health in Derna-Libya. J RegenBiol Med. 2019; 1(1): 1-8
8. For summaries of existing evidence, see Cairns, G., Angus, K., Hastings, G. and Caraher, M. (2013). 'Systematic reviews of the evidence on the nature, extent and effects of food marketing to children: A retrospective summary', Appetite 62, pp. 209–215; Boyland, E. and Tatlow Golden, M. (2017). 'Exposure, power and impact of food marketing on children: Evidence supports strong restrictions', European Journal of Risk Regulation 8(2), pp. 224–236.
9. Joseph N, Nelliyanil M, Rai S, Y P RB, Kotian SM, Ghosh T, Singh M. Fast Food Consumption Pattern and Its Association with Overweight Among High School Boys in Mangalore City of Southern India. J Clin Diagn Res. 2015 May;9(5):LC13-7.
10. Alam MM, Hawlader MDH, Wahab A, Hossain MD, Nishat SA, Zaman S, Ahsan GU. Determinants of overweight and obesity among urban school-going

children and adolescents: a case-control study in Bangladesh. Int J Adolesc Med Health. 2019 May 9;33(1). doi: 10.1515/ijamh-2018-0034. PMID: 31075080.

11. Muktadir M.H.A., Islam M.A., Amin M.N., Ghosh S., Siddiqui S.A., Debnath D., Islam M.M., Ahmed T., Sultana F., Nutrition transition – Pattern IV: Leads Bangladeshi youth to the increasing prevalence of overweight and obesity,Diabetes & Metabolic Syndrome: Clinical Research & Reviews, Volume 13, Issue 3, 2019, Pages 1943-1947,ISSN 1871-4021,
12. Rabi, F.A.; Al Zoubi, M.S.; Kasasbeh, G.A.; Salameh, D.M.; Al-Nasser, A.D. SARS-CoV-2 and coronavirus disease 2019: What we know so far. Pathogens 2020, 9, 231. [CrossRef] [PubMed]
13. World Health Organization. WHO Director-General's Opening Remarks at the Media Briefing on COVID-19–11 March 2020. Available online: https://www.who.int/dg/speeches/detail/who-director-generals-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
14. Maliszewska, M.; Mattoo, A.; Van Der Mensbrugghe, D. The Potential Impact of COVID-19 on GDP and Trade a Preliminary Assessment; Policy Research Working Paper, No. 9211; The World Bank: Washington, DC, USA, 2020.
15. Rawat D., Dixit V., Gulati S.,Gulati S., Gulati A.,Impact of COVID-19 outbreak on lifestyle behaviour: A review of studies published in India, Diabetes & Metabolic Syndrome: Clinical Research & Reviews, Volume 15, Issue 1, 2021, Pages 331-336, ISSN 1871-4021,
16. Ghosh A., Arora B., Gupta R., Anoop S., Misra A. Effects of nationwide lockdown during COVID-19 epidemic on lifestyle and other medical issues of patients with type 2 diabetes in north India. Diabetes & Metabolic Syndrome. Clin Res Rev. 2020;14(5):917–920.
17. Ranjan P., Kumar A., Chowdhury S., Pandey S., Choudhary A., Bhattacharya A. Clinical Research & Reviews; 2020. Is excess weight a risk factor for the development of COVID 19 infection? A preliminary report from India. Diabetes & Metabolic Syndrome.
18. Rehman U., Shahnawaz M.G., Khan N.H., Kharshiing K.D., Khursheed M., Gupta K. Depression, anxiety and stress among Indians in times of Covid-19 lockdown. Community Ment Health J 2020.
19. Roy D., Tripathy S., Kar S.K., Sharma N., Verma S.K., Kaushal V. Study of knowledge, attitude, anxiety & perceived mental healthcare need in Indian population during COVID-19 pandemic. Asian J Psychiat. 2020;51
20. Ghosh A.,Arora B.,Gupta R., Anoop S.,Misra A., Effects of nationwide lockdown during COVID-19 epidemic on lifestyle and other medical issues of patients with type 2 diabetes in north India, Diabetes & Metabolic Syndrome: Clinical Research & Reviews, Volume 14, Issue 5,2020,Pages 917-920, ISSN 1871-4021

Review Article

An Update Review on Childhood Interstitial Lung Diseases (chILD)

Habib RB[1], Kabir ARML[2]

Abstract

In recent times, we have encountered several cases of Childhood Interstitial Lung Disease (chILD) in our clinical practice in Bangladesh. In developed world, there has been tremendous progress in the approach to chILD, with particular recognition that (chILD) in infants is often distinct from the forms that occur in older children and adults. Confirmation of diagnosis is challenging because of the rarity of Interstitial Lung Disease (ILD) and the fact that the presenting symptoms of ILD often overlap those of common respiratory disorders. There are few case reports and almost no study on chILD in Bangladesh from net search.

A growing part of the etiologic spectrum of chILD is being attributed to molecular defects. The pathogenesis of the various chILD is complex and the diseases share common features of inflammatory and fibrotic changes of the lung parenchyma that impair gas exchanges. We are trying to diagnose chILD by excluding methods of suspected children in our aspects. However, in developed nations, clinical practice guidelines emphasize the role for high resolution computed tomography (HRCT) of chest, genetic testing, and lung biopsy in the diagnostic evaluation. Despite improvements in patient management, the therapeutic strategies are still relying mostly on corticosteroids although specific therapies are emerging. Larger longitudinal cohorts of patients are being gathered through on-going international collaborations to improve disease knowledge and targeted therapies. Thus, it is expected that children with ILD will be able to reach the adulthood transition in a better condition.

Keywords: Review, Childhood, Interstitial Lung Diseases

Introduction

The term 'childhood interstitial lung disease' (chILD) that are associated with significant morbidity and mortality. Historically, these diseases have been defined based on lung biopsy histopathological findings. However, recent advances have facilitated increased non-invasive diagnosis through genetic testing and use of chest computed tomography (CT) scans.

Definition

'Interstitial lung disease' (ILD) is a term that refers to a heterogeneous collection of disorders characterized by abnormal gas exchange because of altered structure of the interstitial region of the lung. As many entities also affect the distal bronchioles and alveolar spaces, the term 'diffuse lung disease' is probably a more accurate description.[1] ILD occurs in a variety of clinical contexts, including isolated pulmonary disorders, because of environmental exposures, and as part of systemic processes, such as autoimmune diseases. Although some of the conditions that cause ILD in children and adults are similar, however distinct forms only seen in infants.

Epidemiology

The prevalence of ILDs in children in Bangladesh is not well-established. ILDs are generally considered rare, and specific epidemiological data are limited. We have found some cases of chILD formar clinical practioner and published than as case report in Bangladesh. Environmental factors, including air pollution (indoor and outdoor), exposure to biomass fuels, and other pollutants, may contribute to the development or progression of ILDs in children in Bangladesh.

It is important to note that the epidemiology of ILDs in children can vary within south east Asia based on

1. Assistant Professor (Paediatrics), Saheed Sayed Nazrul Islam Medical College & Hospital, Kishoreganj, Phone- +88 0191236818, Gmail- ssmcdmc@gmail.com
2. Professor, Department of Paediatrics, Ad-Din Women's Medical College Hospital, Magbazar, Dhaka

Correspondence: Dr. Rahat Bin Habib, Assistant Professor (Paediatrics), Saheed Sayed Nazrul Islam Medical College & Hospital, Kishoreganj, Phone- +88 0191236818. Gmail- ssmcdmc@gmail.com

Received Date : 10 September, 2023

Accepted Date : 20 November, 2023

regional and socioeconomic factors, access to healthcare, and environmental exposures. Due to the rarity of pediatric ILDs, larger-scale studies, collaboration among healthcare professionals, and establishment of dedicated registries can help improve our understanding of the epidemiology and management of ILDs in children in these countries.

Overall, ILD is rare in children. Studies have estimated a prevalence of 3.6 cases per million in the United Kingdom and Ireland[2], and 1.32 cases per million in Germany[3], 4 cases per million in Denmark. There is no data in Bangladesh from net search.

Classification

Children less than 2 years of age often have unique disease processes. Deutsch et al. [4] applied a new classification system to 186 biopsies in children under the age of 2 years from 11 centres as part of the North America Children's Interstitial Lung Disease Research Network.

- **Diffuse developmental disorders**

Disorders in this category occur early in lung development, and diagnosis is via lung biopsy or post-mortem. Alveolar capillary dysplasia associated with misalignment of pulmonary veins (ACDMPV) is a universally fatal disease, with term neonates presenting early in life with rapidly progressive respiratory failure and severe pulmonary hypertension, refractory to intensive therapies[5]. In this disorder, there is inadequate development of the pulmonary capillary bed and malposition of pulmonary veins in the bronchiolovascular bundles adjacent to pulmonary arteries. There are often associated anomalies of the cardiovascular, gastrointestinal, or genitourinary systems. Recently, micro deletions in the FOX gene cluster on 16q24.1 and mutations of FOXF1 have been identified with cases of ACDMPV with different phenotypic associated congenital anomalies.[6]

Pulmonary growth abnormalities

Growth abnormalities are the most common cause of diffuse lung disease in infants. They are usually related to prematurity or pulmonary hypoplasia, but can also be associated with congenital heart disease or chromosomal abnormalities, and, in term infants, with early postnatal lung injury.

Prematurity-associated lung disease is a well-known entity, with the 'new' bronchopulmonary dysplasia consisting of alveolar simplification. Pulmonary hypoplasia, resulting from restricted lung growth in utero, can be acquired because of oligohydramnios, congenital diaphragmatic hernia, hypoxemia, or nutritional deficiencies, among other causes.

In a review of 259 biopsies by Langston and Dishop [7], 11 biopsies fit into the category of congenital heart disease affecting lung growth. Infants with Trisomy 21 (with and without cardiac disease) are known to have simplified alveolar architecture and can be noted to have more severe and earlier pulmonary arterial hypertensive changes. Growth abnormalities in term infants can result from a combination of in-utero and postnatal factors, such as infant of a diabetic mother and infectious insults. Pulmonary vascular disease is a frequent association in this group as well.

- **Surfactant dysfunction disorders**

Mutations in the genes encoding the surfactant proteins B and C (SP-B and SP-C), ATP-binding cassette transporter protein ABCA3, and thyroid transcription factor-1 (TTF-1) have been recognized to cause significant morbidity in infants and children. SP-B deficiency is an autosomal recessive disorder, presents early in life with progressive respiratory distress and failure, and is usually fatal by 3–6 months of age. The typical histopathology is alveolar proteinases with foamy, eosinophilia, lipoproteinaceous material filling alveoli, thickened alveolar septa with alveolar epithelial hyperplasia, and abnormal lamellar bodies on electron microscopy.[8] Other histologic patterns, including infantile DIP, may be seen occasionally. Lung transplant is currently the only therapeutic option for SP-B deficiency.

The presentation of SP-C deficiency is variable, with a large proportion of patients presenting in late infancy/early childhood, although some present in early infancy, and still others are discovered in adulthood. In a recent Dutch study, SP-C mutations accounted for approximately 25% of adult familial pulmonary fibrosis cases.[9] It is an autosomal dominant disorder, but about half of the cases are sporadic with de-novo mutations. Late presentation is associated with symptoms of ILD. The histopathologic picture is of uniform alveolar epithelial hyperplasia with mild alveolar wall thickening with mild lymphocytic inflammation and often masculinization of the alveolar septa, foamy alveolar macrophages, and variable amounts of granular to globular alveolar proteinases with a few cholesterol clefts.[10] Pharmacologic approaches for SP-C deficiency

are based on anecdotal evidence, and include pulse corticosteroids, hydroxychloroquine, and azithromycin. Outcome is variable, as some children with SP-C mutations improve over time,[10] although others progress to end-stage lung disease.[11] Most affected infants present in respiratory failure in the newborn period. Mutations in genes encoding ABCA3 are the most common genetic cause of respiratory failure in full-term infants. Mutations in the TTF-1 (also known as NKX2-1) gene are associated with a syndrome of neurologic (cerebral dysgenesis, chorea, developmental delay), thyroid (hypothyroidism), and pulmonary dysfunction.[12]

- **Pulmonary alveolar proteinases (PAP)**

Pulmonary alveolar proteinases (PAP) is a rare disorder of the lung caused by impaired surfactant homeostasis and characterized by the accumulation of lipoproteinaceous material within the alveolar spaces, resulting in respiratory insufficiency or failure. There are three forms: congenital, primary, and secondary. Primary PAP is an autoimmune disorder and accounts for the majority of cases in adults. Primary PAP is due to high levels of granulocyte/ macrophage-colony stimulating factor (GM-CSF) autoantibodies, resulting in altered surfactant homeostasis and impaired surfactant clearance. GM-CSF is required for pulmonary alveolar macrophage catabolism of surfactant, and also is a critical regulator of innate immunity and lung host defence.[13]

- **Neuroendocrine cell hyperplasia of infancy (NEHI)**

Originally described as persistent tachypnea of infancy, neuroendocrine cell hyperplasia of infancy (NEHI) typically presents in children less than 1 year of age with tachypnea, retractions, hypoxemia, and crackles on examination.[14] The diagnosis is based on the identification of an increased proportion of bombesin-immunopositive neuroendocrine cells in bronchioles, suggested to be at least 10% in any individual airway and to be found in more than 70% of bronchioles in the sample.[7] Lung biopsy otherwise usually has a near-normal appearance. Neuroendocrine cell (NEC) prominence has been shown to be significantly increased in NEHI, as compared with other pulmonary disorders.[15] In their findings, the authors note that the increase in neuroendocrine cells did not correlate with signs of airway injury, suggesting that NEC prominence is not a reparative phenomenon, but is the primary disorder. Characteristic CT findings in NEHI and the presence of normal KL-6, a serum biomarker of type II epithelial cell activation, can help differentiate NEHI from other infant lung disorder entities, such as errors of surfactant metabolism.[16,17] The term 'NEHI syndrome' is used when diagnosis is based on characteristic clinical and CT findings, rather than lung biopsy.

- **Pulmonary interstitial glycogenesis (PIG)**

Although previously described with other names, the entity now known as pulmonary interstitial glycogenesis (PIG) was best detailed in 2002 by Canakis et al.[18] They identified lung biopsies from infants presenting with tachypnea, hypoxemia, and diffuse interstitial infiltrates with a characteristic histology of alveolar septal widening by no inflammatory bland interstitial cells without alveolar epithelial hyperplasia. Periodic acid Schiff-positive material consistent with glycogen was seen irregularly and in minimal amounts in these cells; however, on electron microscopy the interstitial cells contained abundant monoparticulate glycogen. Infants present with respiratory distress in the first weeks of life. Treatment for PIG is largely supportive, and the use of corticosteroid therapy for this condition has been contentious.

Diagnosis

Children with ILD typically manifest nonspecific respiratory signs and symptoms, including tachypnea, hypoxemia, crackles, cough, and poor growth. Because these symptoms overlap those seen in many more common conditions, the first step in diagnostic evaluation is to exclude more common causes of diffuse lung disease (i.e. cystic fibrosis, immunodeficiency, congenital heart disease, pulmonary infection, primary ciliary dyskinesia, and recurrent aspiration). After excluding or treating these more common causes of lung disease, the term 'chILD syndrome' [19] is then used to refer to children who meet three out of four of the following criteria: respiratory symptoms (e.g. cough, rapid and difficult breathing, or exercise intolerance); respiratory signs (e.g. resting tachypnea, adventitious sounds, retractions, digital clubbing, failure to thrive, or respiratory failure); hypoxemia; and diffuse parenchymal abnormalities on chest imaging. The recently published ATS clinical guideline describes the primary diagnostic tools used for the evaluation of chILD: bronchoscopy with bronchoalveolar lavage (BAL), chest CT, genetic testing, and lung biopsy.[20] Not all tests are needed in all cases. Generally, the evaluation proceeds from the least to the most invasive procedures, although the sequence depends on the context, acuity, and severity of the patient's condition.

- **Pulmonary function studies**

Pulmonary function tests (PFTs) done in older children typically demonstrate a restrictive pattern with reduced total lung capacity (TLC), forced vital capacity (FVC), and forced expiratory volume in 1 s (FEV1), with a normal or elevated FEV1/FVC ratio. However, air trapping is suggested by a normal or elevated residual volume, and an elevated residual volume/TLC ratio, resulting in a mixed obstructive/restrictive picture. Infant PFTs can be useful in evaluating paediatric ILD syndromes. The finding that the extent of neuroendocrine cell prominence and severity of small airway obstruction on PFTs are correlated suggests that infant PFTs may aid in the assessment of NEHI. [15]

Pulmonary function testing (PFT) and assessment of oxygenation with sleep and exercise (or feeding in infants) are used to characterize the degree and nature of physiologic impairment. Further, screening for pulmonary hypertension may influence the pace of diagnostic evaluations, alter treatment, and impact prognosis, as pulmonary hypertension associated with ILD predicts higher mortality.[8,21]

Bronchoscopy with bronchoalveolar lavage

This is a common, invasive procedure that is performed to evaluate children with suspected ILD. In addition to enabling evaluation of airway anatomy and physiology, airway and alveolar samples are obtained for cytology and microbiologic diagnosis. Bronchoscopy is relatively well tolerated, widely available, and may help diagnose infection, aspiration, haemorrhage, or pulmonary alveolar proteinases (PAP).

BAL can aid in the diagnosis of specific disease types. In the appropriate clinical setting, the presence of hemosiderin-laden macrophages (diffuse alveolar haemorrhage), lipid-laden macrophages (aspiration syndromes), lymphocytes (hypersensitivity pneumonitis, sarcoidosis), or eosinophil (eosinophilic pneumonia) can help distinguish among disorders, although controversy remains regarding the specificity of some of these alterations. Recent data suggest BAL fluid cytokine levels differ between ChILD syndromes and disease controls [cystic fibrosis (CF), aspiration syndrome, non-CF bronchiectasis], with interleukin (IL)-8 and macrophage inflammatory protein (MIP)-1b found to be significantly lowers.[22] Although lung biopsy remains the gold standard for diagnosis of most of the individual entities that result in ChILD syndrome, this is no longer uniformly the case, as less invasive studies may ascertain diagnosis in some conditions in typical clinical settings.

Imaging studies

Chest CT is very useful for defining the extent and pattern of disease with resolution that is superior to plain chest radiographs. Common findings in chILD may include ground-glass pacification, consolidation, and sepal thickening. Findings may be suggestive of or even specific for some types in cases in which lung biopsy is required, CT imaging will guide the choice of biopsy sites. In infants, anaesthesia or controlled ventilation techniques are often needed to decrease motion artefact and atelectasis that may obscure the detection of lung disease.[23,24] Imaging protocols designed specifically for young children at experienced centres significantly reduce the radiation exposure.[24] The CT sensitivity and specificity for this classic pattern were at least 78 and 100%, respectively. HRCT may also provide prognostic information.

Genetic tests

The availability of clinical genetic testing now allows non-invasive definitive diagnosis in some cases. The currently known genetic causes of chILD include abnormalities in the genes encoding surfactant protein B (SFTPB), surfactant protein C (SFTPC), ATP-binding cassette transporter A-3 (ABCA3), granulocyte- macrophage colony stimulating factor (GM-CSF) receptors a and b (CSFRA and CSFRB), and thyroid transcription factor-1 (NKX2.1/TTF1).[20] The choice of specific genetic tests should be guided by the family history and clinical context. A specific diagnosis provides clinically useful information for the great majority of cases as it informs management, prognosis, and genetic counselling. Currently, only a subset of types of chILD has a defined genetic basis. However, it is likely that additional disease-associated genes will be identified in the future.

Lung biopsy

In the absence of genetic diagnosis, lung biopsy remains the gold standard for diagnosis of many forms of chILD. To optimize the diagnostic yield, standardized protocols have been developed[25], which require timely and effective communication between the clinician, radiologist, and surgeon to select proper biopsy site(s) and process tissue, including fixation in glutaraldehyde for electron microscopy.

Diagnosis of ChILD syndromes A systematic approach, combining history and physical exam, pulmonary function studies, imaging studies, bronchoalveolar lavage (BAL), and lung biopsy, is crucial in establishing the diagnosis.

Discussion

In this systematic review of the literature on chILD we have identified significant gaps in research knowledge in the field. Because chILD is rare there have been few studies of large patient groups and these studies have used different case inclusion/exclusion criteria. The different methods used in the studies included in this review along with the heterogeneity of the chILD group of disorders mean that results are not directly comparable between studies. Notwithstanding these difficulties, this systematic review indicates that:

- # chILD is associated with high morbidity and mortality but there is wide variability between and within chILD disorders
- # No specific treatment is effective for all cases of chILD
- # The impact of chILD on families and the burden on health services has not been evaluated.
- # There is a need to establish surveillance, registries and randomised controlled trials to provide an evidence base to inform prognosis, resource requirements, and treatments.

The diversity of outcomes associated with chILD reflects the wide range of aetiologies and clinical presentations. chILD is commonly associated with severe respiratory deficit that limits physical activity, may impede physical growth, and necessitates respiratory support, usually oxygen supplementation. It is possible that the morbidity in this review is skewed towards more severe cases because mild cases are less likely to be identified in hospital record reviews. In some studies only children who had a lung biopsy were included, implying a sample skewed towards severe disease. Not all cases of chILD require lung biopsy for diagnosis. For example, NEHI can be diagnosed from chest computed tomography and pulmonary function test findings consistent with air trapping and obstruction, without the need for a lung biopsy.[26,27] Furthermore, genetic diagnosis has helped avoid the need for lung biopsy in children with inherited surfactant disorders. Prospective, cohort studies including well phenotype groups would give a more accurate picture of the morbidity associated with chILD.

At 13%, childhood mortality associated with chILD is high, but varies considerably both between and within chILD disorders. Age of disease onset may contribute to outcome, worse outcomes being associated with earlier onset of disease.[28] Among inherited surfactant disorders the type of mutation will influence outcome. In 2014, a review of 185 cases of chILD or neonatal respiratory failure associated with homozygous or compound heterozygous ABCA3 mutations was published.[29] That study found that by 1 year of age all children (n ¼ 45) with two ABCA3 mutations likely to result in non-functional proteins ("null" mutations) had died or undergone lung transplantation compared with 62% of children with nonnull ABCA3 mutations that did not reliably predict prognosis. chILD inherited surfactant disorders are associated with high morbidity and mortality but for most of these disorders there is considerable heterogeneity in the severity of disease.

Among studies in our review that reported outcomes, the duration of follow-up varied or was not reported, restricting comparisons between studies. Furthermore, no study has reported outcomes beyond 6 years follow-up. In many studies[25,30-32] definitions of outcomes were limited to imprecise descriptions such as "improved" or "stable" making them difficult to interpret.

Since each individual chILD disorder is rare, and therefore rarely encountered by paediatricians, diagnosis may be difficult. Diagnostic delay may have a negative impact on outcome, especially in chILD disorders that progress rapidly, although we did not find evidence for this. Only two studies [34,35] reported the time taken to determine a diagnosis but neither study analysed the association between time to diagnosis and outcome.

The evidence base for chILD treatments is limited because the disorders are so rare and there have been no clinical trials. The general principle of treatment is that minimising inflammation may prevent progression to fibrosis.[36] Corticosteroids and hydroxychloroquine are widely used in the treatment of chILD, not always with success. Both have anti-inflammatory properties but they also may have other effects, for example hydroxychloroquine may inhibit the intracellular processing of the precursor protein of surfactant protein C.[37]As chILD disorders are generally incurable, supportive care (nutritional supplementation, influenza vaccination, oxygen supplementation) is important.[38] chILD disorders have a diverse range of aetiologies and

pulmonary pathologies, thus a common treatment strategy is unlikely to be effective for all chILD disorders. Current treatments are not based on rigorous scientific evidence but on the experience of individual health professionals and the preferences of individual centres. There is an impetus to standardise treatment, follow-up, and collection of biological samples in observational studies with a view to providing evidence to support the first randomised controlled trial of treatment for chILD. It is hoped that the establishment of the United States chILD Research Network (ChILDRN) [39] and a recent $3.0 million European FP7 grant [40] will help to achieve that aim.

The impact of chILD on families and the burden on health services has not been studied. Bronchopulmonary dysplasia, a diffuse lung disease[28] that is usually associated with prematurity [40] and is not a chILD disorder[41] has been studied in this context.[42,43] These studies give an indication of the health services burdens and costs that might be expect for chILD. The median length of the first hospital stay for children with bronchopulmonary dysplasia was 120 days, at a median cost of US $172,717.[42] An analysis of health services use and costs for a single case of chILD due to surfactant protein C deficiency showed 443 days of in-patient care at a cost of AUS $966,531. Families caring for children with bronchopulmonary dysplasia incur loss of wages, loss of jobs, and emotional stress associated with caring for their child.[42,43] From what is known about the chronic morbidity of chILD it is likely that there is a high impacton families. This remains to be demonstrated through rigorous study.

The classification and nomenclature of chILD has rapidly evolved over recent years as underlying genetic causes and new diseases such as NEHI[44] have been identified. The changes in nomenclature and classification causes confusion amongst clinicians who rarely encounter these conditions.[45]

Recent American Thoracic Society clinical practice guidelines for child[41] highlight that the term "interstitial" is confusing in children who present with the clinical features of chILD but with the histopathological process occurring outside the intersititium. The guidelines proposed that the term "diffuse lung disease" encompass specific chILD diagnoses, as a subset of "chILD syndrome". chILD syndrome includes cases that remain unclassified. Classification is also hampered by the use of similar terms for different entities such as infantile cellular interstitial pneumonitis and chronic pneumonitis of infancy.[28]

These changes in classification schemes are also a potential limitation of this review as some relevant papers may not have been included due to different diagnostic labels being used inconsistently. Furthermore, some of the studies in this review have included diseases that do not fit into the current classification for chILD.

Despite their limitations, the current chILD classification systems serve the important function of distinguishing these disorders from ILD more commonly seen in adulthood. It is likely that the classification of chILD will continue to evolve over the next few years and systematic terminology will be an important step forward. The inadequacy of ICD codes for the classification of rare diseases such as chILD is also an impediment to research. There are initiatives by Orphaned to assign specific codes (Orpha Codes) to individual rare disorders.[46] These would complement ICD codes and, if adopted by clinicians and researchers, would aid in data pooling to improve statistical power and meta-analysis.

Treatment

Management is largely supportive, including supplemental oxygen and ventilator support, nutritional support, proper immunizations, and avoidance of harmful environmental exposures. Lung transplantation is an option for children with end-stage lung disease.[49] Genetic counseling and family support are also important components of care. Treatment is directed to the specific disorder. Corticosteroids remain the first-line therapy for a number of these disorders, including the surfactant dysfunction disorders, idiopathic interstitial pneumonias, hypersensitivity pneumonia, eosinophilia pneumonia, alveolar haemorrhage, and connective tissue diseases. We recommend the use of intravenous pulse steroids, given as 10– 30 mg/kg with a maximum of 1 g once weekly or on three consecutive days monthly instead of daily steroids, as this appears to be associated with fewer side-effects, though no controlled trials exist. Steroid-sparing agents with anti-inflammatory properties, such as hydroxychloroquine, azathioprine, methotrexate, cyclophosphamide, and intravenous immunoglobulin, have also been used with some success.[47] This is based on anecdotal evidence, as there have been no randomized controlled trials in children with ILD. Lung transplantation is an option for children

with end stage diffuse lung disease, with long-term outcomes that appear to be comparable to those with CF and pulmonary hypertension.[48]

Conclusion

In conclusion, the disorders that together constitute the group of diseases known as chILD are extremely heterogeneous and associated with high morbidity and mortality. Prospective, active surveillance of chILD through strategic international collaboration is needed to provide more accurate estimates of frequency. It is important that a single classification system for chILD is adopted globally to support direct comparisons of research evidence. Patient registries and randomised controlled intervention trials through international collaboration are required to provide an evidence based for improving the lives of children with these rare disorders. An increasing proportion of cases are now diagnosed without lung biopsy through the use of chest CT imaging patterns and genetic testing. Obtaining a specific diagnosis often has important implications in patient management and prognosis, as well as for genetic counselling. For health services planning and to support families, the impacts of chILD should be addressed in prospective studies.

References

1. Deutsch GH, Young LR, Deterding RR, et al. Diffuse lung disease in young children: application of a novel classification scheme. Am J Respir Crit Care Med 2007; 176:1120–1128.
2. Dinwiddie R, Sharief N, Crawford O. Idiopathic interstitial pneumonitis in children: a national survey in the United Kingdom and Ireland. Pediatr Pulmonol 2002; 34:23–29.
3. Griese M, Haug M, Brasch F, et al. Incidence and classification of pediatric diffuse parenchymal lung diseases in Germany. Orphanet J Rare Dis 2009; 4:26
4. Deutsch GH, Young LR, Deterding RR, et al., Pathology Cooperative Group: ChILD Research Co-operative. Diffuse lung disease in young children: application of a novel classification scheme. Am J Respir Crit Care Med 2007; 176:1120–1128.
5. Sen P, Thakur N, Stockton DW, et al. Expanding the phenotype of alveolar capillary dysplasia (ACD). J Pediatr 2004; 145:646–651.
6. Stankiewicz P, Sen P, Bhatt SS, et al. Genomic and genetic deletions of the FOX gene cluster on 16q24.1 and inactivating mutations of FOXF1 cause alveolar capillary dysplasia and other malformations. Am J Hum Genet 2009; 84:780–791.
7. Langston C, Dishop M. Diffuse lung disease in infancy: a proposed classification applied to 259 diagnostic biopsies. Pediatr Dev Pathol 2009; 12:421–437.
8. Wert SE, Whitsett JA, Nogee LM. Genetic disorders of surfactant dysfunction. Pediatr Dev Pathol 2009; 12:253–274.
9. Van Moorsel CHM, van Oosterhout MFM, Barlo NP, et al. Surfactant protein C mutations are the basis of a significant portion of adult familial pulmonary fibrosis in a Dutch cohort. Am J Respir Crit Care Med 2010; 182:1419– 1425.
10. Gower WA, Popler J, Hamvas A, et al. Clinical improvement in infants with ILD due to mutations in the surfactant protein C gene (SFTPC). Am J Respir Crit Care Med 2010; 181:A6733.
11. Glasser SW, Hardie WD, Hagood JS. Pathogenesis of interstitial lung disease in children and adults. Pediatr Allerg Immunol Pulmonol 2010; 23:9–14.
12. Krude H, Schutz B, Biebermann H, et al. Choreoathetosis, hypothyroidism, and pulmonary alterations due to human NKX2-1 haploinsufficiency. J Clin Invest 2002; 109:475–480.
13. Martinez-Moczygemba M, Huston DP. Immune dysregulation in the pathogenesis of pulmonary alveolar proteinosis. Curr Allergy Asthma Rep 2010; 10:320–325.
14. Deterding RR, Pye C, Fan LL, Langston C. Persistent tachypnea of infancy is associated with neuroendocrine cell hyperplasia. Pediatr Pulmonol 2005; 40:157–165.
15. Young LR, Brody AS, Inge TH, et al. Neuroendocrine cell distribution and frequency distinguish neuroendocrine cell hyperplasia of infancy from other pulmonary disorders. Chest 2010.
16. Brody AS, Guillerman RP, Hay TC, et al. Neuroendocrine cell hyperplasia of infancy: diagnosis with high-resolution CT. AJR Am J Roentgenol 2010; 194:238–244.
17. Doan ML, Elidemir O, Dishop MK, et al. Serum KL-6

differentiates neuroendocrine cell hyperplasia of infancy from the inborn errors of surfactant metabolism. Thorax 2009; 64:677–681.

18. Brody AS, Guillerman RP, Hay TC, et al. Neuroendocrine cell hyperplasia of infancy: diagnosis with high-resolution CT. AJR Am J Roentgenol 2010; 194:238–244.
19. Fan LL, Deterding RR, Langston C. Pediatric interstitial lung disease revisited. Pediatr Pulmonol 2004; 38:369–378.
20. Kurland G, Deterding RR, Hagood JS, et al. An official American Thoracic Society clinical practice guideline: classification, evaluation, and management of childhood interstitial lung disease in infancy. Am J Respir Crit Care Med 2013; 188:376–394.
21. Dinwiddie R, Sharief N, Crawford O. Idiopathic interstitial pneumonitis in children: a national survey in the United Kingdom and Ireland. Pediatr Pulmonol 2002; 34:23–29.
22. Popler J, Wagner BD, Accurso F, Deterding RR. Airway cytokine profiles in children's interstitial lung diseases. Am J Respir Crit Care Med 2010; 181:A3316.
23. Long FR, Castile RG, Brody AS, et al. Lungs in infants and young children: improved thin-section CT with a noninvasive controlled-ventilation technique – initial experience. Radiology 1999; 212:588–593.
24. Frush DP. Pediatric CT: practical approach to diminish the radiation dose. Pediatr Radiol 2002; 32:714–717; discussion 751–754.
25. Langston C, Patterson K, Dishop MK, et al. A protocol for the handling of tissue obtained by operative lung biopsy: recommendations of the chILD pathology co-operative group. Pediatr Dev Pathol 2006; 9:173–180.
26. Kerby GS, Wagner BD, Popler J, Hay TC, Kopecky C, Wilcox SL, Quinones RR, Giller RH, Accurso FJ, Deterding RR. Abnormal infant pulmonary function in young children with neuroendocrine cell hyperplasia of infancy. Pediatr Pulmonol 2013;48:1008–1015.
27. Brody AS, Guillerman RP, Hay TC, Wagner BD, Young LR, Deutsch GH, Fan LL, Deterding RR. Neuroendocrine cell hyperplasia of infancy: diagnosis with high-resolution CT. Am J Roentgenology 2010;194:238–244.
28. Deutsch GH, Young LR, Deterding RR, Fan LL, Dell SD, Bean JA, Brody AS, Nogee LM, Trapnell BC, Langston C. et al. Diffuse lung disease in young children: application of a novel classification scheme. Am J Respir Crit Care Med 2007;176:1120–1128.
29. Wambach JA, Casey AM, Fishman MP, Wegner DJ, Wert SE, Cole FS, Hamvas A, Nogee LM. Genotype-phenotype correlations for infants and children with ABCA3 deficiency. Am J Respir Crit Care Med 2014;189:1538–1543
30. Krude H, Schutz B, Biebermann H, et al. Choreoathetosis, hypothyroidism, and pulmonary alterations due to human NKX2-1 J Clin Invest 2002; 109:475–480.
31. Shulenin S, Nogee LM, Annilo T, et al. ABCA3 gene mutations in newborns with fatal surfactant deficiency. N Engl J Med 2004; 350:1296–1303
32. Brasch F, Schimanski S, Muhlfeld C, et al. Alteration of the pulmonary surfactant system in full-term infants with hereditary ABCA3 deficiency. Am J Respir Crit Care Med 2006; 174:571–580
33. Agrawal A, Hamvas A, Cole FS, et al. An intronic ABCA3 mutation that is responsible for respiratory disease. Pediatr Res 2012; 71:633–637.
34. Griese M, Haug M, Brasch F, Freihorst A, Lohse P, von Kries R, Zimmermann T, Hartl D. Incidence and classification of pediatric diffuse parenchymal lung diseases in Germany. Orphanet J Rare Dis 2009;4:26
35. Nathan N, Taam RA, Epaud R, Delacourt C, Deschildre A, Reix P, Chiron R, de Pontbriand U, Brouard J, Fayon M, et al. A national internet-linked based database for pediatric interstitial lung diseases: the French network. Orphanet J Rare Dis 2012;7:40
36. Beers MF Inhibtion of cellular processing of surfactant protein C by drugs affecting intracellular pH gradients. J Biol Chem 1996;271: 14361–14370. 14. Vece TJ, Fan LL. Diagnosis and management of diffuse lung disease in children. Paediatr Respir Rev 2011;12:238–242.
37. Vece TJ, Fan LL. Diagnosis and management of diffuse lung disease in children. Paediatr Respir Rev 2011;12:238–242.
38. Bush A, Anthony G, Barbato A, Cunningham S,

Clement A, Epaud R, Gilbert C, Goldbeck L, Kronfeld K, Nicholson AG, et al. on behalf of the ch-ILD collaborators. Research in progress: Put the orphanage out of business. Thorax 2013;68:971-973.

39. chILD Research Network. Norman (OK): Childrens Interstitial and Diffuse Lung Disease www. childfoundation. com/research/child- research-network/.

40. Coalson JJ. Pathology of new bronchopulmonary dysplasia. Semin Neonat 2003;8:73–81.

41. Kurland G, Deterding RR, Hagood JS, Young LR, Brody AS, Castile RG, Dell S, Fan LL, Hamvas A, Hillman BC, et al. An official american thoracic society clinical practice guideline: classification, evaluation, and management of childhood interstitial lung disease in infancy. Am J Respir Crit Care Med 2013;188:376–394.

42. McAleese KA, KnappMA, Rhodes TT. Financial and emotional cost of bronchopulmonary dysplasia. Clin Pediatr 1993;32:393–400.

43. Miller VL, Rice JC, DeVoe M, Fos PJ. An analysis of program and family costs of case managed care for technology-dependent infants with broncho-pulmonary dysplasia. J Pediatr Nurs 1998; 13:244–251.

44. Deterding RR, Pye C, Fan LL, Langston C. Persistent tachypnea of infancy is associated with neuro-endocrine cell hyperplasia. Pediatr Pulmonol 2005;40:157–165.

45. Nicholson AG, Bush A. Classification of diffuse lung disease in infants: the reality of groups. Am J Respir Crit Care Med 2007;176:1060–1061.

46. Orphanet Report Series: List of rare diseases and synonyms. www.orpha.net/orphacom /cahiers n/docs/GB/List_of_rare_diseases_ in_alphabetical_ order

47. Lenney W, Boner AL, Bont L, et al. Medicines used in respiratory diseases only seen in children. Eur Respir J 2009; 34:531–551.

48. Rama JA, Fan LL, Faro A, et al. Long term outcomes of pediatric lung transplantation for interstitial lung disease. Am J Respir Crit Care Med 2009; 179:A4596

49. Rama JA, Fan LL, Faro A, et al. Lung transplantation for childhood diffuse lung disease. Pediatr Pulmonol 2013; 48:490–496.

Review Article

Understanding the Hereditary Factors in Cancer-Recent Insights and Developments: An Updated Review

Waseka Nowshin[1, 2]

Abstract

Background: Although cancer (Ca) etiology can be multifactorial, it is nearly universally intertwined with genetic mutations that instigate tumor genesis or progression. This updated review aims at describing if this dispute remains meaningful based on a thorough literature survey.

Methodology: This updated review was conducted over the last 2.5 decades using 3 (three) search engines: Web of Science (WoS), Pubmed and Science direct that encompassed all associated information and hypothetical considerations, globally, utilizing information from 1998 through 2022. All such, concepts, logically deducted explanations and scientifically assumed points if Ca remains hereditary is the main focus of this review.

Results/ Findings: This appraisal on cancer, though yielded some instances of hereditariness in origin, mostly remains of genetic origin. Reportedly, cancers can be passed down from one family member to another through genes, and, may cause by genetic mutation present in eggs or sperms cell during fertilization which are actually considered as hereditary cancer, like breast, colon, and prostate cancer, as well as less common cancers, viz., pancreatic and ovarian cancer.

Therefore, understanding the hereditary factors of Ca is critical not only for assessing the genetic contribution to cancer, but also for designing preventive and therapeutic strategies. It allows identifying people who are at a higher risk due to family history and/or genetic makeup, allow early detection through improved surveillance and, more importantly, for tailored therapeutic modality. By addressing recent advancement, this review will provide an overview on the hereditary factors of cancers and/or raising awareness on significant role of development in Ca genetics.

Keywords: Cancer, BRCA1, BRCA2; Genetic factors; Hereditariness; Public health.

Introduction

Cancer is a complex disease marked by the uncontrolled spread of abnormal cells, which can infiltrate nearby tissues and potentially metastasize to other parts of the body.[1] According to world health organization (WHO) fact sheets, Ca is the second leading cause of death globally,[2] accounting for an estimated 9.96 million deaths, or 1 in 6 deaths, in 2020.[3,4]

The loss of life years is not only causing harm and damages to the society but also poses economic consequences. As an example, productivity losses linked to premature Ca deaths were estimated at €104·6 billion or 0·62% of the national gross domestic product in Europe,[5] and at US$46·3 billion or 0·33% of the combined gross domestic product of the BRICS countries (Brazil, Russia, India, China, and South Africa).[6]

Cancer encompasses a diverse group of malignancies, with common types distinguished by their origin and affected organs such as female breast cancer, lung cancer, colorectal cancer, prostate cancer, stomach cancer, liver cancer, etc. According to Global Cancer Statistics 2020,[4] female breast Ca stands as the most frequently identified cancer, constituting 11.7% of the total cases, closely followed by lung Ca at 11.4%, colorectal Ca at 10.0%, prostate Ca at 7.3%, and stomach Ca at 5.6%.

While female breast Ca stands as the most frequently identified cancer types, lung Cancer on the other hand is regarded as the leading contributor to cancer-related fatalities globally, accounting for 18.0% of total Ca deaths including man and women, followed by colorectal Ca at 9.4%, liver Ca at 8.3%, stomach Ca at 7.7%, and female breast Ca at 6.9%.[4]

Correspondence: [1]Medical Research Unit, Ad-din Women's Medical College (AWMC), 2, Bara Moghbazar, Dhaka-1217, Bangladesh & [2]Bangamata National Cellular and Molecular Research Center (BNCMRC), Bangladesh Medical Research Council (BMRC), Dhaka-1212, Bangladesh E-mail address:waseke2810 @gmail.com

Received Date : 02 August, 2023

Accepted Date : 10 November, 2023

The development of Ca in human body can be influenced by a range of factors, including but not limited to genetics,[7,8] lifestyle choices,[9] and environmental exposures.[10] Considering various factors leading to cancer, 22% of cases result from tobacco use, while 10% stem from factors like an unhealthy diet, obesity, insufficient physical activity, excessive alcohol consumption, and other contributors, including exposure to ionizing radiation, environmental pollutants, and infections.[11]

Infections such as hepatitis B, hepatitis C, human papillomavirus (HPV), helicobacter pylori, immuno-deficiency virus (HIV), and Epstein-Barr virus are responsible for around 15% of all Ca cases worldwide.[4] In general, about 90% of the cancers are caused by above factors. Along with that, at least 5-10% of Ca cases are caused by inherited genetic mutations Ca also known as hereditary Cancer.[12] Based on causes of cancer, these cases can be divided into three categories such as, sporadic, familial, and hereditary. Figure 1 depicts the distribution of cancer categories.

Sporadic cancers are the cancers occurs by chance or due to environmental and lifestyle factors. Familial cancers and hereditary cancers are distinct from one another. The term "familial cancer" accounts for 15-20% of all cancer cases refers to a situation in which more members of a specific family are diagnosed with a particular type of Ca than would be statistically predicted, but it is unknown why this is the case;[13,14] hereditary and lifestyle factors may individually or jointly contribute to the high incidence in the family.[15]

On the other hand, familial tumors with a known genetic basis or genetic mutations are referred to as having "inherited cancer".[16] These mutations confer an increased susceptibility to specific Ca types and are typically inherited from one's parents. Hereditary Ca syndromes often manifest as autosomal dominant inheritance patterns, meaning that a single mutated allele is sufficient to confer an elevated Cancer risk.[17]

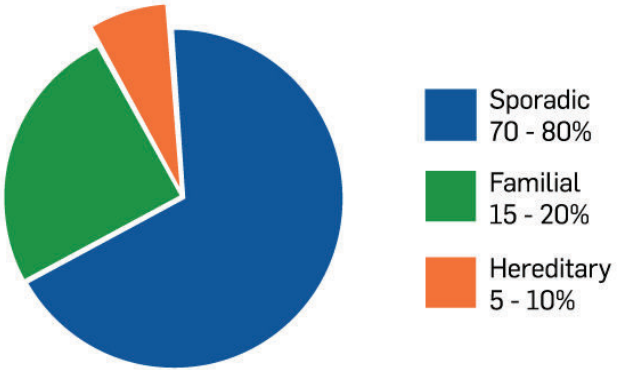


Figure 1: *Distribution of cancer categories.*

The genetic mutations underlying hereditary Ca syndromes typically involve critical tumor suppressor genes or oncogenes, which perturb cellular homeostasis and regulatory mechanisms, thus fostering carcinogenesis.

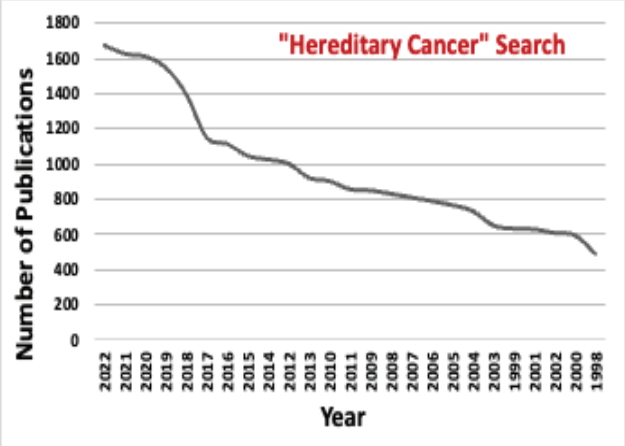


Figure 2: *Record of growing interest among scientific community regarding the hereditary factors in cancer. (source: Web of Science data based)*

Recently, there has been a growing interest among the scientific community regarding the hereditary factor in Ca as presented in Figure 2 (searched under the keyword “hereditary cancer”). According to the past 25 years of publication statistics, the number of publications related to understanding the hereditary factors, treatment, remedies has increased in ever year, showing the importance of this factor for Ca and interest towards its understanding.

However, the accumulation of the knowledge available in various research based on recent insight may play key role on the understanding of the hereditary factors in Ca among the young researchers. To the best of our knowledge, the accumulated knowledge addressing the recent insight is missing, hence this study focused on the understanding of the basics of hereditary factors in Ca including the molecular mechanisms, global perspective, well-known genetic mutations that passes on to children from the parents and the hereditary factor on different common Ca types.

This study and the topic are particularly important as it provides education for healthcare professionals, enabling individuals to make informed health choices and equipping medical practitioners to deliver superior care. On a global scale, it will contribute to the public health strategies, addressing genetic mutations and their implications in hereditary Ca among diverse populations.

Table-I

Syndromes of inherited Ca predisposition in clinical oncology syndrome

	Component Tumors	Inheritance Mode	Genes
Hereditary breast cancer syndromes			
Hereditary breast cancer and ovarian cancer Syndrome	Breast cancer	Dominant	BRCA1 BRCA2
	Ovarian cancer		
	Prostate cancer		
	Pancreatic cancer		
	Fanconi anemia/medulloblastoma	Recessive	BRCA2
Li-Fraumeni Syndrome	Soft tissue sarcoma	Dominant	P53 CHEK2
	Breast cancer		
	Osteosarcoma		
	Leukemia		
	Brain tumors		
	Adrenocortical carcinoma		
Cowden Syndrome	Breast cancer	Dominant	PTEN
	Thyroid cancer		
	Endometrial and other cancers		
Bannayan-Riley-Ruvalcaba syndrome	Breast cancer Dominant	Dominant	PTEN
	Meningioma		
	Thyroid follicular cell tumors		
Hereditary gastrointestinal malignancies			
Hereditary gastric cancer	Stomach cancers	Dominant	CDH1
Juvenile polyposis	Gastrointestinal cancers	Dominant	SMAD4/DPC4
	Pancreatic cancer		BMPR1A
Peutz-Jeghers syndrome	Colon cancer	Dominant	STK11
	Small bowel cancer		
	Breast cancer		
	Ovarian cancer		
	Pancreatic cancer		
Hereditary melanoma pancreatic cancer	Pancreatic cancer	Dominant	CDKN2A/p16
	Melanoma		
Hereditary pancreatitis	Pancreatic cancer	Dominant	PRSS1
Turcot Syndrome	Colon cancer	Dominant	APC MLH1 PMS2
	Basal cell carcinoma		
	Ependymoma		
	Medulloblastoma		
	Glioblastoma		
Familial gastrointestinal stromal tum	Gastrointestinal stromal tumors		KIT
Genitourinary cancer predisposition syndromes			
Hereditary prostate cancer	Prostate cancer	Dominant	HPC1, HPCX HPC2/ELAC2 PCAP PCBC PRCA
Hereditary bladder cancer	Bladder cancer	Sporadic Unknown	Unknown
Hereditary testicular cancer	Testicular cancer	Possibly x- linked, Possibly recessive	Unknown
Central nervous system/vascular cancer predisposition syndromes			
Hereditary Paraganglioma	Paraganglioma Pheochromocytoma	Dominant	SDHD SDHC SDHB

SDHB(Source: Garber, J. E., & Offit, K. (2005).[16]

2. Hereditary cancer genes

Hereditary cancer genes play a pivotal role in our understanding of the genetic basis of cancer susceptibility. These genes are responsible for the transmission of cancer predisposition from one generation to the next within families. Over the past several decades, substantial research efforts have been dedicated to identifying and characterizing these genes.[16,18] Their discovery has provided valuable insights into the mechanisms underlying cancer development and progression.

Hereditary cancer genes can encompass a wide array of mutations, including those in tumor suppressor genes, oncogenes, and DNA repair genes. The presence of such mutations within an individual's genetic makeup can significantly increase their risk of developing specific types of cancer.

These mutations disrupt cellular equilibrium and regulatory processes, thereby promoting carcinogenesis. A detailed list of syndromes of cancer predisposition is listed in Table 1 with component tumors, the mode of inheritance and corresponding genes. The data underscore key findings from the past two decades, a period marked by the discovery of numerous cancer susceptibility genes.

Epidemiological investigations have uncovered the inherent genetic diversity in even rare tumors. This means that the predisposition to specific cancers can be ascribed to mutations in various genes which includes but not limited to BRCA2, BRIP1, APC, ATM, BARD1, BRCA1, CDH1, CDKN2A, CDK4, CHEK2, EPCAM, HOXB13, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, SKT11, TP53. While all genes can be responsible for various cancers, BRCA1 and BRCA2 predispose to cause common Ca such as breast, ovarian and pancreatic cancer 18-21 as shown in Figure 3.

Heritable mutations in the mentioned genes, such as lead to different further genetic alterations that are specifically involved in the development of each of these types of breast tumor. BRCA1, BRCA2 are known as high penetrance Ca of which mutations can be found both among men and women.[18,22]

MLH1, MSH2, and MSH6, which are responsible for most hereditary forms of hereditary nonpolyposis colon cancer (HNPCC) and are associated with up to a 70% chance of endometrial cancer.[23] The APC and MYH genes, which cause the adenomatous polyposis syndromes.[24] The RET oncogene, which is responsible for medullary thyroid cancer in patients who have the multiple endocrine neoplasia type 2 syndrome.[25]

There are several other high penetrance genes responsible for breast cancer are PALB2[26], TP53[27], PTEN[28], CDH1.[29] Several moderate penetrance Ca genes

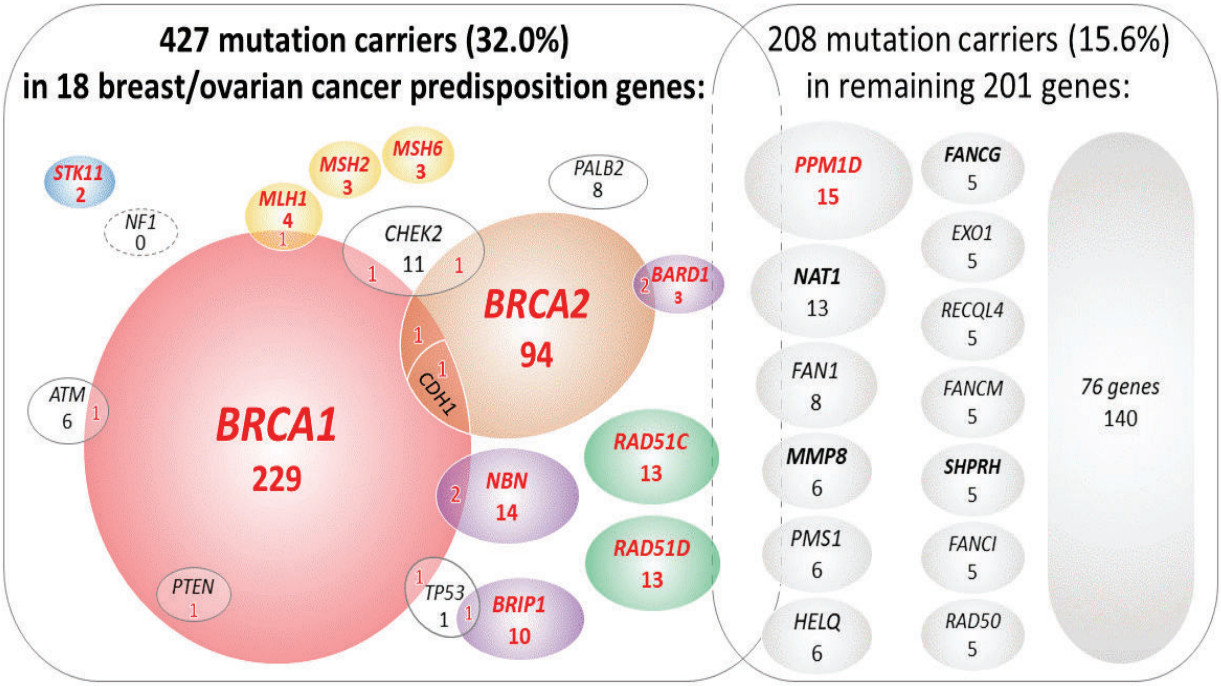


Figure 3: *Mutations in 18 known/anticipated hereditary breast and ovarian cancer genes. (Source: Lhotova, K. Et al. (2020)[21])*

such as ATM[29], CDKN2A[30], BARD1,[31] were also reported for common cancer types including breast and ovarian cancer.

According to leading medical oncologist and Clinical Director of the Clinical Genetics Service at Memorial Sloan Kettering, moderate-penetrance genes can affect how the medical practitioner counsel and care for patients, particularly if they also have a family history of cancer as patients who have a mutation in a moderate-penetrance gene along with a strong family history of Cancer, being at high risk.[32]

Understanding hereditary cancer genes is of critical importance from both clinical and research perspectives. These genes elucidate the genetic predisposition to cancer, facilitating precise risk assessment and stratification. Early detection and intervention strategies are significantly enhanced by this understanding, leading to improved patient outcomes.[16]

Furthermore, the identification of hereditary cancer genes has a direct impact on therapeutic approaches, enabling the development of tailored treatments that target the specific genetic aberrations associated with each case. It also informs the design of preventive measures and risk-reduction strategies.[8,16,17] From research perspective, the study of hereditary cancer genes continues to shed light on the molecular mechanisms underlying cancer initiation and progression, fostering the discovery of novel therapeutic targets, and advancing overall comprehension of cancer genetics.

Molecular mechanisms of hereditary tumor formation

The molecular mechanisms of hereditary tumor formation encompass a complex interplay of genetic factors and cellular processes. These mechanisms often involve mutations in key tumor suppressor genes and oncogenes, disrupting the finely tuned regulatory pathways that maintain cellular homeostasis.[12,16] Genes exist in pairs, operating synergistically to facilitate the production of proteins. One of these gene alleles is maternally inherited, while the other is paternally inherited. The genesis of tumors primarily arises from dysregulated cell proliferation.

Within the human genome, a multitude of gene variants intricately govern cell growth in a highly precise manner. When these genes harbor errors in their DNA sequences, they may malfunction, giving rise to "altered" or mutated forms.[12]

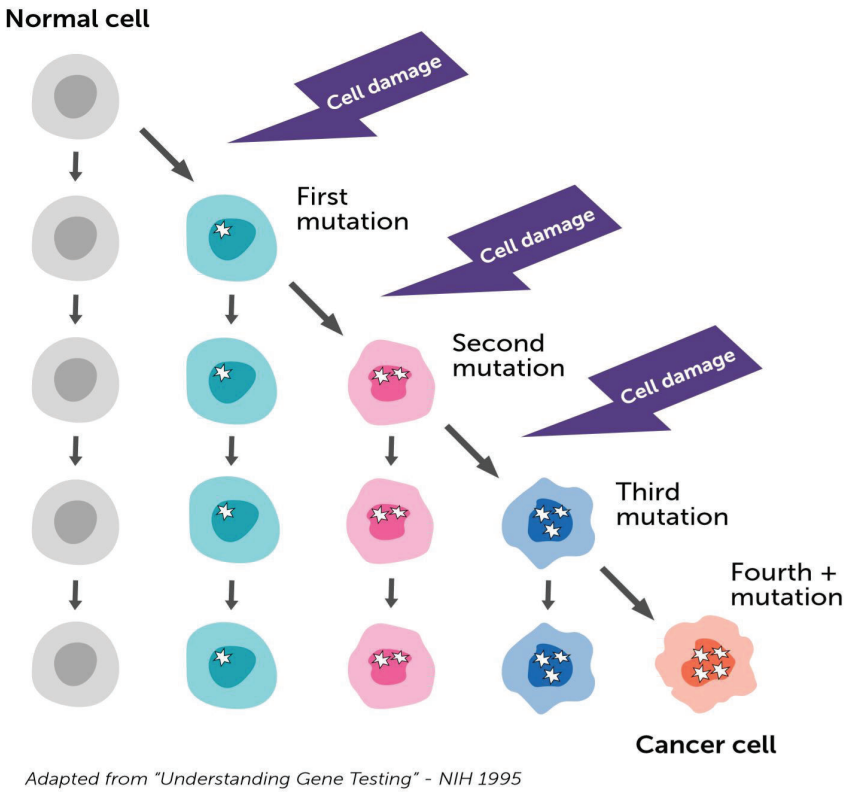


Figure 4: *Schematic illustration of DNA damage and gene mutations.*[33]

The cumulative occurrence of numerous mutations across diverse genes within a specific population of cells over an extended period is a prerequisite for the initiation of malignancy or the emergence of cancer cells, as elucidated in Figure 4.**33** In case of hereditary cancers, the initial mutations are inherited and are already present from birth.[16] As time progresses, additional mutations accrue, eventually giving rise to cancerous cells. This stepwise accumulation of mutations is a fundamental process in the development of cancer in individuals with a genetic predisposition to the disease.[8]

It's crucial to understand that the emergence of cancer typically necessitates mutations in multiple genes.[12] The precise triggers for these mutations remain largely mysterious. Nevertheless, mutations can be inherited or acquired. The process of formation of tumors may include mutation in proto-oncogenes, tumor suppressor gene mutations, DNA repair gene mutations, chromosomal aberrations, epigenetic changes and so on.[16]

Mutation in Proto-oncogenes: Proto-oncogenes are normal genes that are involved in regulating cell growth and division. When these genes undergo mutations, they can become oncogenes, which promote uncontrolled cell growth. One well-known example is the BCR-ABL fusion gene, which is associated with chronic myeloid leukemia (CML).[34]

Tumor Suppressor Gene Mutations: Tumor suppressor genes are responsible for preventing the formation of tumors. Mutations in these genes can result in the loss of their function, allowing uncontrolled cell growth. For example, mutations in the TP53 gene are common in various cancers.[35]

DNA Repair Gene Mutations: DNA repair genes are responsible for fixing errors in DNA replication. Mutations in these genes can lead to the accumulation of genetic mutations, increasing the risk of cancer. For instance, mutations in the BRCA1 and BRCA2 genes are linked to breast and ovarian cancer.[36]

Chromosomal Aberrations: Large-scale genetic changes, such as chromosomal translocations and amplifications, can lead to the activation of oncogenes or inactivation of tumor suppressor genes. One notable example is the Philadelphia chromosome in chronic myeloid leukemia.[37]

Epigenetic Changes: While not strictly genetic, epigenetic alterations, such as DNA methylation and histone modifications, can also contribute to Cancer development by silencing tumor suppressor genes.[38]

4. High risk individuals for hereditary cancer

High-risk individuals for hereditary cancer are those who possess specific genetic mutations or a strong family history of cancer, predisposing them to an elevated risk of developing certain types of cancer.[8] The risk of hereditary and sporadic cancer is unique due to practical reason as the Sporadic cancer arises from random mutations in somatic cells, often due to environmental factors or chance occurrences during cell division.[39,40] It typically lacks a significant family history of the disease. In contrast, hereditary cancer is characterized by specific inherited genetic mutations that predispose individuals to cancer as illustrated in Figure 5.

In case of hereditary cancer, a person receives a working copy of the growth control gene from one parent and a copy of the gene with a mutation from the other parent. The altered gene is also known as a "Cancer susceptibility gene." Every cell in the body contains the inherited Cancer susceptibility gene, but only the functional copy of the gene allows each cell to function normally. But if a cell's working copy of the gene is compromised by a mutation, that cell may no longer be able to regulate its own development and develop cancer. As a result, those who inherit a Cancer susceptibility gene have a considerably higher risk of specific types of Cancer However, not everyone with an inherited Cancer susceptibility gene may not develop cancer.[16]

As for example, if father and mother pass any mutated BRCA1 & BRCA2 gene to their offspring the child may remain at higher risk of developing cancer, more like breast, ovarian cancer, and others. Both men and women can be inherited damage Cancer suspectable gene, in of which have a 50% chance to inherit that very Cancer gene, being suspectable to produce cancer. Moreover, the affected child also has a 50% chance of inheriting that Cancer gene through its working copy.

Literature shows risk of Cancer in those children remain risky than general population. Notably, some Cancer suspectable genes only links to Cancer but may not be equally affected between male and female children. Not only that, but parent of the unaffected sex may also still carry and pass on those genes.[8,16,18]

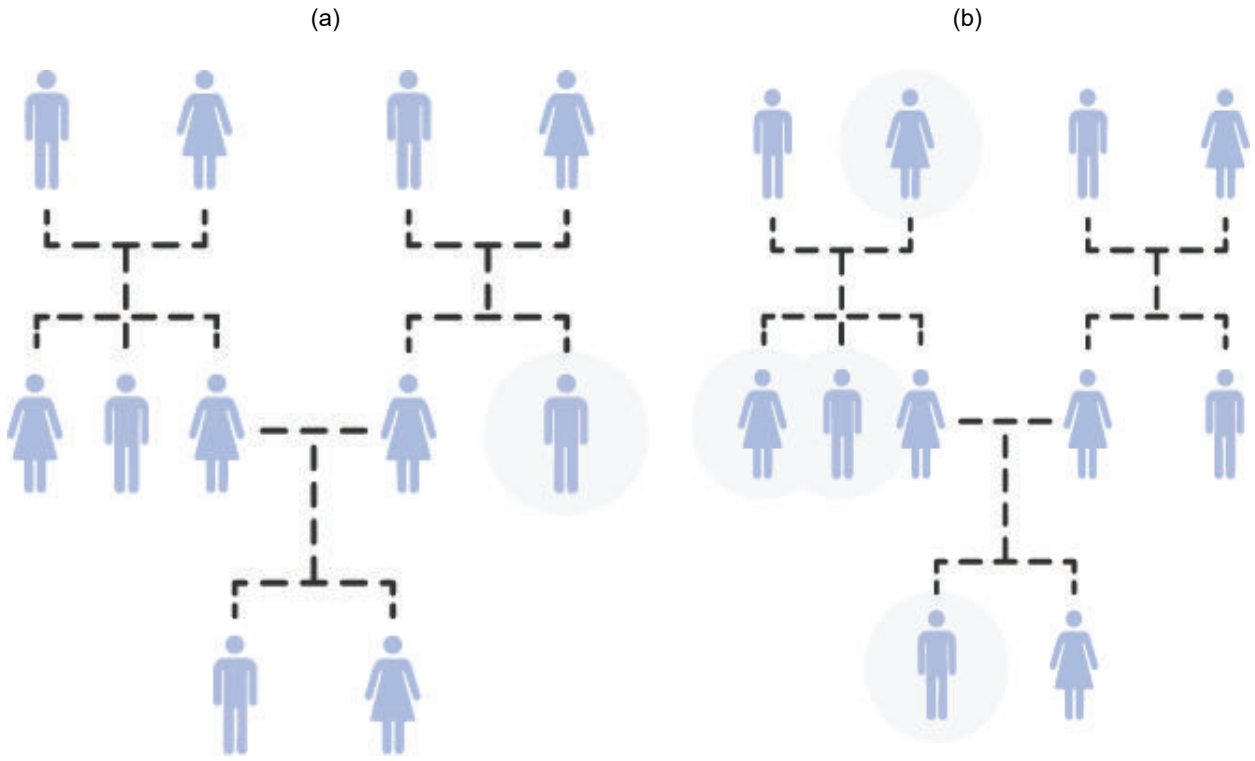


Figure 5: *Illustration of high-risk individuals for (a) sporadic and (b) hereditary cancer.*

Hereditary cancers typically lack significant distinguishing features when compared to non-hereditary cancers. The distinction arises from familial patterns of occurrence. Key signs suggestive of hereditary Cancer encompass:

(a) Presence of two or more family members afflicted by the same Cancer type, particularly on the same side of the family lineage, the persistence of this pattern across multiple generations,

(b) Manifestation of Cancer at an early age,

(c) Occurrence of multiple primary cancers in an individual, the coexistence of genetically linked cancers within a family, such as breast and ovarian Cancer or colon and uterine cancer,

d) The identification of physical attributes associated with hereditary cancer, such as the presence of moles and melanoma or polyps and colon cancer, and the emergence of specific rare Cancer types within the familial context.[41]

Global perspectives on hereditary cancer research

More than a century ago, investigators made clinical observations on the hereditary characteristics of cancer, such as cancers diagnosed in patients at a younger age and in many members of the family. Since then, the global perspective on hereditary cancer research had witnessed significant advances in the identification of genetic mutations associated with hereditary cancer syndromes, including well-known genes like BRCA1 and BRCA2.[8,16]

International collaborations among researchers and institutions had been on the rise, fostering the sharing of genetic data and research findings to gain a more comprehensive understanding of hereditary cancers.[42] Based on multigenerational collaboration and commitment leading to foundational discoveries, in recent years, understanding the germ line defects and related biologic consequences helped scientist to develop effective drugs for some of the common hereditary syndromes.[43]

Among these drugs, HIF2α inhibitors were specifically developed for treating von Hippel-Lindau syndrome, while anti-PD-1 pembrolizumab was designed to target high microsatellite instability/mismatch repair deficient colorectal cancer and various solid tumors. PARP inhibitors, on the other hand, have shown promise in addressing breast and pancreatic cancer.

The development of these medications for hereditary cancer syndromes represents the culmination of over a century's worth of collective efforts from dedicated

physicians and scientists. Their contributions have been instrumental in establishing clinical diagnostic methods and uncovering the underlying biological mechanisms of these diseases, ultimately paving the way for the recent advancements in novel drug development for hereditary cancer syndromes.[44]

It's important to emphasize that hereditary cancer syndromes make up less than 5% of all cancer cases. However, the valuable biologic and clinical insights obtained during the development of drugs for these genetic disorders have had a broader impact. The investigation and utilization of these agents have expanded to encompass sporadic cancers that share similar underlying mechanisms.

This cross-application of knowledge and treatments derived from hereditary cancer research has significantly benefited the understanding and management of a wider range of malignancies beyond the hereditary context.[18]

Apart from drugs, globally the cancer research field has developed significantly through use of new equipment and technology of which hereditary cancer. One example of new technology is Next-Generation Sequencing (NGS). Also known as high-throughput sequencing. Along with that, liquid biopsy, also known as fluid biopsy or fluid phase biopsy has gain momentum in detecting cancers.[18,44]

Conclusion

Recent insights and in-depth progress on the understanding of hereditary factors of cancer, though yielded a multifactorial etiology, it mostly entangled with genetic origin. Cancer is passed down to family descendants via genes or causing genetic mutation present in eggs or sperms cell during fertilization, considered to be hereditary cancer (breast, colon, prostate, pancreas, ovary).

Understanding Cancer-hereditariness remains critical not only to assess genetic pathways but also to design preventive &/or therapeutic strategies, and also, allows identifying risky group of people having family history and/or genetic makeup. Early detection through improved surveillance and it is important to tailor therapeutic modality.

Acknowledgement

My sincere appreciation goes to Ad-din Women's Medical College (AWMC) and Bangamata National Cellular and Molecular Research Center (BNCMRC) and Bangladesh Medical Research Council (BMRC) due assistance. Particular thanks go to Dr. Kazi Selim Anwar, Md, Mphil. and Dr. Mohammad Neaz Morshed, PhD for all sorts of expert assistance in preparing, writing and revising this manuscript.

References:

1. Bisoyi, P., A brief tour guide to cancer disease, in Understanding cancer. 2022, Elsevier. p. 1-20.
2. Bray, F., et al., The ever-increasing importance of cancer as a leading cause of premature death worldwide. Cancer, 2021. 127(16): p. 3029-3030.
3. Frick, C., et al., Quantitative estimates of preventable and treatable deaths from 36 cancers worldwide: a population-based study. The Lancet Global Health, 2023.
4. Sung, H., et al., Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians, 2021. 71(3): p. 209-249.
5. Ortega-Ortega, M., et al., Paid and unpaid productivity losses due to premature mortality from cancer in Europe in 2018. International Journal of Cancer, 2022. 150(4): p. 580-593.
6. Pearce, A., et al., Productivity losses due to premature mortality from cancer in Brazil, Russia, India, China, and South Africa (BRICS): A population-based comparison. Cancer epidemiology, 2018. 53: p. 27-34.
7. Petrakis, N.L., Genetic factors in the etiology of breast cancer. Cancer, 1977. 39(6): p. 2709-2715.
8. Lynch, H.T., R.M. Fusaro, and J. Lynch, Hereditary cancer in adults. Cancer detection and prevention, 1995. 19(3): p. 219-233.
9. Kispert, S. and J. McHowat, Recent insights into cigarette smoking as a lifestyle risk factor for breast cancer. Breast Cancer: Targets and Therapy, 2017: p. 127-132.
10. Thomas, R.F. and J. Scotto, Estimating increases in skin cancer morbidity due to increases in ultraviolet radiation exposure. Cancer investigation, 1983. 1(2): p. 119-126.
11. Blackadar, C.B., Historical review of the causes of cancer. World journal of clinical oncology, 2016. 7(1): p. 54.

12. Fymat, A.L., Genetics, epigenetics and cancer. Cancer Ther. Oncol. Int. J, 2017. 4: p. 555634.
13. Frank, C., et al., Population landscape of familial cancer. Scientific reports, 2015. 5(1): p. 12891.
14. Lindor, N.M., et al., Concise handbook of familial cancer susceptibility syndromes. Journal of the National Cancer Institute Monographs, 2008. 2008(38): p. 3-93.
15. Nagy, R., K. Sweet, and C. Eng, Highly penetrant hereditary cancer syndromes. Oncogene, 2004. 23(38): p. 6445-6470.
16. Garber, J.E. and K. Offit, Hereditary cancer predisposition syndromes. Journal of clinical oncology, 2005. 23(2): p. 276-292.
17. Strate, L.L. and S. Syngal, Hereditary colorectal cancer syndromes. Cancer Causes & Control, 2005. 16: p. 201-213.
18. Seppälä, T.T., R.A. Burkhart, and B.W. Katona, Hereditary colorectal, gastric, and pancreatic cancer: comprehensive review. BJS open, 2023. 7(3): p. zrad023.
19. Miki, Y., et al., A strong candidate for the breast and ovarian cancer susceptibility gene BRCA1. Science, 1994. 266(5182): p. 66-71.
20. Wooster, R., et al., Identification of the breast cancer susceptibility gene BRCA2. Nature, 1995. 378(6559): p. 789-792.
21. Lhotova, K., et al., Multigene panel germline testing of 1333 Czech patients with ovarian cancer. Cancers, 2020. 12(4): p. 956.
22. Palacios, J., et al., The molecular pathology of hereditary breast cancer. Pathobiology, 2008. 75(2): p. 85-94.
23. Abdel-Rahman, W.M., J.-P. Mecklin, and P. Peltomäki, The genetics of HNPCC: application to diagnosis and screening. Critical reviews in oncology/hematology, 2006. 58(3): p. 208-220.
24. Galiatsatos, P. and W.D. Foulkes, Familial adenomatous polyposis. Official journal of the American College of Gastroenterology| ACG, 2006. 101(2): p. 385-398.
25. Dionigi, G., et al., Medullary thyroid carcinoma: surgical treatment advances. Expert review of anticancer therapy, 2007. 7(6): p. 877-885.
26. Couch, F.J., et al., Associations between cancer predisposition testing panel genes and breast cancer. JAMA oncology, 2017. 3(9): p. 1190-1196.
27. Hanahan, D. and R.A. Weinberg, Hallmarks of cancer: the next generation. cell, 2011. 144(5): p. 646-674.
28. Vargas, A.C., J.S. Reis-Filho, and S.R. Lakhani, Phenotype-genotype correlation in familial breast cancer. Journal of mammary gland biology and neoplasia, 2011. 16: p. 27-40.
29. Domagala, P., et al., Prevalence of germline mutations in genes engaged in DNA damage repair by homologous recombination in patients with triple-negative and hereditary non-triple-negative breast cancers. PLoS One, 2015. 10(6): p. e0130393.
30. Buys, S.S., et al., A study of over 35,000 women with breast cancer tested with a 25-gene panel of hereditary cancer genes. Cancer, 2017. 123(10): p. 1721-1730.
31. González-Rivera, M., et al., Frequency of germline DNA genetic findings in an unselected prospective cohort of triple-negative breast cancer patients participating in a platinum-based neoadjuvant chemotherapy trial. Breast cancer research and treatment, 2016. 156: p. 507-515.
32. 3 Cancer Genes You've Never Heard Of. [Webpage] 2019 2019 [cited 2023 October 15]; Available from: https://www.mskcc.org/news/3-cancer-genes-you-ve-never-heard#:~:text=%E2%80%9CWhat's%20really%20important%20about%20moderate,Service%20at%20Memorial%20Sloan%20Kettering.
33. FORCE-Facing Our Risk of Cancer Empowered, I. DNA damage and gene mutations. 2023 [cited 2023 Ocotber 15]; Available from: https://www.facingourrisk.org/info/hereditary-cancer-and-genetic-testing/hereditary-cancer/genes-and-cancer#:~:text=DNA%20damage%20and%20gene%20mutations,of%20control%20and%20become%20cancerous.
34. Druker, B.J., et al., Efficacy and safety of a specific inhibitor of the BCR-ABL tyrosine kinase in chronic myeloid leukemia. New England Journal of Medicine, 2001. 344(14): p. 1031-1037.
35. Hollstein, M., et al., p53 mutations in human cancers. Science, 1991. 253(5015): p. 49-53.
36. Venkitaraman, A.R., Cancer susceptibility and the functions of BRCA1 and BRCA2. Cell, 2002. 108(2): p. 171-182.

37. Rowley, J.D., A new consistent chromosomal abnormality in chronic myelogenous leukaemia identified by quinacrine fluorescence and Giemsa staining. Nature, 1973. 243(5405): p. 290-293.

38. Kanwal, R. and S. Gupta, Epigenetic modifications in cancer. Clinical genetics, 2012. 81(4): p. 303-311.

39. Souglakos, J., Genetic alterations in sporadic and hereditary colorectal cancer: implementations for screening and follow-up. Digestive diseases, 2007. 25(1): p. 9-19.

40. Jones, P.A. and S.B. Baylin, The epigenomics of cancer. Cell, 2007. 128(4): p. 683-692.

41. Trepanier, A., et al., Genetic cancer risk assessment and counseling: recommendations of the national society of genetic counselors. Journal of genetic counseling, 2004. 13(2): p. 83-114.

42. Bell, K.A., et al., Development of a comprehensive approach to adult hereditary cancer testing in Ontario. Journal of Medical Genetics, 2023. 60(8): p. 769-775.

43. Riley, L.B. and D.C. Desai, The molecular basis of cancer and the development of targeted therapy. Surgical Clinics of North America, 2009. 89(1): p. 1-15.

44. Hasanov, E., et al., Current systemic treatments for the hereditary cancer syndromes: drug development in light of genomic defects. American Society of Clinical Oncology Educational Book, 2022. 42: p. 808-824.

Perspective

Metamorphosis of a medical graduate: From a general physician to a public health expert

Tanzila Naureen

After completion of SSC and HSC successfully, I could enter the MBBS course, in the Dhaka Medical College (DMC), thanks to the Almighty!! Here, in this communication, I intend to present my own perspective humbly scribbling down my brief bio-sketch as a doctor (physician).

To begin with, I started my 1st year-MBBS course with full enthusiasm but got halted a bit- understanding how huge a load my brain, memory and mental strength should be required to prepare in dedicating to learn medical science at a modest level. Nevertheless, by the Almighty's grace I could successfully cross over that vast ocean of MBBS.

I joined my internship right at the DMCH starting with the Dept. of Medicine. As an intern I actually started feeling the amazing vibe as a doctor so much so, that I forgot all my hard past of 5 year-long medical college days. I must admit, here, that 'Community Medicine' really got my heart and full devotion shaking as we completed our training in rural health complex (part of internship).

Right within a year or so of my internship, I appeared the exam of Govt. BCS (Health Cadre) and passed out. I was posted first in Choddogram, Cumilla.

Soon after, I applied for Australia Awarded Scholarship and was nominated to study MPH and in January 2014, I flew to Australia to pursue an MPH degree from the University of Melbourne- one of world's best universities.

Correspondence: Dr. Tanzila Naureen, Faculty Member, Department of Community Medicine, Dhaka Medical College, Dhaka 1000, Bangladesh.

Received Date : 02 November, 2023
Accepted Date : 05 November, 2023

Though I always had a keen interest in public health, this very course opened an unknown door of medical science when we started learning:

- Epidemiology and Biostatistics,
- Health Policy and Hospital management, etc….
- Public Health, Public Health Nutrition, Food safety & food security, etc.,
- Environmental Health/ Climate Change…..etc.. what not!

I was much eager to utilize the expertise that I learnt in Melbourne University to apply or replicate those in Bangladesh. Thus, on coming back to my motherland, I joined back to my Govt. Health Services and got posted at the Institute of Epidemiology, Disease Control and Research (IEDCR) in in 2016. I was so fortunate to work with country's eminent public health experts, like Prof. M Mahmudur Rahman, the frontliner in One Health Sector home and abroad, and also with Prof. Meerzadi Sebrina Flora, the most versatile lady who took care of our country's massive on-going COVID-19 pandemic (during 2018 through 2021)- the two personalities who really supported me a lot to build up my career in public health, so much so!

Currently, in 2019, I had been posted at the Dhaka Medical College (DMC)- my parent institution, as one of the faculty members at the Dept. of Community Medicine. However, I must spell it out aloud that it was not an easy task for me to leave my beloved IEDCR which was so exciting and enjoyable. Though teaching and mentoring young minds have always intrigued me, leaving IEDCR was difficult since I gathered a lot of practical working experience in epidemiology and public health quite seriously.

Well, getting back to Dhaka Medical College, I got the opportunity of my choice to teaching community medicine/ public health to both under- and, post-graduate medical students, my primary responsibility remains to teach and mentor undergraduate ones. Currently, I conduct tutorial classes, take item examinations for MBBS course and also guide them often to various field and lab surveys.

Recently, I guided my students for field level research activities for the residential field site training program (RFST) and, also, supervise day visits to certain places of huge public health importance.

I get to attend/ supervise various training programs and lead workshops both within Dhaka Medical College and in other national level institutions, hospitals & research organizations.

To sum up:

As a public health expert, I do enjoy teaching young minds who I render constant encouragement and motivate them to learn more about details of public health. I can assure there is a lot of opportunities in Bangladesh to grow as a public health personnel- which our country demands a lot more than existing ones, including devoting to public/community health research which has enough possibilities and potential in our country. Finally, it is crucial to mention our recent experience on COVID-19 Pandemic that made everyone (from public to administrators to clinicians, all including emergency room doctors) fully realize the importance of public health towards saving lives of million people not only in our country but also across the globe.

Bottom Line:

- This is in short, my humble journey, on how a general physician could flourish as a public health expert. Hope these pathways, will encourage our future physicians to evolve as public health experts!
- It's not that easy a task to excel as a public health expert but is largely possible, I believe in! Any new generation physician can shine as a public health expert if he/ she is determined!

Welcome to the world of our public health community!!

Case Report

Bilateral Toxoplasma Retinitis: Rare But Devastating Condition - A Case Report

Dr. Md. Abdullah-Al Kafi

Introduction

Toxoplasma gondii, an obligate intracellular protozoan, is the most frequent cause of infectious retinitis in immunocompromised individuals. Although some cases may occur as a result of reactivation of prenatal infestation but the vast majority are acquired postnatally.

Recurrent episodes of inflammation are common and occur when the cysts rupture and release hundreds of tachyzoites into normal retinal cells. Recurrences usually take place between ages of 10 and 35 yrs. The scars from which recurrences arise may be the residua of previous congenital infestations or more frequently, remote acquired involvements.

Toxoplasmosis is one of the more common parasitic zoonoses world-wide. Its causative agent, Toxoplasma gondii, is a facultatively heteroxenous, polyxenous protozoon that has several potential routes of transmission within &/or between different host species.

If T. gondii is first contracted during pregnancy, it may be transmitted vertically by tachyzoites that are passed to the fetus via the placenta. Horizontal transmission of T. gondii may involve three life-cycle stages, i.e. ingesting infectious oocysts from the environment or ingesting tissue cysts or tachyzoites which are contained in meat or primary offal (viscera) of many different animals.

Correspondence: Dr. Md. Abdullah-Al Kafi, Chief Ophthalmologist, Shyamoli Eye Hospital, Ring Road, And, CEO. Ex. Asst. Prof. National Inst. Of Ophthalmology & Hospital, Shere-Bangla Nagar, Dhaka. e-mail: kafi68@yahoo.com

Received Date : 10 July, 2023

Accepted Date : 10 August, 2023

Transmission may also occur via tachyzoites contained in blood products, tissue transplants, or unpasteurized milk. However, it is not known which of these routes is more important epidemiologically. In the past, the consumption of raw or undercooked meat, in particular of pigs and sheep, has been regarded as a major route of transmission to humans.

However, recent studies showed that the prevalence of T. gondii in meat-producing animals decreased considerably over the past 20 years in areas with intensive farm management.[1]

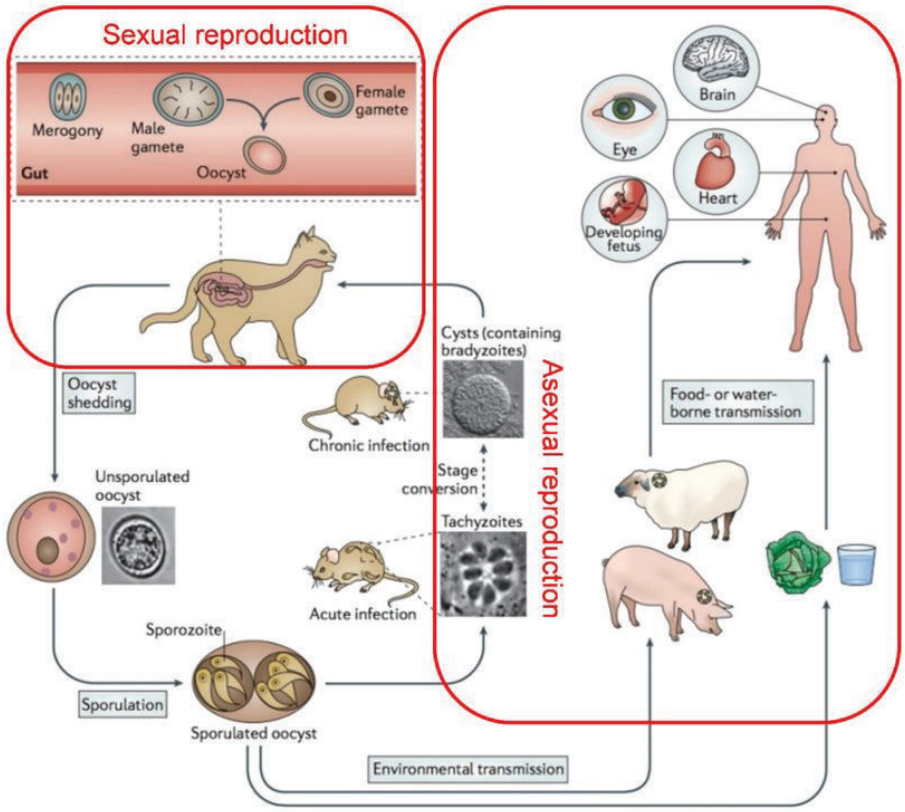
Cat is the definitive host of the parasite and other beings, such as mice, livestock and humans are intermediate host.

Organisms exist in the following three forms:

a) **Sporozoites** are contained within an oocyst (sporocyst) and are the result of sexual reproduction of the organisms with the intestinal mucosa of the cat. They are excreted in the faeces and spread to intermediate host.

b) **Bradyzoites**are relatively inactive and are contained within tissue cysts that most commonly develop in the brain, eye, heart, skeletal muscles and lymph nodes. They may lie dormant for many years without provoking an inflammatory reaction.

c) **Tachyzoites** (trophozoites) are the proliferating active form responsible for tissue destruction and inflammation following rupture of cell wall containing bradyzoites.



Mode of human infection:

a) Ingestion of undercooked meat (lamb, pork, beef) containing bradyzoites of an intermediate host.

↓

Ingestion of sporocysts from accidental contamination of hands when disposing of cat litter trays and then subsequent transfer on to food.

↓

Infants may also become infested by eating dirt (pica) containing sporocysts.

↓

In rural areas water contamination may plays important role in transmission.

↓

Parasite (tachyzoite) may spread transplacentallyfrom infected pregnant woman.

Congenital Toxoplasmosis:

Toxoplasmosis is transmitted to the fetus through the placenta when a pregnant woman become infested. If the mother is infected before pregnancy, the fetus will be unscathed.

Severity of involvement of the fetus is dependent on the duration of gestation at the time of maternal infestation. Involvement in early pregnancy may resultin stillbirth, whereas if it occurs during late pregnancy it may result in convulsions, paralysis, hydrocephalus and visceral diseases.

Manifestations:

Intracranial calcification may be seen on CT scan. In most cases of congenital systemic toxoplasmosis are subclinical. In these children, bilateral healed chorio-retinal scars may be discovered later in life, either

by chance or when the child is found to have defective vision.

Infestation towards the end of second trimester usually results in disease that can be detected at birth such as macular scars. That ocurring later in third trimester may results in normal examinations at birth but the development of uveitis or neurological disease in the future.

Acquired Toxoplasmosis:

In immunocompetent patients subclinical is the most frequent. Lymphadenopathic syndrome, usually self-limiting and characterized by cervical lymphadenopathy, fever, malaise and pharyngitis. Meningoencephalitis may occur rarely.

In immunocompromised patients may be life-threatening. The most common manifesta-tion in AIDS patients is an intracerebral space occupying lesion which resembles a cerebral abscess on MRI.

Diagnosis of Toxoplasma Retinitis:

The diagnosis of Toxoplasma retinitis is based on a compatible fundus lesion. Positive serology for toxoplasma antibodies is significant in early cases but in recurrent ocular toxoplasmosis no correlation exists between the titer and the activity of retinitis.

Aims:

a) To reduce the duration and severity of acute inflammation.

b) To lessen the risk of permanent visual loss by reducing the size of the eventual retinochorhoroidal scar.

c) To reduce the the risk of recurrences.

Where we should treat?

a) A lesion involving the macula, papillomacular bundle, optic nerve head or a major blood vessels.

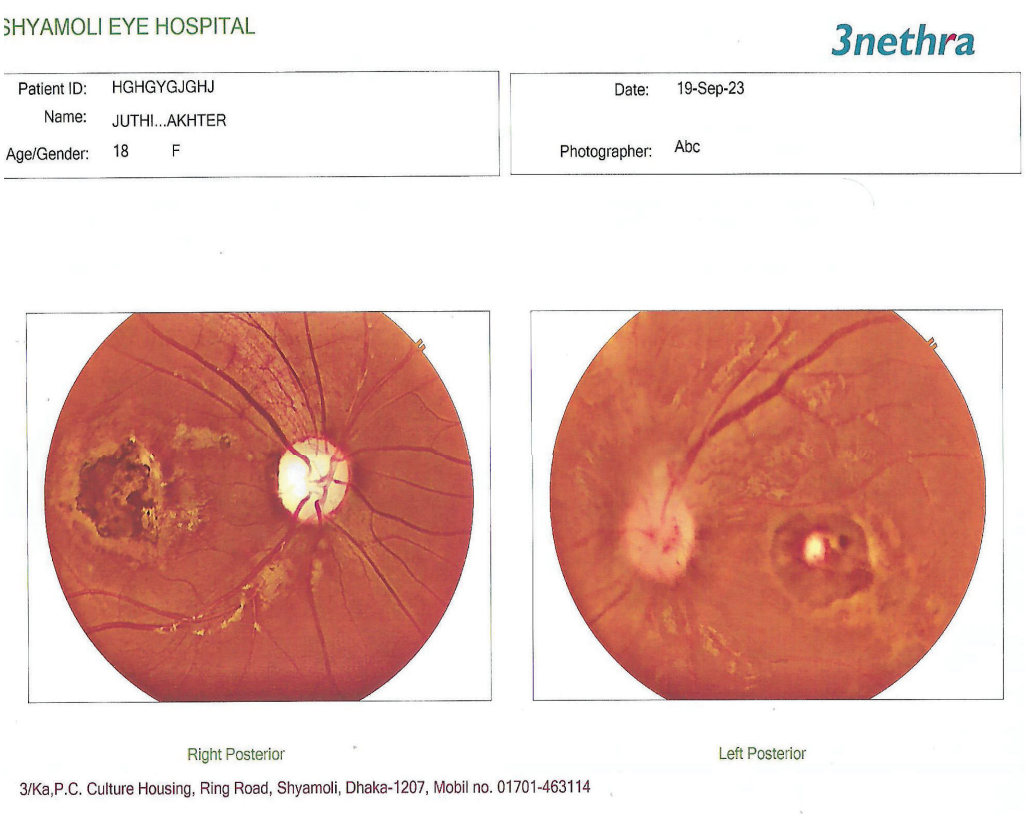
b) Very severe vitritis because of the risk of vitreous fibrosis and Tractional retinal detachment.

c) In immunocompromised patients all lesions should be treated irrespective of location & severity.

Treatment options:

There is no universally agreed therapeutic regimen and no evidence to support the specific form of treatment.

In line of aforementioned background based on updated literature review the case report on bilateral Toxoplasma Retinitis- a rare but devastating condition is delineated in next page:



The Case

A 18 years woman, **Juthy Akter**, attended my chamber (Eye Care Center, Shyamoli, Dhaka) with the complain of severe dimness of vision in both eyes, persisting for last 2- months. Often, she felt pain and had redness in both her eyes, including photophobia.

Procedure followed/ Ophthalmological Examination

On examination, her visual acuity of is 6/60 both eyes and no visual improvement with refraction. Her intraocular pressure of both eyes is 14mm of Hg. Anterior segment of both eyes shows normal.

Posterior segment of both her eyes showed a large macular lesion in retina. The left eye center of macula had active inflammation and optic nerve head was inflamed (optic neuritis).

Discussion

Programs for the prevention of congenital toxoplasmosis have been tested or discussed in several countries or states.[2-7] To our knowledge, France and Austria are the only countries in which testing for toxoplasmosis is required by law in women of childbearing age. France has the most stringent program, but its epidemiologic impact on ocular toxoplasmosis has not been assessed.

No national registry is available, and data were acquired by asking patients or their mothers to recollect the results of their previous serologic tests. Therefore a recall bias, which could have affected the assignment of cases as congenital or acquired, cannot be ruled out. In children who are known to have been congenitally infected, a systematic ophthalmic longitudinal follow-up is recommended. The role of acquired infections in ocular toxoplasmosis has also been highlighted in specific epidemiologic circumstances.[2]

Diagnosis of toxoplasmosis in humans is made by biological, serological, histological, or molecular methods, or by some combination of the above. Clinical signs of toxoplasmosis are non-specific and are not sufficiently characteristic for a definite diagnosis. Toxoplasmosis in fact mimics several other infectious diseases. Detection of T. gondii antibody in patients may aid diagnosis[8]

It is known that T. gondii is a protozoan parasite that infects 30% of humans, mainly in the chronic stage, which is the parasite's most resistant stage. This resistant form is unaffected by current drugs that are used to treat toxoplasmosis, which are pyrimethamine and sulfadiazine; these drugs control the parasite's acute stage, tachyzoites.[9,10]

Although these compounds are most often used to treat toxoplasmosis, they cause severe side effects [11-13]they are not active against the bradyzoites found in the cyst.[14] Some studies have pointed out to the need to establish new in vitro and in vivo experimental models to test new compounds against T. gondii tachyzoites and bradyzoites.[15]

Highlights:

- Infection by T. gondii a protozoan parasite is widely prevalent in humans and animals.
- T. gondii causes serious disease in congenitally infected children & depressed immunity.
- To prevent human infection, all meat should be cooked well before consumption.
- Gloves should be worn while gardening, & sandboxes used by children be covered when not in use to prevent exposure to soil contaminated T. gondii oocysts excreted in cat feces.
- Extreme care should be used in handling litterboxes for cats; & pregnant women, children & immunocompromised individuals should avoid litterboxes always.[16]
- A better understanding of clinical characteristics & course of ocular toxoplasmosis will have prudent implication for developing effective prevention & treatment strategies.[17]

Conclusion:

Infection by T. gondii -a protozoan parasite is widely prevalent in human and animals. It can cause devastating disease in congenitally infected children with depressed immunity. Reassessment of older publications in the light of recent observations provides a richer understanding of ocular toxoplasmosis, although knowledge about the disease remains incomplete.

Recommendations:

- It is advisable to have eye examination early.
- Mandatory step is to take medication in time.
- Primary treatment involves anti-parasitic medication against T. Gondi infection.
- Regular follow-up with the ophthalmologist remains essential.
- Ophthalmologist must monitor progress of retinitis to assess response of treatment and check to prevent potential complications.
- In case of active retinal lesions that threaten vision, retinal therapy may be considered to prevent destroying active tissue and further damage.

- Lastly patient should be educated on the importance of compliance with medication & need for regular follow-up appointments with ophthalmologists.

References

1. Tenter AM, Heckeroth AR, Weiss LM*Toxoplasma gondii*: from animals to humans Int J Parasitol, 30 (2000), pp. 1217-1258
2. Delair E, Monnet D, Grabar S, Dupouy-Camet J, Yera H, Brézin AP. Respective roles of acquired and congenital infections in presumed ocular toxoplasmosis. American journal of ophthalmology. 2008 Dec 1;146(6):851-5.
3. Ricci M, Pentimalli H, Thaller R, Rava L, Di Ciommo V. Screening and prevention of congenital toxoplasmosis: an effectiveness study in a population with a high infection rate. J Matern Fetal Neonatal Med 2003;14:398 – 403.
4. Eskild A, Fallas Dahl G, Melby KK, Nesheim BI. Testing for toxoplasmosis in pregnancy: a study of the routines in primary antenatal care. J Med Screen 2003;10:172–175.
5. Raeber PA, Biedermann K, Just M, Zuber P. Prevention of congenital toxoplasmosis in Europe. Schweiz Med Wochenschr Suppl 1995;65:96S–102S.
6. Breugelmans M, Naessens A, Foulon W. Prevention of toxoplasmosis during pregnancy—an epidemiologic survey over 22 consecutive years. J Perinat Med 2004; 32:211–214.
7. Hsu HW, Grady GF, Maguire JH, Weiblen BJ, Hoff R. Newborn screening for congenital Toxoplasma infection: five years experience in Boston, Massachusetts. Scand J Infect Dis Suppl 1992;84:59 – 64.)
8. Hill D, Dubey JP. Toxoplasma gondii: transmission, diagnosis and prevention. Clinical microbiology and infection. 2002 Oct 1;8(10):634-40.
9. Mcauley J, Boyer KM, Patel D, Mets M, Swisher C, Roizen N, Wolters C, Stein L, Stein M, Schey W, Remington J, Meier P, Johnson D, Heydeman P, Holfels E, Withers S, Mack D, Brown C, Patton D, McLeod R (1994) Early and longitudinal evaluations of treated infants and children and untreated historical patients with congenital toxoplasmosis: the Chicago Collaborative Treatment Trial. Clin Infect Dis 18:38–72
10. Montoya JG, Liesenfeld O (2004) Toxoplasmosis. Lancet 363
11. Haverkos HW (1987) Assessment of therapy for toxoplasma encephalitis. The TE Study Group. Am J Med 82:907–914.
12. Leport C, Raffi F, Matheron S, Katlama C, Regnier B, Saimot AG, Marche C, Vedrenne C, Vilde JL (1988) Treatment of central nervous system toxoplasmosis with pyrimethamine/sulfadiazine combination in 35 patients with the acquired immunodeficiency syndrome. Efficacy of long-term continuous therapy. Am J Med 84: 94–100.
13. Georgiev VS (1994) Management of toxoplasmosis. Drugs 48:179–188.
14. Dunay IR, Gajurel K, Dhakal R, Liesenfeld O, Montoya JG (2018) Treatment of toxoplasmosis: historical perspective, animal models, and current clinical practice. Clin Microbiol Rev 31(4)
15. Portes JA, De Souza W. Development of an in vitro system to study the developmental stages of Toxoplasma gondii using a genetically modified strain expressing markers for tachyzoites and bradyzoites. Parasitol Res. 2019 Dec;118(12): 3479-3489. doi: 10.1007/s00436-019-06493-6. Epub 2019 Nov 14. PMID: 31728720.
16. Hill D, Dubey JP. Toxoplasma gondii: transmission, diagnosis and prevention. Clinical microbiology and infection. 2002 Oct 1;8(10):634-40.
17. Holland GN. Ocular toxoplasmosis: a global reassessment: Part I: epidemiology and course of disease. American journal of ophthalmology. 2003 Dec 1;136(6):973-88

News and Views

Poster Presentation on Vitamin D [Serum 25(OH) cholecalciferol] Insufficiency is Associated with Childhood Asthma: Recent Findings among Bangladesh Children"

Nabila Tabassum

Dr. Nabila Tabassum, Core Trainee, Dept of Pediatrics, University hospital Leicester, shared with Medical Research Unit (MRU), AWMC her poster presentation titled "**Vitamin D [Serum 25(OH) cholecalciferol] Insufficiency is Associated with Childhood Asthma: Recent Findings among Bangladesh Children**" which was formerly presented as poster at the **Royal College of Pediatrics and Child health (RCPCH) conference in Glasgow, Scotland** in January 2023.

Contributors:

Nabila Tabassum[1], Kazi S. Anwar[2], Md. Abid H. Mollah[3], Probir K. Sarkar[4]

Department of Pediatrics, Bangladesh Inst. of Child Health and Dhaka Shishu Hospital, Dhaka, Bangladesh.

1. Core Trainee, Dept of Pediatrics, Leicester Royal Infirmary, University hospital Leicester
2. Leicester, England Head, Medical Research Unit, Ad-din Women's Medical College (AWMC), Dhaka.
3. Head & Senior Consultant, Dept. of Pediatrics, BIRDEM- 2
4. Deputy Director, Department of Pediatrics, Bangladesh Inst. of Child Health and Dhaka Shishu Hospital, Dhaka, Bangladesh.

Correspondence: Dr. Nabila Tabassum, Core trainee, Department of Pediatrics, UK.

Received Date : 20 July, 2023
Accepted Date : 25 September, 2023

Background:

Vitamin D has a role in asthma due to its effects on airway epithelium, bronchial smooth muscle & immune-modulatory effects on innate and adaptive immune systems. Lower level of *S.25(OH) cholecal- ciferol* is associated with increased childhood asthma prevalence, less responsiveness to corticosteroids, frequent exacerbations, increased disease severity & hospitalizations. We examined interaction between childhood asthma & Vit. D.

Objectives:

Assess the clinico-epidemiological features of childhood asthma, aiming to determine if Vitamin D among asthmatic children (cases) differ from that of non-asthmatic ones (controls).

Methods:

- Study Type: Case control study
- Place of Study: Child asthma clinic, Bangladesh Shishu Hospital & Inst.
- Tenure: March-August 2021.
- Case: Asthmatic children, (2-12 years), diagnosed based on the GINA
- Control: Age & sex-matched children having no respiratory illness.
- Method: Compared mean *S. 25 (OH) cholecalciferol* between asthmatic & non-asthma children, *S.* Vit-D estimated using immunofluorescence technique.

Results:

Children with asthma between the ages of 2 and 12 were the respondents whereas children with no respiratory illness served as the control group. Around 60% of the asthma case group had vitamin D deficiency, compared to the control group's adequate vitamin D levels. Insufficient/deficient S. Vitamin D level was detected in a significantly higher (p 0.01) percentage of asthmatic children compared to the control children.

Conclusion:

Mean levels of S. Vitamin D were significantly lower among asthmatic children compared to controls. Significantly higher (p<0.01) proportion of asthmatic children had insufficient/ deficient S. Vitamin D status compared to controls. Likelihood of having Low Vitamin D (deficient + insufficient) is 3.4 times higher in asthmatic patients than non-asthmatic control Low vitamin D status remain a predictive factor for developing asthma.

Vitamin D [Serum 25(OH) cholecalciferol] Insufficiency is Associated with Childhood Asthma: Recent Findings among Bangladesh Children

Nabila Tabassum[1], Kazi S. Anwar[2], Md. Abid H. Mollah[3], Probir K. Sarkar[4]
Department of Pediatrics, Bangladesh Inst. of Child Health and Dhaka Shishu Hospital, Dhaka, Bangladesh.

BACKGROUND

- Vitamin D has a role in asthma due to its effects on airway epithelium, bronchial smooth muscle & immune-modulatory effects on innate and adaptive immune systems.
- Lower level of *S.25(OH) cholecalciferol* is associated with increased childhood asthma prevalence, less responsiveness to corticosteroids, frequent exacerbations, increased disease severity & hospitalizations.
- We examined interaction between childhood asthma & Vit. D

OBJECTIVES

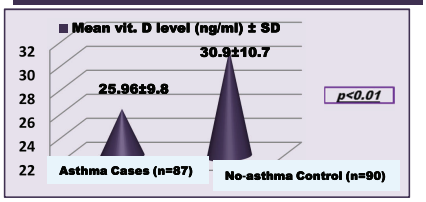
- Assess the clinico-epidemiological features of childhood asthma, aiming to determine if Vitamin D among asthmatic children (cases) differ from that of non-asthmatic ones (controls).

METHODS

- **Study Type:** Case control study
- **Place of Study:** Child asthma clinic, Bangladesh Shishu Hospital & Inst.
- **Tenure:** March-August 2021.
- **Case:** Asthmatic children,*(2-12 years)*, diagnosed based on the GINA
- **Control:** Age & sex-matched children having no respiratory illness.
- **Method:** Compared mean *S. 25 (OH) cholecalciferol* between asthmatic & non-asthma children, *S.* Vit-D estimated using immunofluorescence technique.

RESULTS

Mean Vit. D level among case & control



Vit. D status among Asthma & Non asthma

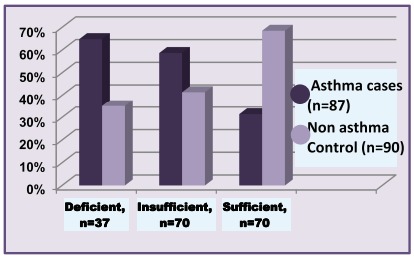


Table: Evaluation of crude association of Vit. D status between asthmatic & non-asthmatic

Serum Vitamin D status	Asthma Children (n=87)	Non asthma children (n=90)	Odd ratio (OR) 95% CI	P value
Low (deficient+ insufficient) (n=107)	65 (75%)	42 (47%)	3.37 (1.78-6.38)	<0.01
Sufficient (n=70)	22	48		

CONCLUSION:

- Mean levels of S. Vitamin D were ***significantly lower*** among asthmatic children compared to controls.
- ***Significantly higher (p<0.01) proportion of asthmatic children had insufficient/ deficient S. Vitamin D status compared to controls.***
- Likelihood of having Low Vitamin D (deficient + insufficient) is **3.4 times** higher in asthmatic patients than non-asthmatic control
- Low vitamin D status remain a predictive factor for developing asthma.

LESSON LEARNT/FUTURE DIRECTIONS

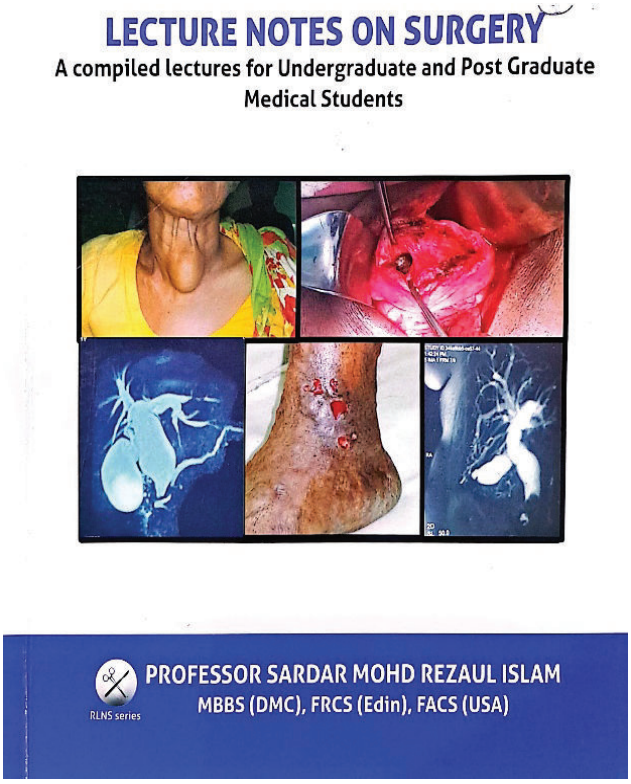
Data recommends routine vit- D screening in asthma is crucial

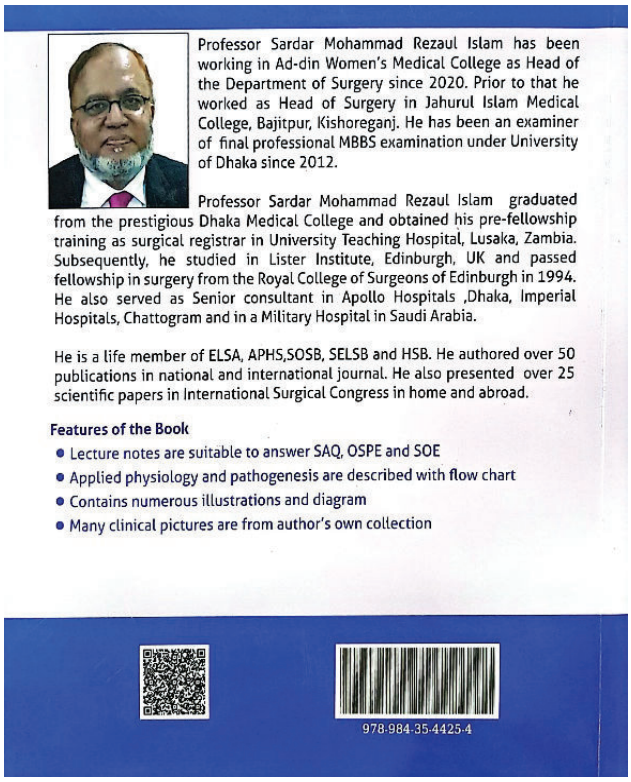
Underscores importance of potential future efficacy trial of Vit-D supplementation in asthmatic children to minimize asthma morbidity in LMICs/ BD

News and Views

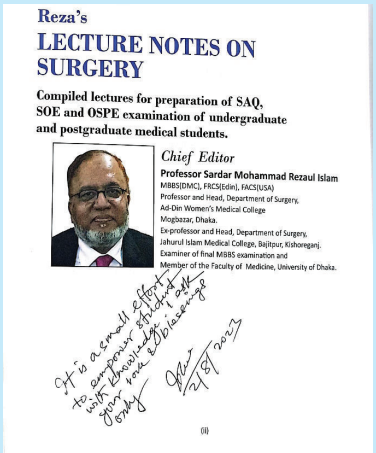
Published Books: Prof. Dr. Sardar Md. Rezaul Islam Reza

The MRU wishes to accord hearty congratulations and a large applaud to Prof. Sardar Mohammad Rezaul Islam for his excellent drive in publishing an invaluable yet largely demanding book on Lecture Notes on Surgery. All the MBBS and post graduate students will be largely beneficial in utilizing this clinical surgery lecture notes.





Cover of the book



The contents of this excellent book remain as follows

- Principles of Surgery
- Breast and Endocrine
- Hepatobiliary
- Alimentary System
- Operative Surgery
- Hernia

Preface of first Edition

The book is primarily aimed at undergraduate students, who are preparing for SAQ, SOE and OSPE parts of surgery final MBBS examination. Every topics are presented in a summarized way with explanation, wherever appropriate. Chapters are selected considering the latest syllabus and curriculum adopted by BMDC.

Publishing this book has been my dream since I came to teaching. My hand written lecture notes (done by my students) were compiled as book form and were being sold in photocopy shop. This made me realize that my lecture notes need to be published in a book form for student's smooth preparation for final MBBS surgery examination. I furnished my lecture notes with diagram, flow chart, X-ray and clinical pictures from my own collection. Clinical pictures and diagram which are not available in my archives are collected from text books and open access publications. I sincerely express my thankfulness and gratitude to all these resources whose contributions were utilized in this book.

This is probably the first attempt to publish a comprehensive lectures notes on surgery aiming under-graduate medical students in our country. I hope this book will be well acknowledged by students and teachers and other members of surgical fraternity. I tried my best to correct factual error and misspelling. I beg my apology if still some errors remained unnoticed. I welcome any suggestion and recommendation to improve the book in its subsequent edition.

I, sincerely, express my gratitude to my beloved wife **Dr Sanjida Parveen** and my children, who have been encouraging me to publish this book for medical students since a long time. Their support were always my strength to accomplish this difficult task of publishing a book. I am so grateful to my teachers of undergraduate education in **Dhaka medical college** and my trainers in **University Teaching Hospital Lusaka, Zambia.** I am immensely indebted to **Prof. Malcolm Wright,** Professor of applied physiology of **University of Edinburgh** for his great lectures in **'Scientific Foundation of surgery'** course in **Lister Institute**, Edinburgh, UK. I have got a strong foundation of surgical physiology through his lectures.

I am grateful to my colleagues and students in **JIMC** and in **AWMC,** who have been constant source of inspiration in this journey of my teaching career. I am thankful to my patients who contributed immensely by allowing their pictures to be publish for educational purpose. All my efforts will be successful if this book becomes beneficial for medical students and ease their final professional and postgraduate examination. The second volume of the book will cover the remaining part of the BMDC syllabus of surgery, Insha Allah.

Professor Sardar Mohammad Rezaul Islam
MBBS(DMC), FRCS(Edin), FACS(USA)