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From the Desk of Editor-in-Chief

We are delighted to inform that the Volume 9, Number 2 of the Dhaka Central International Medical College Journal (DCIMCJ) is going to be published very soon. In this issue we have added a new section, Medical Quiz: Images. We are grateful to Almighty Allah. We are sending the complimentary copies of the journal to the libraries of most of the medical college and other medical institutions in Bangladesh. Already our journal has been approved by Bangladesh Medical & Dental Council (BMDC). We invite the doctors of medical colleges and institutes to submit their research articles to the journal committee for publication. We accept both hard & soft copies of the articles. We go through the papers and if necessary, communicate the authors. We also thank all the authors for giving us opportunity to publish their research papers in this journal. We have tried our best to avoid erroneous information. We like to add here that DCIMC Journal and its editorial board accept no liability for any inaccurate and misleading information, opinion and statements. It is the responsibility of the individual author (s). We have mentioned the instruction for the authors in this issue. We request the contributing authors to follow the instructions for their manuscripts. We appreciate our chairman, editors, members and advisors for their encouragement and also appreciate the contributors and reviewers for their participation. Last of all we welcome valuable suggestion, opinion, advice and constructive criticisms for improvement of the quality of the journal.



Prof. Bidhu Bhushan Das
Editor-in- Chief

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Electronic submission of manuscripts is strongly encouraged, provided that the text, tables, and figures are included in a single Microsoft Word file (preferably in Arial font).

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Five types of manuscripts may be submitted:

Editorials:

It will be preferably written invited only and usually covers a single topic of contemporary interest.

Original articles:

These should describe new and carefully confirmed findings, and experimental procedures should be given in sufficient detail for others to verify the work. The length of a full paper should be the minimum required to describe and interpret the work clearly.

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I. A. Preparing manuscript for submission to DCIMCJ Editors and reviewers spend many hours reading manuscripts that are easy to read and edit. Much of the information in this journal`s Instructions to Authors is designed to accomplish that goal in ways that meet each journal`s particular editorial needs. The following information provides guidance in preparing manuscripts for this journal.

Condition for submission of manuscripts:

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2. Margin should be 5 cm for the header and 2.5 cm for the remainder.
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   - Title page
   - Summary/abstract
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Page should be numbered consecutively at the upper right hand corner of each page beginning from the title page

I. A. 1.a. General Principles:

- The text of observational and experimental articles is usually (but not necessarily) divided into the following section: Introduction, Methods, Results, and Discussion. This so-called “IMRAD” structure is a direct reflection of the process of scientific discovery.

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- Double-spacing all portions of the manuscript- including the title page, abstract, text, acknowledgments, references, individual tables, and legends- and generous margins make it possible for editors and reviewers to edit the textline by line and add coments and queries directly on the paper copy.
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- Authors should number on right upper corner of all of the pages of the manuscript consecutively, beginning with the title page, to facilitate the editorial process.

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Research reports frequently omit important information. Reporting guidelines have been developed for a number of study designs that DCIMC journals ask authors to follow. Authors should consult the information for Authors of this journal. The general requirements listed in the next section relate to reporting essential elements for all study designs. Authors are encouraged also to consult reporting guidelines relevant to their specific research design. A good source of reporting guidelines in the EQUATOR network (http: //www.equator-network.org/home/) or CONSORT network (http://www.consort-statement. org).

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- Should be limited to 250 words
- The abstract should provide the introduction of the study and blinded state and should state the study's purpose, basic procedures (selection of study subjects or laboratory animals, observational and analytical methods), main findings (giving specific effect sizes and their statistical significance, if possible), and principal conclusions. It should emphasize new and important aspects of the study or observations. Articles on clinical trials should contain abstracts that include the items that the CONSORT group has identified as essential (http: //www. consort-statement. org).
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- Provide only directly pertinent primary references, and do not include data or conclusions from the work being reported.

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- Link the conclusions with the goals of the study but avoid unqualified statements and conclusions not adequately supported by the data. In particular, avoid making statements on economic benefits and costs unless the manuscript includes the appropriate economic data and analyses. Avoid claiming priority or alluding to work that has not been complete. State new hypotheses when warranted, but label them clearly as such.

I. A 9. References:

I. A. 9. a. General considerations related to

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- Tables capture information concisely and display it efficiently.

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- Type or print each table with double-spacing on a separate sheet of paper. Number tables consecutively in the order of their first citation in the text and supply a brief title for each.

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- Identify statistical measures of variations, such as standard deviation and standard error of the mean.

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  - Word limit 150-200 words
  - Pertinent information only

- **Material and methods:**
  - Study Design
  - Duration and place of study
  - Ethical consent
  - Patient consent
  - Statistical analysis and software used.
- **Result:**
  - Clearly present the data
  - Avoid data redundancy
  - Use table information at the end of the sentence before full stop between the small bracket
- **Discussion:**
  - Avoid unnecessary explanation of someone else work unless it is very relevant to the study
  - Provide and discuss with literatures to support the study
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- **Conclusion:**
  - Give your conclusion
  - Any recommendation
- **Acknowledgement:**
  - Acknowledge any person or institute who have helped for the study
- **Reference:**
  - Abide by the Vancouver style
  - Use reference at the end of the sentence after the full stop with superscript
- **Legends:**
  - Table
  - Figures

The editor reserves the right to style and if necessary, shorten the material accepted for publication and to determine the priority and time of publication

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DCIMCJ

Editorial

DCIMCJ 2022 July;9(2):13-16

Online Medical Education/Teaching During and After Covid-19 Pandemic

Begum R[1], Chowdhury MAA[2]

Introduction:

The dawn of the year 2020 has brought the world to face off with the worst reality of the millennium in the form of one of the most contagious respiratory infections caused by the novel corona virus, named coronavirus-2019 (COVID-19). Within a short time span, the disease had acquired such a mammoth proportion that World Health Organization had to declare the corona virus outbreak to be a pandemic on March 11, 2020.

2019 Coronavirus disease is a disease caused by a novel coronavirus called severe acute respiratory syndrome coronavirus. On December 31, 2019, WHO first learned of a cluster of pneumonia cases of the novel coronavirus reported in the city of Wuhan, People's Republic of China. This major outbreak has had a profound impact on all walks of life.. In particular, in the education sector, the decision to close, partially close or reopen schools should be guided by a risk management mindset, more so to maximize the education, well-being and health benefits for students, teachers, staff and the broader community, and to help prevent another outbreak of COVID-19 in the community. The decision to resume classes should be based on a careful assessment of the situation and consultation with various stakeholders, including Page 3/29 health and education decision makers, teachers and other school staff, parents, and medical and community workers. Thus, changing the current classroom approach becomes a new and viable measure.

1. Dr. Rahana Begum, Associate Professor, Department of Community Medicine, Dhaka Central International Medical College.

2. Dr. Md. Anwarul Alam Chowdhury, Associate Professor, Department of Biochemistry, Dhaka Central International Medical College.

The World Health Organization states, "If children are unable to attend school, they should be supported to ensure that students have continued access to educational materials and technologies."

Online education is an educational system where information technologies and communications are used for the acquisition of knowledge from remote locations. It uses internet and video, audio, text communications as well as software to create the learning environment. The synonyms of online classes are virtual class, e-learning, distance learning, etc. The online classroom replaces the traditional classroom of blackboard, whiteboard, projectors of an educational institute with a virtual environment. Moving smoothly from an environment of conventional education to a virtual platform could not happen overnight. However, the massive efforts made by many institutions in a short time proved that change is possible2020.The government of Bangladesh closed all in campus educational activities due to the COVID-19 pandemic since 18th of March 2020 and that clicked a sudden pause of teaching-learning activities. As like in other countries, the online class has introduced a major focus in the education system of Bangladesh. However, virtual teaching had been a new experience in almost all medical colleges; sudden closures of face-to-class gave the least opportunity to both the faculty and students to get adopted with the new option of virtual class and classroom.

Since 2000, online education has become an important research direction in the field of education as an important supplement to the traditional education model. As the Internet industry continues to upgrade, the software and hardware equipment

required for online teaching continues to change, making the effect of online education medical education's networking process has been ahead of other disciplines. Online education in medicine has played an extremely important role for the majority of undergraduate and postgraduate teaching work and even for the continuing education of clinicians. Since the novel coronavirus outbreak, social factors have contributed to the flourishing of online education, and the hotspots and directions of research have changed.

Medical education involves pre-clinical and clinical teaching to build a strong knowledge foundation and clinical experience for the medical students. Their physical presence in inpatient and outpatient clinical settings is imperative for the successful practice of early clinical experiences and the clerkship curriculum.1 However, the COVID-19 pandemic has caused substantial ramifications on the medical education system. This paper aims to critically evaluate the impact of the COVID-19 pandemic on medical education and to recommend possible solutions.

The severe contagious nature of the coronavirus SARS-CoV-2, its high mortality rate combined with a lack of knowledge of the virus pushed the world to change the daily lifestyle to isolation, staying at home, quarantine, wearing mask, social distancing by remaining two meters apart from others, and work from home, etc. Consequently, medical education is facing many challenges on teaching, assessment, and feedback to the students. The pandemic has also caused worldwide mental health anxiety, depression, and suicidal attempts. The pandemic has had grave repercussions on medical education in that the students have had reduced exposure to clinical specialties that would ultimately lead to a detrimental effect on their examination performance, confidence, and competency. Pre-clinical medical students face challenges as the face-to-face teaching and other hands-on training such as cadaveric dissections, practical sessions using physical aids such as bones, specimens, and models and laboratory classes cannot take place.

On the other hand, online teaching sessions broke the monotonous routine and were a major stress reliever from this ongoing pandemic along with the pressure of completion of subject course. It has been suggested that universities should consider utilizing other modes of learning like live teleteaching, video conferencing so that student engagement and interactivity can be preserved.

Online teaching is helpful in the way to guide the student in learning in context to their curriculum rather than leaving the students on their own in the current situation. Adaptation and understanding to online teaching among students have to be assessed at regular intervals. Their points of view are of paramount importance in decision-making process for further medical education. Recently, the National Medical Commission has also mooted online teaching as valid for medical education. Medical students are interested in being part of this process which may impact their education.

Difficulty to understand and no prior training were major lacunae cited by teachers and the taught. Bangladesh, being a developing country seems managed to cope with the COVID-19 catastrophe in terms of medical education. However, more needs to be done to supplement the existent teaching pattern and preparedness of teaching faculty by incorporating online assignments and assessment methods, strengthening digital infrastructure in medical schools, and training support for teachers.

Conclusion:

"Necessity is the mother of invention," this age-old proverb finds its supreme relevance in today's scenario. It's been more than a decade since when the policymakers are advocating the use of online resources in routine teaching and practical skills (e.g., simulation laboratories).[1] A sudden disruption in education during Corona Virus Disease 2019 (COVID-19) has precipitated the practice of online education in a big way.

Promoting student motivation and participation at all levels were the main lessons learned for enhancing online learning and teaching experiences in undergraduate medical education. Key elements to reach this goal are, among others, planning, coordination, communication, and pedagogical coherence.

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DCIMCJ

Original Article

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Role of HRCT Imaging in Diagnosis and Evaluation of Novel Corona (Covid-19) Pneumonia, Correlated With RT-PCR.

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Abstract:

Background: Pneumonia and respiratory failure due to the coronavirus disease 2019 (COVID-19) is recognized as the global health hazard now. Recent studies support that HRCT is the most useful tool for diagnosis, treatment planning and follow up of COVID-19 patients. Objective: To assess radiological findings of high resolution CT scan in diagnosis of COVID-19 and also to see the sensitivity specificity, accuracy, positive and negative predictive value against RT-PCR. Materials and Method: This cross sectional prospective observational study was carried out in department of Radiology and imaging, Dhaka Central International Medical College Hospital Dhaka, Bangladesh. 230 inpatients with diagnosed or suspected COVID-19 were included and sent for HRCT and RT-PCR testing. Detailed clinical data, chest HRCT basic performances and certain signs (Ground-glass opacity, consolidation, crazy paving pattern, fibrosis and air trapping) were quantified. HRCT diagnosis was compared with RT-PCR diagnosis. Results: Extent of HRCT lung involvement were mild 66 cases (30.27%), moderate 61 cases (27.98%) and severe in 41 cases (18.80%). Common CT finding was ground glass opacity (GGO) in 198 (90.82%) cases. Among them 163 (74.77%) cases had GGO plus consolidations and ground glass opacity alone were 60 (27.52%) cases, crazy paving pattern was seen in 72 (33%) cases, consolidation alone in only 8 (3.67%) cases. Most of the lesions were multiple and involved all the 5 lobes in 132 (60.55%) cases. The lesions were distributed mostly at the periphery 198 (90.82%) and posterior 187 (85.77%) region. In 129 (59.17%) cases the distribution were diffuse but predominantly peripheral. Most commonly involved lobe was right lower lobe 189 (86.70%) followed by left lower lobe 186 (85.32%). Among other findings reverse halo sign 33 (15.130%), sub-pleural band 24 (11%), thickened vessels 121 (55.50%), pleural effusion 11 (5.04%) were found in our study. There were 9 (4.12%) cases with unilateral and 200(91.74%) cases with bilateral lung involvement. No abnormal finding in HRCT chest was seen in 4 (1.83%) cases who were RT-PCR positive. Conclusion: HRCT can detect COVID-19 changes in different phases, and treatment outcome can be accessed with the help of the follow-up chest scans. HRCT can also assess lung condition and guide treatment steps. HRCT carries acceptable sensitivity and specificity for covid-19 diagnosis, so it can be the diagnostic tool in symptomatic patients where RT-PCR facilities are not available or time consuming.

Keywords: HRCT, RT-PCR, Covid-19, GGO

Introduction:

COVID-19 viral infection has killed millions of people worldwide in last 2 years. Among them thousands died here in Bangladesh with complications of this viral infection. Major cause of deaths is lungs fibrosis andrespiratory failure.

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It is a novel pathogenic human coronavirus first identified in Wuhan, Hubei Province, China in December 2019. It transmits human-to-human between close contacts, and can cause serious coronavirus disease (COVID-19), especially pneumonia.

On January 30, 2020 the World Health Organization (WHO) announced that the outbreak of COVID-19 has become a Public Health Emergency of International Concern, and declared it a pandemic on March 11, 2020[1]. First case was reported in 8th March 2020 in Bangladesh and first death was recorded in 18th March 2020. Up to May 27th of 2020, number of confirmed cases in Bangladesh raised to 36751, of which 522 died[2]. As it is an infectious disease, early diagnosis is the only way to isolate the infected patients and to protect the other people. COVID -19 RT-PCR of viral nucleic acid collected from bronchial or nasopharyngeal swab is regarded as the reference standard. Nucleic acid amplification testing (NAAT), most commonly with a reverse-transcription polymerase chain reaction (RT-PCR) assay, to detect SARS-CoV-2 RNA from the upper respiratory tract is the preferred initial diagnostic test for COVID-19 [3]. Rapid RT-PCR tests appear to perform comparably to standard laboratory-based NAAT, but rapid isothermal tests may be less sensitive[4-7]. A positive nucleic acid amplification test (NAAT; eg, RT-PCR) for SARS-CoV-2 generally confirms the diagnosis of COVID-19.

However, false-negative RT-PCR from upper respiratory specimens have been well documented. Repeat testing is generally performed 24 to 48 hours after the initial test. False-positive results are rare but have been reported with certain platforms[8]. Reported false-negative rates have ranged from less than 5 to 40 percent[9-11]. The sensitivity of the RT-PCR assay is approximated to around 60-71% [12]. A high number of false negatives are likely because of ongoing genomic mutations of SARS-CoV-2, technical and operator, lack of resources, and prowess needed for this genomic test[13-14]. A high-resolution computed tomography (HRCT) chest is a rapid diagnostic technique for COVID-19 that has an added benefit of determining the severity, complications, andtreatment plan for infected patients[15-16].

HRCT chest findings typical of COVID-19 pneumonia include bilateral multifocal peripheral - based ground - glass opacities, crazy paving, consolidation and intra & inter lobular septal thickening and few emerging manifestations like pleural changes, fibrosis and nodules and reverse halo sign[17]. HRCT has a higher sensitivity of approximately 89% and a moderate specificity of up to 68%[18]. Many types of research show HRCT to be one step ahead of RT-PCR as a first-line screening investigation for COVID-19 in emergency and hospital settings owing to its higher sensitivity and propose the idea of using chest CT or HRCT as a standard of reference along with clinical and laboratory evaluation for the diagnosis of COVID-19. Computed tomography (CT) of the chest is increasingly recognized as strong evidence for early diagnosis, because the changes in chest imaging sometimes maybe earlier than clinical symptoms. Chest CT can be used for a rapid triage of patients in multiple emergency departments during COVID- 19 epidemic. The aim of this study is to analyze the typical lung features in HRCT films of COVID patients and also to compare sensitivity and specificity against RT-PCR.

Materials and methods:

This prospective observational cross sectional study was carried out in department of Radiology & imaging Dhaka Central International Medical College Hospital in collaboration with Department of Medicine, Virology and COVID unit from March 11th to 30th May 2021. Patients referred from COVID unit of DCIMCH with RT-PCR positive or suspected COVIDS were included in this study. RT-PCR negative, clinically not suspected as covid-19 and unwilling to participate this study were excluded. We selected random 230 patients during the research period, but we failed to collect all reports of 12 patients. So, our final sample size is 218. All 218 patients had RT-PCR reports, and underwent HRCT scan of chest without contrast in a 128 slice CT scanner Scnaria machine with reconstructions of the volume at 0.625mm to 1.5mm slice thickness for high resolution reconstruction scan and scanning time is less than 5 sec. Patients were placed in supine position with head first. Axial data was taken with coronal reconstruction. For each patient HRCT scan

of chest was evaluated for the following characteristics: Presence of ground glass opacities, consolidation, crazy paving pattern, mixed ground glass opacities with consolidation, reverse halo sign, sub-pleural bands, thick vessels, pleural effusion, number of lobes affected and degree of involvement of each lung lobe. The signs of ground-glass opacity (GGO), consolidation, fibrosis and air trapping were analyzed quantitatively using a radiologic scoring system ranging from 0-25 points, which was an adaptation of the method previously used to describe idiopathic pulmonary fibrosis and SARS (Ng et al., 2004). Each lung lobe was evaluated by 0-5 points, on the basis of the area involved, with score 0 for normal performance, 1 for less than 5% of lung lobe areas involved, 2 for 6%–25%, 3 for 26%–50%, 4 for 51%–75%, and 5 for more than 75%. A total score was eventually recorded via the addition of the score of each lobe. [a). No involvement- no lobe- Score 0; b). Minimum involvement – 1 lobe-score: 1; c). Mild involvement –lobe 2 Score 2; d). Moderate involvement- no of lobe 3 score 3; d). Severe involvement–No of lobe 4 score 4. Four stages are observed in COVID-19 pneumonia. Early initial stage (0-4 days) Normal CT findings or GGO only. Progressive (5-8 days) Increased GGO and crazy paving appearance. Peak stage (9-13 days) consolidation with mixed GGO. Absorption stage (>14 days) Fibrotic stripes. Short personal history and detail clinical features were enlisted.

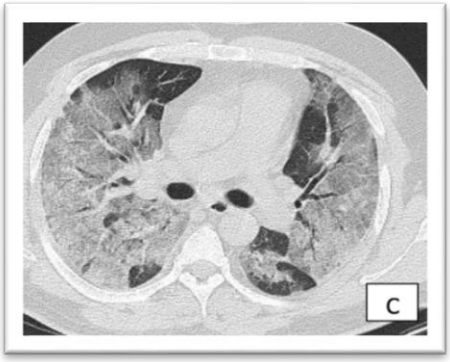


Figure 1: Dense ground glass infiltration and consolidation diffusely affecting both lungs.

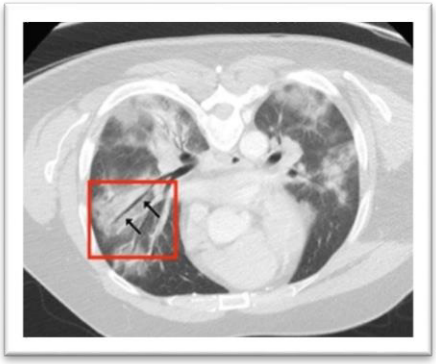


Figure2: Bilateral patchy ground glass and consolidative changes with areas of confluence. Here is a linear air bronchogram (black arrow) surrounded by peri-bronchial consolidation and GGO.

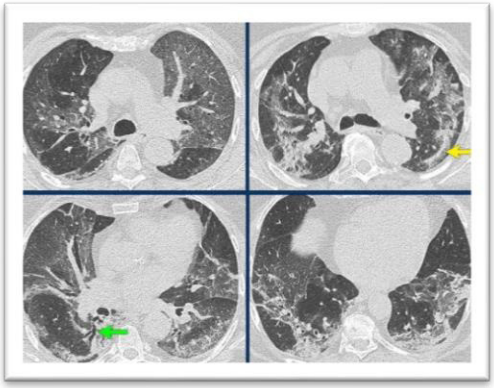


Figure 3: There is bilateral subpleural GGO, consolidation in right lower lobe with bronchiectasis (green arrow), fibrous bands (yellow arrow).

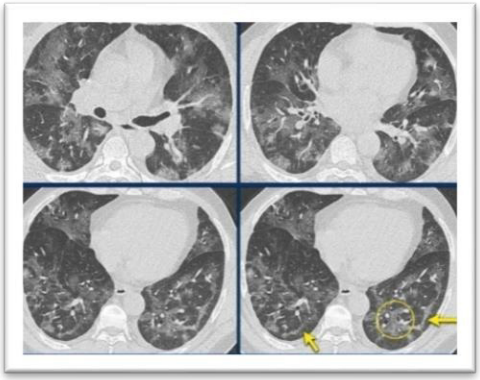


Figure 4: Showing bilateral GGO, fibrotic bands (arrow) and dilated vessels (circle).

Result:

Total 218 confirmed patients was included in our final study. 110 (50.46%) of them were male, and 108 (49.54%) were female. Mean age was 52.65±11.6 (SD), with majority were in 51-60 years group (33%). 6 patients were younger than 20 years and 58 were more than 60 years age. Radiology room history revealed smoking 30 (13.76%), diabetes 26 (11.92%), bronchial asthma 7 (3.2%) and COPD 9 (4.12%). Major presentation were fever 185 (84.85%), sore throat 94 (43.11%), fatigue 91 (41.74%), shortness of breath 70 (32.11%), headache 41 (18.80%), dry cough 37 (16.97%) and running nose 156 (6.88%). HRCT showed no lung involvement in 12 (5.5%) cases, mild involvement in 66 (30.27%) cases, moderate involvement in 61 (27.98%) cases and severe involvement in 41 (18.80%) cases. Among the 218 patients, 203 had positive findings of COVID-19 in HRCT, and were counted as positive by HRCT. 15 patients had no radiological findings of covid, and were counted as negative in HRCT. Among the 218 patients, 204 were RT-PCR test positive, of them 200 were also positive for HRCT, they are true positive (TP). Among 203 HRCT positive patients, 3 patients were negative in RT-PCR, hence were false positive (FP) due to pathology other than COVID- 19. 11 patients among 15 HRCT negative cases were also tested negative in RT-PCR, they are true negative (TN). There were 4 patients tested positive in RT-PCR but negative in HRCT, they are false negative (FN). Overall HRCT sensitivity was 98%, specificity 78%, PPV 98% and NPV 73%, and Accuracy 96% respectively. Common CT finding was ground glass opacity in 198 (90.82%) cases. Among them 163 (74.77%) cases had GGO plus consolidations and ground glass opacity alone were 60 (27.52%) cases, crazy paving pattern was seen in 72 (33%) cases, consolidation alone in only 8 (3.67%) cases. Most of the lesions were multiple and involved all the 5 lobes in 132 (60.55%) cases. The lesions were distributed mostly at the periphery 198 (90.82%) and posterior 187 (85.77%) region. In 129 (59.17%) cases the distribution were diffuse but predominantly peripheral. Most commonly involved lobe was rightlower lobe 189 (86.70%) followed by left lower lobe 186 (85.32%). Among other findings reverse halo sign 33 (15.130%), sub-pleural band 24 (11%), thickened vessels 121 (55.50%), pleural effusion 11 (5.04%) were found in our study. There were 9 (4.12%) cases with unilateral and 200 (91.74%) cases with bilateral lung involvement. No abnormal finding in HRCT chest was seen in 4 (1.83%) cases who were RT-PCR positive.

Table- I: Comparison of HRCT and RT-PCR diagnosis (n= 218)

HRCT Total	RT-PCR +ve	RT-PCR –ve
Positive 203	200 (TP)	03(FP)
Negative 15	04 (FN)	11 (TN)
Total 218	204	14

Table- II: Sensitivity, specificity, positive and negative predictive value and accuracy of HRCT considering RT-PCR as gold standard.

Sensitivity	98.03%
Specificity	78.57%
PPV	98.53%
NPV	73.33%
Accuracy	96.78%

Table- III: HRCT findings of case series (n= 218)

Findings	Case	Percentage
Ground Glass Opacity	209	90.82%
GGO + Consolidation	163	74.77%
Consolidation	171	78.44%
Crazy paving	72	33%
Reverse halo	33	15.13%
Thickened vessels	121	55.50%
Sub-pleural band	24	11%
Pleural effusion	11	5.04%

Table- IV: Degree of lung involvement in HRCT

Degree of involvement	% of involvement	Lobe involved	Patient number	(%)
None	0%	0	12	(5.5%)
Minimum	1-25%	1	38	(17.43%)
Mild	26-50%	2	66	(30.27%)
Moderate	51-75%	3	61	(27.98%)
Severe	75-100%	4	41	(18.80%)
Total: 218				

Table - V: Clinical history of patients

Feature	Patient number	(%)
Smoking	30	(13.76%)
Diabetes	26	(11.92%)
Asthma	7	(3.2%)
COPD	9	(4.12%)
Fever	185	(84.86%)
Fatigue	91	(41. 74%)
Sore throat	94	(43.11%)
Headache	41	(18.80%)
Dry cough	37	(16.97%)
Running nose	15	(6.88%)

Figure- 5: Age distribution of case group (n= 218)

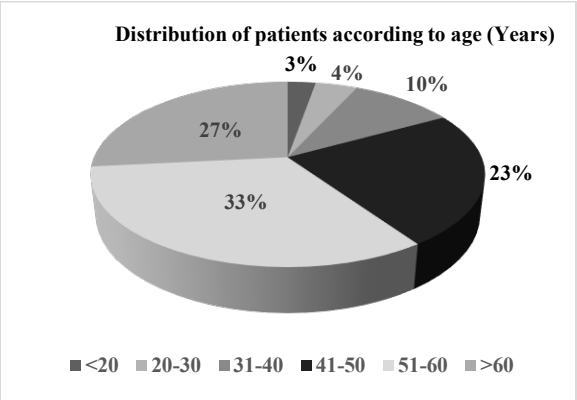
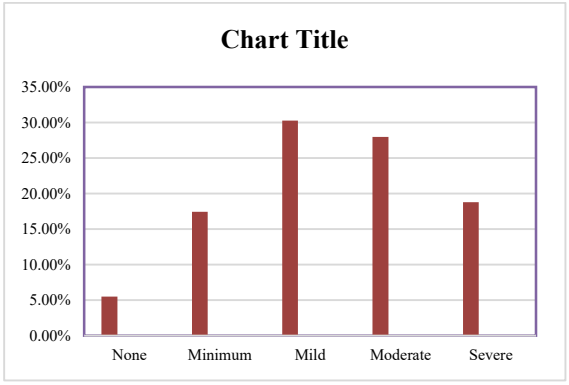


Figure – 6: Degree of lung involvement in Covid-19 (n=218)



Discussion:

Total 218 confirmed patients was included in our final study. 110 (50.46%) of them were male, and 108 (49.54%) were female. Mean age was 52.65±11.6 (SD), with majority were in 51-60 years group (33%). 6 patients were younger than 20 years and 58 were more than 60 years age. Radiology room history revealed smoking 30 (13.76%), diabetes 26 (11.92%), bronchial asthma 7 (3.2%) and COPD 9 (4.12%). Major presentation were fever 185 (84.85%), sore throat 94 (43.11%), fatigue 91 (41.74%), shortness of breath 70 (32.11%), headache 41 (18.80%), dry cough 37 (16.97%) and running nose 156 (6.88%).

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In a study of Qureshi et al published in 2020- Out of 116/121 diagnosed covid-19 patients, 38(32.75%) showed sub-pleural consolidation, 19(16.37%) consolidation with air-bronchogram, 29(25.0%) crazy paving sign, one pleural effusion (0.86%) and 18 cases (15.51%) displayed reticulations. 11cases(9.48%) had isolated ground glass appearances, while all categories showed it to variable extent. 65/116 patients (56.03%) were PCR-positive. HRCT-Thorax revealed sensitivity: 97.41 %, specificity: 80%, PPV: 99.12%, NPV: 57.14%, and diagnostic accuracy of 96.69% for COVID-19 pneumonia[19].

Yousuf et al in 2021 found amongst 48 suspects with negative RT-PCR assay, 38 (79.2%) showed ground-glass opacities, a hallmark feature of COVID-19 pneumonia. A total of 22 (57.89%) of these 38 patients had ground-glass opacities with a crazy-paving pattern, nine (23.68%) mixed ground-glass opacities with consolidation, and seven (18.42%) had pure ground-glass opacities. Among these 79.2% suspects, ground-glass opacities were multifocal in 37 (97.37%), bilateral in 35 (92.10%), peripheral in 36 (94.74%), and dorsally located in 32 (81.6%) cases. Subpleural atelectatic bands were seen in 18 (47.36%) of these, bronchovascular markings were prominent in 15 (39.47%), and reverse halo sign was positive in nine (23.68%) cases. Out of the rest of the cases, three were diagnosed as interstitial lung disease, two as chronic lung disease, and one as active pulmonary tuberculosis. They concluded- the majority of clinically suspected cases for COVID-19 showed hallmark findings on non-contrast HRCT chest scans in keeping with coronavirus disease regardless of a negative RT-PCR assay[20].

Khan et al published their work in 2021 - glass ground opacity was the most prevalent finding in 99% of the patients, followed by lymph node involvement, consolidation, and crazy-paving pattern. Pleural effusion was observed in only 10% of the patients while pericardial effusion and hiatal hernia were present in 5%. In RT-PCR-positive patients, the posterior basal segment of the lower lobe of the right and left lungs were found to be dominantly involved; however, the upper and middle lobes of the right lung were more commonly involved than the left lung. The mean CTSS was significantly higher in patients aged above 50 years ($p<0.001$). The mean CTSS of RT-PCR-negative patients was higher than that of RT-PCR-positive patients (15.18 vs. 14.31, $p=0.537$). They concluded as- RT-PCR has a limited role in the diagnosis of COVID-19. The HRCT scan can detect typical COVID-19 findings even in patients with negative RT-PCR results. Moreover, the use of HRCT scan in determining the disease severity and extent of lung damage can lead to a better assessment of critically ill patients[21].

Hanif et al in 2021 researched 94 patients, 55 (58.5%) males and 39 (41.5%) were females. Out of them, 83% patients had positive HRCT chest findings of COVID-19,17% had negative HRCT chest findings; while 40.4% had positive and 59.6% had negative first PCR. Among the repeat second PCR, 19.6% had negative, 1.8% had positive PCR results; while 78.6% patients didn't undergo repeat PCR. The sensitivity, specificity, NPV, PPV and accuracy of HRCT chest was 92%, 23%, 81%, 45%, and 51%; while of first RT-PCR was 45%, 81%, 23%, 92% and 51%, respectively[22].

Ai et al in a study to find out the correlation of chest CT and RT-PCR testing in corona virus disease 2019 in China concluded that HRCT has 97% sensitivity in diagnosing COVID-19. Wen et al found that HRCT chest has a sensitivity of 93 [23,24].

Among the 218 patients, 204 were RT-PCR test positive, of them 200 were also positive for HRCT, they are true positive (TP). Among 203 HRCT positive patients, 3 patients were negative in RT-PCR, hence were false positive (FP) due to pathology other than COVID- 19. 11 patients among 15 HRCT

negative cases were also tested negative in RT-PCR, they are true negative (TN). There were 4 patients tested positive in RT-PCR but negative in HRCT, they are false negative (FN). Overall HRCT sensitivity was 98%, specificity 78%, PPV 98% and NPV 73%, and Accuracy 96% respectively, which is very similar to all other studies. Thus HRCT images can play an important role in the rapid diagnosis and evaluation of COVID-19 and can be used as a standard method in timely management of patients.

Conclusion:

HRCT scan of chest is the best modality for COVID - 19 patients for diagnosis, treatment planning, response to treatment and assessing patient outcome. HRCT diagnosis can help in symptomatic patients with RT-PCR negative or, where RT-PCR facilities are not available. We radiologists must to be familiar with different key findings on HRCT, to help clinicians and the covid-19 patients. Together with RT –PCR, HRCT findings will increase the sensitivity and specificity of covid-19 diagnosis.

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Original Article

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Coronary Artery Disease and Vitamin D

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Abstract:

Background: Vitamin D deficiency is a prevalent condition in Bangladesh. The aim of this study is to find out whether deficient vitamin D status is associated with coronary artery disease considering cardiovascular risk factors. Methods: We measured 25 (OH) D levels in 50 patients that were diagnosed with coronary artery disease and 50 individuals in the control group who were matched for age and sex with the patients and examined the association between serum 25 (OH) D and coronary artery disease with regard to cardiovascular risk factors. Patients were considered to have confirmed coronary artery disease if they had previous episodes of ST elevation/Non-ST elevation myocardial infarction (MI) or angiographically proven CAD. The control group was family or friends of the patients, which were matched with them for sex and age and didn't have any history of angina pectoris upon clinical evaluation. Results: There was no significant difference in the age and sex between the two groups (P > 0.05). Smoking status, Obesity, high blood cholesterol was significantly different between the patients and the control group (P < 0.05). Despite the higher percentage of the individuals with hypertension in the patient group, the difference between the two groups was not significant. Vitamin D deficiency (25 (OH) D <10 ng/ ml), was significantly higher in the patients (P =0.003). Conclusion: Low vitamin D levels are associated with prevalent coronary artery disease independent of cardiovascular risk factors.

Keywords: Coronary artery disease, 25 (OH) D, cardiovascular risk factors

Introduction:

Vitamin D deficiency is prevalent in most parts of the world. Vitamin D exists in two forms: Ergocalciferol (D2) and cholecalciferol (D3). Ergocalciferol is made in herbal resources and cholecalciferol through UVB (Ultraviolet B) radiation to the body skin. Generally, humans receive vitamin D by being exposed to the sun light or dietary intake, such as fish oil and nutritional supplements[1].Although vitamin D can be obtained from diet or supplements, exposure to sunlight is the main source of this vitamin[2].Solar UV radiation penetrates the skin and converts 7-dehydrocholesterol (7DHC) into previtamin D3, which is rapidly transformed into vitamin D3. Vitamin D from diet and from skin is hydroxylated in the liver to 25 hydroxyvitamin D [25(OH)D], the main determinant of vitamin D status. It is then metabolized in the kidneys in its active form, 1,25-dihydroxyvitamin D, in a tightly regulated process controlled by plasma parathyroid hormone (PTH) levels and serum calcium and phosphorus levels,among others[2].

Although the best-characterized sequelae of vitamin D deficiency involve the musculoskeletal system, a growingbody of evidence suggests that low levels of vitamin D may adversely affect the cardiovascular system[3]. Vitamin D receptors have a broad tissue distribution that includes vascular smooth muscle,[4,5] endothelium,[6] and cardiomyocytes[7].

Invitro, activated 1,25-dihydroxyvitamin D (1,25-OH D) directly suppresses renin gene expression[8], regulates thegrowth and proliferation of vascular smooth muscle cells andcardiomyocytes[9], and inhibits cytokine release from lymphocytes[10]. Studies in knockout mice confirm that the absence ofvitamin D receptor activation leads to tonic upregulation

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ofthe renin-angiotensin system, with the developmentof hypertension and left ventricularhypertrophy[11]. Clinical studies have reported cross-sectional associationsbetween lower vitamin D levels and plasma renin activity[12], blood pressure[13], coronary artery calcification[14], andprevalent cardiovascular disease[15]. Additionally, ecological studies have reported higher rates of coronary heartdisease and hypertension with increasing distance from theequator, a phenomenon that has been attributed to the higherprevalence of vitamin D deficiency in regions with lessexposure to sunlight[16,17].

Many studies have shown an association between vitamin D deficiency and dyslipidemia[18]. A very significant result of the effect of vitamin D on lipid profile was reported by Ponda et al.[19]. In their study, a group of 108,711 subjects with differentserum 25(OH)D and lipid measurements taken from 4 to 26 weeks apart were selected fromamong four million laboratory test results. Investigations of these subjects revealed thathigher serum levels of 25(OH) D correlated with lower levels of total cholesterol, LDL-C, and triglycerides and higher levels of HDL-C in both men and women[19].

The mechanism which causes the protective effect of vitamin D against cardiovascular diseases is not fully understood but several mechanisms have been proposed such as the effect of the vitamin D on the renin-angiotensin system, vessel compliance, blood pressure, parathyroid hormone level and also glycemic control. In addition, vitamin D has anti-inflammatory effects and prevents cholesterol removal by macrophage and foam cell formation on vessels walls. Also, an inverse relation has been seen between vitamin D serum level and coronary artery calcification[20].

The effect of vitamin D status on serum lipids is especially interesting considering that vitamin D and cholesterol share a common precursor, 7DHC, although previous studies yielded divergent results[21].The aim of this study was to investigate the association of vitamin D status with coronary artery disease.

Methods:

This was a cross sectional study that was conducted in BIRDEM General Hospital from July 2021 to December 2021. Fifty Patients were included in case group known to have coronary artery disease. Patients were considered to have confirmed coronary artery disease if they had previous episodes of ST elevation/Non-ST elevation myocardial infarction (MI) or angiographically proven CAD. The control group was family or friends of the patients, which were matched with them for sex and age and didn't have any history of angina pectoris upon clinical evaluation. Written consent was obtained from the. The exclusion criteria of the study were unwillingness to cooperate, presence of chronic renal diseases, neoplastic disease, heart failure, recent major surgical procedure, evidence of hypercalcemia and systemic inflammatory conditions, any infection, liver, disease. The patients on vitamin D and calcium supplements were also excluded.

Study variables including age, sex, smoking status, presence of diabetes and hypertension, usage of antihyperlipidemic, antidiabetic and antihypertensive drugs were gathered through checklist. Weight, height and also the blood pressure of the participants were measured by the standard protocol. The blood pressure was measured two times with a five-minute interval in a sitting position and from the right brachial artery. Then the mean blood pressure was calculated. Body mass index (BMI) wascalculated as weight/height^2 (kg/m^2).

Although 1,25 (OH) 2D is the active form of vitamin D, it is not suitable for measuring vitamin D serum level. 25 (OH) D has a longer half – life and it can more precisely show the food intake and skin production of vitamin D.[22] 2.5 cc of patients and control group blood samples were obtained after 8 hrs of fasting and centrifuged, andwas frozen at -20 c in capped plastic pipes. The levels of 25 (OH) D, Cholesterol and Fasting blood sugar were measured in the laboratory.

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Diabetes was considered as FBS levels ≥7mmol/l or the consumption of antidiabetic drugs. Hypertension was considered as blood pressure≥140/90 or the consumption of antihypertensive drugs. Hypercholesterolemia was considered as blood cholesterol ≥240 mg/dl or the consumption of antihyperlipidemic drugs.

Vitamin D level were measured in the form of 25-hyroxyvitamin D (25(OH) D). 25-hyroxyvitamin D was estimated by HPLC (High Performance liquid Chromatography) method. Patients with 25-hyroxyvitamin D level <10ng/ml were considered vitamin D deficient, 10-40ng/ml considered insufficient and 41-100ng/ml considered as sufficient.

Statistical tests used were Chi–square, independent t test and log regression.The gathered information were analyzed by the statistical software SPSS version 19 (IBM corporation, USA) and $P < 0.05$ was considered significant.

Results:

50 Patients with coronary artery disease and50 healthy individuals participated in this study from whom 31 were females and 69 were males ($P = 0.653$). Table 1 shows the base line characteristics of the participants. There was no significant difference in the age and sex between the two groups ($P > 0.05$). Smoking status, Obesity, high blood cholesterol was significantly different between the patients and the control group ($P < 0.05$). Despite the higher percentage of the individuals with hypertension in the patient group, the difference between the two groups was not significant. Vitamin D deficiency (25 (OH) D <10 ng/ ml), was significantly higher in the patients ($P =0.003$).

Table 1: Baseline characteristics of the studied individuals.

Studied variables	Patient %(N)	Control %(N)	*P*value
Age (Years)			
<50	22(11)	12(6)	0.314
>50	78(39)	88(44)	
Sex			
Male	72(36)	66(33)	0.653
Female	28 (14)	34(17)	
BMI (kg/m2)			
<30	86(43)	10(5)	0.006
≥30	14(7)	90(45)	
Smoking			
Current	26(13)	16(8)	
Past	6(3)	4(2)	0.035
Never	68(34)	80(40)	
DM	58(29)	30(15)	0.020
HTN	62(31)	52(26)	0.082
High Total Cholesterol (240≥mg/dl)	68(34)	28(14)	0.001
Vitamin D level			
<10ng/ml	52(26)	30(15)	0.003
10-40ng/ml	20(10)	12(6)	
40-100ng/ml	28(14)	58(29)	

Discussion:

In our study, it was found that low levels of vitamin D was associated with coronary artery disease. Very low levels of vitamin D (<10 ng/ml) was found in 52% of patient group, whereas it was only 30% in control group. Conversely, sufficient level of vitamin D was found in only 28% of patient group, which was 58% in control group.

Previous studies also conform with the findings of the present study. Kumar et al (2017) found that vitamin D level was significantly lower in patient group (CAD patients) compared with control group (18.2±10.9 vs 28.8±21ng/mL). Vitamin D deficiency was present in 81.4% patient in CAD patients whereas 57.7% in control group. Vitamin D deficiency was found to be an independent predictor of CAD after adjusting effect of other risk factors like hypertension, diabetes, smoking, obesity, high blood cholesterol and level of physical activity with adjusted odds ratio (95% confidence interval) 2.695 (1.148-6.330). They concluded that Vitamin D deficiency is an independent predictor of CAD after adjusting other risk factors emphasizing that vitamin D can be a potential risk factor for development of coronary artery disease. This study was done in Uttar Pradesh of India, which matches with the ethno-demographic pattern of our country[23].

Wang et al performed a longitudinal study on 1739 Framingham Offspring Study participants (mean age 59 years; 55% women; all white) without prior cardiovascular disease. Vitamin D status was assessed by measuring 25-dihydroxyvitamin D (25-OH D) levels. During a mean follow-up of 5.4 years, 120 individuals developed a first cardiovascular event. Individuals with 25-OH D 15 ng/mL had a multivariable-adjusted hazard ratio of 1.62 (95% confidence interval 1.11 to 2.36, P0.01) for incident cardiovascular events compared with those with 25-OH D 15 ng/mL. There was a graded increase in cardiovascular risk across categories of 25-OH D, with multivariable-adjusted hazard ratios of 1.53 (95% confidence interval 1.00 to 2.36) for levels 10 to 15 ng/mL and 1.80 (95% confidence interval 1.05 to 3.08) for levels 10 ng/mL (P for linear trend0.01). Further adjustment for C-reactive protein, physical activity, or vitamin use did not affect the findings. They concluded that vitamin D deficiency is associated with incident cardiovascular disease[24].

Siadat et al (2012) measured 25 (OH) D serum levels in 57 patients that were diagnosed with coronary artery disease upon coronary angiography and 62 individuals in the control group who were matched for age and sex with the patients and examined the association between serum 25 (OH) D and coronary artery disease with regard to cardiovascular risk factors. They found that the odds ratio of being affected by coronary artery disease in individuals with vitamin D deficiency (25 (OH) D < 30 ng/ml) was 5.8 (1.77 - 18.94) after adjustment with cardiovascular risk factors, i.e., blood pressure, diabetes, smoking, obesity, physical activity and high blood cholesterol in comparison with the control group. They concluded that low levels of 25 (OH) D are associated with prevalent coronary artery disease independent of cardiovascular risk factors[25].

Conclusion:

Our study this study suggests that low vitamin D levels are associated with prevalent coronary artery disease independent of cardiovascular risk factors. Further investigations could demonstrate the need for vitamin D supplementations in order to prevent cardiovascular disease.

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Original Article

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A Randomized, Double-blind, Placebo Controlled Trial to Assess the Effect of L-carnitine in Patients with Diabetic Peripheral Neuropathy to Relief Pain

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Abstract:

Diabetic peripheral neuropathy is one of the common complication of chronic diabetes mellitus, with a 20-50 % prevalence. The epidemic spread of the disease has raised concern among physicians and researchers. A variety of agents or medicines with potential effect have been studied to control development of peripheral neuropathy. Objectives: To investigate the effect of l-carnitine in pain relief in patients with diabetic peripheral neuropathy. Methods: This study was a randomized, double blind, placebo controlled prospective interventional study which was conducted in the Department of Pharmacology in collaboration with the Department of Endocrinology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from September 2018 to January 2020.A total of 71patientssuffering from diabetic peripheral neuropathy were selected according to inclusion and exclusion criteria and 66 patients (92%) had completed the study. Group (group A) consisted of 32 patients who received anti-diabetics with placebo for 10 weeks. And the intervention group (group B) consisted of 34 patients received anti-diabetics with L-carnitine oral syrup. The pain was assessed by Visual Analogue Scale (VAS).Results: It was observed that the (mean ± SD) VAS score of pain in DPN patients in intervention group (35.58±10.5) was reduced significantly (p<0.001) compared to the placebo group (54.06±10.29) after 10 weeks of treatment. Conclusion: It is being concluded that oral administration of l-carnation in DPN patients had effectively and significantly improved pain of diabetic polyneuropathy. l- carnitine supplementation in diabetic polyneuropathy patients had effectively improved the neuropathic pain.

Keywords: Diabetic polyneuropathy, l-carnitine, neuropathic pain

Globally according to an estimation in the year of 2019, about 463 million people are sufferingfrom DM in the world and by the year of 2045, this figure issupposed to be reach about 700 million[1].

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Thus chronic cases of DM may show many micro vascular complications such as neuropathy, retinopathy, and nephropathy. Among them Diabetic Peripheral neuropathy (DPN) is considered the most dreadful micro vascular complications of both types1 and 2 diabetes mellitus[2]. The international diabetes federation has estimated that DPN affects 20-50% of peoplewith diabetes[3]. DPN is defined as the presence of symptoms and/or signs of peripheral nerve dysfunction in patients with diabetes. Hyperglycemia is an important etiology of DPN and anti-hyperglycemic treatment is fundamental for long term prevention. However, simple blood glucose control is not sufficient for this neuropathy. A variety of agents with potential effect on DPN has been given but the present available management is not satisfactory enough to alleviate or correct the peripheral neuropathy of diabetes mellitus[4].

Materials and methods:

This study was conducted in the Department of Pharmacology and in the Department of Endocrinology, BSMMU, Dhaka. This study was conducted From September2018 to January 2020. The study was conducted on 66 patients was suffering from DPN and inclusion criteria were i. Diabetic patients who had been on stable anti-diabetic therapy for 1 year or more and who met clinical criteria for Diabetic Peripheral Neuropathy: such as pain in lower limbs (dull, aching and worse at night), burning sensation in soles off eet, paresthesia in feet, sense of numbness in feet, reduce ability to detect temperature change, diminished perception of distal vibration. ii. Age: From 18 years to 70 years iii. Glycated hemoglobin (HbA1c) level: 6.5% to10%. The Exclusion criteria were i. Patient who were suffering from other causes of peripheral neuropathy for example chemotherapy and HIV patient, rheumatoid arthritis, SLE, alcoholism, vitaminB12 deficiency ,hypothyroidism, hyperthyroidism etc.i i.Lactating and pregnant women, iii.Patients taking anticonvulsants, antidepressants, opioids and other neuropathic pain medication drugs or medicines.

Process of randomization:

After determining the sample size and patients were randomly allocated into two arms prior to the patient enrollment. Randomization was done by online graph pad software by using computer from the website (http://www.graphpad.com/quickcales/ranMenu).

The software automatically generated two distinct set of random numbers after giving necessary inputs (sample size, sets of number). Here every patient had equal chance to be assigned in anyone of the groups (Group A or Group B).The randomization was conducted by a competent third person, a researcher who had no relationship with this research.

Blinding and grouping of study subjects:

Immediately after randomization, random numbers of the sets were assigned as patient code number. Then the sets of code numbers that belongs to the intervention group were written as patients ID number on the packages contained levocarnitine syrup. On the other hand, the sets belong to the control group were designated as patient ID numbers on the packages contained placebo.

This total procedure was conducted by the persons unrelated to this research. The participants and the investigator who require being blind for such study, were effectively blinded from the knowledge about intervention allocation.

Group A (Control group):

This group consisted of 36 patients suffering from diabetic peripheral neuropathy who were treated with placebo at a dose of 1.5 gram oral solution daily for10 weeks in addition to their anti-diabetic drugs.

Group B (Intervention group):

This group consists of 35 patients suffering from diabetic neuropathy who were treated with anti-diabetic drugs plus L-carnitineat a doseof 1.5gram daily for10 weeks.

Data collection:

After initial screening, the demographic data (age, sex, occupation, marital status) and medical history were recorded in data collection sheets. Written informed consent were taken from each patient. The study consisted of 2 visits: a baseline visit and a follow up visit after 10 weeks. 3µl blood were taken for the measurement of HbA1c with glycol haemoglobin test kit according to inclusion criteria. Patients body weight, height, blood pressure and pulse were obtained at the time of enrollment in the study. At baseline data were collected about diabetic peripheral neuropathic pain was measured by VAS (visual analogue scale).

Then patients were assigned to the respective groups. Group B patients were treated with antidiabetic drug along with l-carnitine at a dose1.5gram or a lsolution daily in three divided dose for 10 weeks and group A patient were treated with same dose of placebo solution along with antidiabetic drugs for same duration. Compliance sheet were provided for each patients. Consumption of medicine was ensured by telephone and from patient's compliance sheet. After10 week's neuropathic pain improvement was estimated again and blood was collected from both group to measure the same parameter. Patients were asked to report for any adverse effects of the medication given during the period of study.

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Assessment Visual Analogue Scale (VAS)

Visual Analogue Scale:

For measurement of pain, a visual analogue scale (VAS) was used. VAS is a 0-10 numeric pain assessing scale usually 10cm in length. Validated Bengali version of VAS[10] was used to measure the pain of diabetic neuropathy patients at baseline and at follow up after 10weeks of intervention by l-carnitine. For pain intensity the scale most commonly anchored by no pain (score 0-3), moderately pain (score 4-6), unbearable pain (7-10). Data were collected in the data collection sheets by interviewing and clinical examination of the subjects and results were recorded in separate result sheets.

Data analysis was done by Microsoft Office Excel and online statistical analysis calculator was used to present the data as mean ± SD. All results were appropriately recorded in the computer in tabulated form. The quantitative variables were expressed as mean ± SD. Differences in mean values between two groups were assess by using paired and unpaired t-test. The level of significance was set at 'p' value less than 0.05, 0.01, and 0.001. Data and results were presented in the form of tables, diagrams such as bar diagram and figure as applicable.

Results:

Total 71 patient were enrolled and were randomized into Control group (A, n=36) and Experimental group (B, n=35). Here every patient had equal chance to be assign in any of the groups (Group A or Group B).3 patients from Group A and 2 patients from group B had dropped out from the experiment due to personal cause, delaying in follow up and not willing to get treatment from BSMMU. So 32 patient from Group A and 34 patient from Group B were ultimately available to complete the study. The demographic characteristics of the patients are shown inTable1. In group A, the mean age was 46.96±11.5years and in group B, the mean age was 51.03 ± 8.86 years. There was no significant difference in age between the two groups obtained statistically (P=0.06).

Table1. Demographic characteristics of Group A and Group B patients

Variables	Group A (Mean ± SD)(n=32)	Group B (Mean ±SD) (n=34)	P value
Age (years)	46.96 ± 11.5	51.03 ± 8.86	0.06 *
Sex Male	14(41.20)	19(55.88)	
Female	18(58.80)	15(44.12)	0.32Ø
Occupational status	17(53.13)	16(47)	
Unemployed Employed	15(46.87)	18(53)	0.98Ø
Duration of DM(Year)	7.09 ±4.79	9.35 ± 5.67	0.082 *
BMI	26.89 ± 3.4	26.33 ± 2.7	0.481 *
Blood pressure			
a) Systolic	119.8 ± 3.5	117.5 ± 11.3	0.491
b) Diastolic	73.75± 7.18	73.97 ± 7.05	*0.657*

Group A= Control group (received anti-diabetic drugs plus placebo)

Group B = Intervention group (receiving with anti-diabetic drugs plus L-carnitine)

Values were expressed as (Mean ± SD)

n=Number of patients in each group.

*Data were analyzed by using independent t-test.

P≥0.05=statistically insignificant

Table-2: The VAS score at baseline and at follow up in Group A

Groups	At Baseline Mean±SD	At follow up Mean±SD	Reduced level Mean±SD	P value
Group A(n=32)	56.87 ± 6.34	54.06 ± 10.29	3.12 ± 10.2	0.09NS
Group B(n=34)	57.64 ± 8.5	35.58 ± 10.5	22.05±10.67	≤ 0.001***

Group A=Control group (received anti-diabetic drugs plus placebo)

GroupB=intervention group (received anti-diabetic drugs plus L-carnitine)

Values were expressed as (mean±SD)

NS= P value statistically non-significant **(**analyzed by paired t-test) Data were analyzed by paired t-test

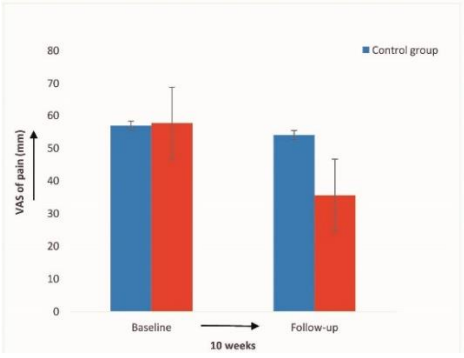
***=P value suggests highly significant decreased invasion group B patients n=number of patients in each group

Comparison of VAS score of DPN in Group A and group B

In group A, the VAS at baseline was 56.87±6.34 (mean ±SD) and VAS in group B was 57.64±8.5 (mean±SD), which suggested that at baseline VAS there was no significant difference in group A and B (p=>0.05).

In group A, at follow up VAS was decreased to 54.06 ± 10.29 (mean ± SD) and at follow-up, VAS was found 35.58 ± 10.5 (mean ±SD). The data suggested that the VAS in group B were decreased after treatment and statistically significant (p<0.0001) difference was obtained in compared to group A.

Figure1. Comparison of VASin GroupA and group B



Bar diagram showing comparison of VAS in Group A and Group B

Group A=Control group receiving placebo and anti-diabetics

Group B= Intervention group receiving l-carnitine in addition with anti-diabetics

Baseline = at the onset of the study

Follow-up= after10 weeks from baseline

Values were expressed as (mean± SD)

Discussion:

The present researcher was interested about the role of l-carnitine (LC) in alleviationor treatment of painful neuropathy. This study shows that chronic treatment with oral l-carnitine (1.5g/day) significantly improves the outcome of painful neuropathy. However a few interventional studies have indicated obvious improvement of symptoms of DPN after use of LC[9,11]. Different tools for assessing of DPN have been recommended among which, the tool used in the present study that was recommended by Young[12]. The present study was a double blind controlled trial which has attempted to assess changes of pain of DPN by a parameter, the VAS (which measures the intensity of pain in a 0-10 numeric pain assessing scale system),

The scoring process of pain by VAS has been accepted as a reliable system of scoring of diagnosis of neuropathic pain including the pain of DPN. The present double blind randomized controlled trial was conducted by administering 500 mg l-carnitine three times per day (1.5gm/day) for10 weeks as conducted in the present study. Previously, it has observed that l-carnitine (500mgor1000mg, three times per day) for 26 weeks was able to significantly improve the pain of DPN7. The therapeutic effect of LCupon pain of DPN was also supported by some other studies, Inwhich0.5mg intramuscular injection of l-carnitine two times per day for 15 days has been able to show improvement of pain when assessed by visual analogscale[13].

In the present study, the VAS score in group B patients (Intervention group) was decreased significantly (P<0.0001) at follow-up compared to placebo group (figure 1). This observation would suggest that, l-carnitine could effectively reduce pain of DPN patients. In the study it was also observed that the mean VAS score after 10 weeks of treatment, were reduced from baseline by 22.05±10.67 in group B or l-carnitine treated patients (Table 2) compared with placebo recipients (group A) which was significant (P<0.0001). Probably the analgesic effect exert by l-carnitine was also able to raise the pain threshold by enhancing the activity of the cholinergicnerves[14].

Conclusion:

Oral administration of L-carnitine in diabetic peripheral neuropathy patients had produced significant reduction of the pain intensity in comparison to placebo.

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Original Article

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A Case Control Study on Risk Factors of Stroke in Pregnancy

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Abstract:

Though stroke in pregnancy is not so common, it leads to considerable maternal mortality and morbidity. It is estimated that 7.7–15% of all maternal deaths worldwide are caused by stroke and 30–50% of surviving women are left with persistent neurological deficits. Few studies have been carried out on epidemiology of stroke in pregnancy.We aimed to find out the risk factors of stroke in pregnancy. It was a case control study conducted from January 2017 to December 2021. 50 antepartum, intrapartum and postpartum stroke cases were taken during this 5 years period. 50 pregnant ladies without stroke were taken as control. 28 cases were haemorrhagic strokes (56%) and most occurred in the postpartum period (26 cases, 52%). Risk factors for stroke included advance maternal age, hypertension, diabetes mellitus, preeclampsia, eclampsia, hyperlipidemia, maternal heart disease, connective tissue disorders, sepsis, obesity, ceasarean section and migraine . Recognition of these risk factors through proper assessment is needed in order to prevent stroke in pregnancy and post partum period.

Keywords: Maternal stroke, risk factors

Background:

Stroke is a neurological emergency and a major cause of disability and death around the world. Data suggest that the rate of maternal stroke has been increasing in recent years. Advance maternal age at the time of child birth and the increasing prevalence of traditional cardiovascular risk factors and other risk factors, as well, such as hypertensive disorders of pregnancy, migraine and infections, may contribute to increased rates of maternal stroke[1,2].

Maternal stroke is an infrequent but debilitating complication of pregnancy and is the most frequent cause of serious long-term disability after pregnancy[3].

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It accounts for at least 7.7% of pregnancy-related deaths worldwide[4] and results in residual neurological deficits in approximately half of maternal stroke survivors[5].

In general population 87% stroke cases are ischemic[6] whereas half of the stroke cases that occur in pregnancy are haemorrhagic (attributable to intracerebral hemorrhage or subarachnoid hemorrhage)[5].

In a meta-analysis of 11 studies including >85 million pregnant and postpartum women, the incidence of maternal stroke was 30 per 100 000 pregnancies; most occurred during the postpartum period (up to 6 weeks)[6]. Another study of >39, 000 deliveries in India from 2006 to 2008 revealed that the incidence of cerebrovascular complications was 66 per 100 000 deliveries[7].The rate of maternal stroke appear higher in the United States than in other developed nations[8].

The risk of thromboembolic events has been estimated to be 15 to 35 times higher in the first postpartum week and the risk remains elevatedup to 12 weeks postpartum[10].

Haemorrhagic strokes, too, occur most frequently in postpartum period. A cross sectional study using administrative data from New York, California and Florida found a 9-fold increased rate of intracerebral hemorrhage in the 12 weeks postpartum in comparison with the nonpregnant state[9,10].

Risk factors for maternal stroke may be broadly classified as traditional cardiovascular risk factors and other risk factors. Traditional risk factors include older age, obesity, chronic hypertension, hyperlipidemia and heart disease. Other risk factors include hypertensive disorders of pregnancy, migraine, infections and hypercoagulable states[10].

Methods:

It was a case control study carried out from January 2017 to December 2021.The aim was to find out the risk factors of maternal stroke. For this study 50 antepartum, intrapartum, and postpartum stroke cases were identified. 50 pregnant lady (age matched) without stroke were taken as controls. Non random sampling was followed for selecting cases and controls.

Patients were evaluated by history, physical examination and related investigations. Inclusion Criteria:1) Female patients of reproductive age group(15-49 years). 2) Confirmed pregnancy. Exclusion criteria:1)patients below 15 years age. 2) Patient above 49 years age. 3) Patients with abortion. Migraine was diagnosed according to third edition of the ICHD (ICHD-3), developed by the International Headache Society[4]. Hypertension was diagnosed according to JNC 8 criteria. Diabetes mellitus was diagnosed according to guideline of American Diabetes Association 2017.Relevent data were collected by means of a questionnaire and a structured interview with the patients or patients' family members. Cases as well as controls were evaluated to explore risk factors. Then risk factors between cases and controls were compared. The results were presented as charts. Statistical analysis were done by appropriate methods. Then the results were compared with those of different studies done previously. Analysis of data was done with help of SPSS version 29 software. Appropriate statistical methods were applied for data analysis and comparison (taking p value ≤0.05 as significant).

Result:

In this study a total of 50 cases and 50 controls were evaluated for presence of risk factors. 28 cases were hemorrhagic stroke (56%) and 22 cases were ischaemic stroke(46%). 9(18%) cases of stroke occurred during antepartum period,15(30%) cases occurred during intrapartum period and most cases occurred during post partum period (26 cases,52%) The mean age was found 32.7 ± 5.08 years in cases and 28.36 ±7.29 years in controls. The mean age difference was statistically significant (p <0.05) between cases and controls. 34 cases had one or more risk factors. In control group, 18 had one or more risk factors. The difference was statistically significant (p< 0.05) in chi square test.

Table 1 : Difference of risk factors between cases aand controls

Risk factors	Cases (n=50)		Controls (n=50)		P-value
	f	%	f	%	
Hypertension	13	26	3	6	0.006 s
Diabetes mellitus	11	22	2	4	0.007 s
Hyperlipidemia	12	24	3	6	0.012s
Preeclampsia/ eclampsia	7	14	1	2	0.027s
Heart disease (congenital/ valvular/cardiomy opathy)	8	16	2	4	0.045 s
Systemic lupus erythematosus	3	6	1	2	0.300 ns
Antiphospholipid antibody syndrome	2	4	0	0	0.152 ns
Sepsis	7	14	1	2	0.027 s
Obesity	6	12	4	8	0.503 ns
Cesarean section	12	24	4	8	0.029 s
Migraine	8	16	2	4	0.045 s

S = significant

NS = not significant

P value was reached from Z test of proportion

The above table shows that hypertension, diabetes mellitus, hyperlipidemia, preeclampsia/ eclampsia, heart disease (congenital/valvular/cardiomyopathy), sepsis, caesarean section and migraine were significantly ($p<0.05$) different between cases and controls.

Discussion:

Pregnancy increases the risk for hemorrhagic stroke much more than for ischemic stroke, with relative risk 2.5 during pregnancy and 28.5postpartum. Hemorrhagic stroke is an important cause of maternal and fetal pregnancy-related mortality[11].

The mean age was found 32.7 ± 5.08 years in cases and 28.36 ±7.29 years in controls .The rising trend in the incidence of maternal stroke might be attributed in part to advance maternal age[10].

Hypertension remains the most prevalent modifiable risk factor for stroke among the general population, and among pregnant and postpartum women, as well.[6] In our study 26% cases were hypertensive.

Wu Pet al found that obesity and hyperlipidemia were increasing among women with maternal stroke[12]. Hyperlipidemia was found to be a significant risk factor in our cases ($p<0.05$).

In a meta-analysis of 22 studies, comprising >6.4 million women, including 250 000 women with preeclampsia showed that preeclampsia was independently associated with a 2-fold increased risk of maternal stroke after adjusting for other potential confounders including traditional cardiovascular risk factors[13]. In our study 14% cases had Preeclampsia/ eclampsia.

Hypertensive disorders of pregnancy are a group of conditions occurring in pregnancy and puerperium with a common background of hypertension, defined as BP ≥ 140/90 mmHg. Included in this group are gestational hypertension, preeclampsia, eclampsia, chronic hypertension and chronic hypertension with superimposed preeclampsia.

Hypertensive disorders of pregnancy are associated with a 1.7–5.2-fold increase in the risk of stroke. Preeclampsia is associated with a 2-fold increased risk of coronary heart disease, stroke, and cardiovascular death[13,14].

In an analysis of the NIS (The National Inpatient Sample of United State) including 18 million pregnancy hospitalizations, migraine was strongly associated with maternal stroke after adjusting for other risk factors[15]. Migraine was also a significant risk factor in our cases.

Infections are now recognized as a trigger for strokes in people of all ages[16]. This association has also been observed among pregnant and postpartum women. Infections have been recognized as a risk factor for maternal stroke even among women with preeclampsia[17]. The risk appears to be higher with genitourinary infections and sepsis[18]. Infections were recognized as a risk factor for maternal stroke in our study. Proposed pathophysiological pathways for the association between infections and maternal stroke include activation of the inflammatory cascade, causing a surge in inflammatory cytokines leading to platelet activation and aggregation; increased oxidative stress and impaired endothelial function, all of which are linked with maternal stroke[19].

An analysis of the New York State Department of Health inpatient database, comprising >88 000 women with preeclampsia, showed that prothrombotic states including systemic lupus erythematosus were associated with a higher risk of maternal stroke[17]. Pregnancy with antiphospholipid syndrome increases the risk of recurrent ischemic stroke, preeclampsia, and preterm delivery[20]. But our study failed to establish strong association of SLE and antiphospholipid syndrome with maternal stroke.

In a study of data from the Healthcare Cost and Utilization Project (1993 – 1994), risk factors for peripartum stroke and venous sinus thrombosis were assessed among 1,408,015 sampled deliveries. In that study, the risk of peripartum stroke was 34.3/100,000

births for women who had a cesarean birth, compared with risk of 7.1/100,000 births for vaginal delivery ($p<0.001$)[21]. Our study also found that cesarean section had strong with maternal stroke ($p<0.05$).

Conclusions:

Stroke in pregnancy is an important cause of maternal morbidity and mortality and is potentially preventable. The prevalence of maternal stroke is increasing day by day. Further research is needed to broaden our understanding of the mechanisms and risk factors to prevent stroke in pregnancy.

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Original Article

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Evaluation of Bohler's Angle in Bangladeshi Population: A Morphometric Study of Calcaneus

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Abstract:

Background: Calcaneus is the largest tarsal bone designed to withstand the daily stresses of weight bearing. Calcaneal fractures are the most common fractures of the hindfoot, accounting 1 to 2% of all fractures of the human skeleton. Bohler's angle is subtended by the calcaneus, which plays a key role in the surgical management of calcaneal fractures.In order to assess the degree of deformity of calcaneal fractures and the effectiveness of reduction, it is crucial to understand the normal limits of the Bohler's angle in Bangladesh.Objective: To assess different morphometry of Bohler's angle of dry adult human left calcaneus and to evaluate the morphological differences of dry left calcaneus between male and female.Materials and Methods: A cross-sectional analytical study was carried out in the Department of Anatomy, Dhaka Medical College, Dhaka from January 2018 to December 2018. A total two hundred dry adult human left calcaneus of unknown sex were collected from the Department of Anatomy and also from the MBBS students of Dhaka Medical College, Dhaka National Medical College, Dr. Sirajul Islam Medical College & Dhaka Community Medical College. The study samples were grouped into male and female by discriminant function analysis technique. Bohler's angle was measured with the help of goniometer. Measurement of goniometer was recorded in degree°.The statistical analyses were done by unpaired Student's't' test for comparison between variables by using SPSS program. Data were expressed as mean ± SD with minimum and maximum values.Results: The mean ± SD Bohler's angle was greater in the male than in the female and when compared between male and female it was found to be statistically insignificant (p=0.087). Conclusion: A sound knowledge of the Bohler's angle and measurements would assist better treatment and management options for the calcaneal fractures and for further research efforts.

Keywords: Bohler's angle, calcaneus, morphometric study

Introduction:

Foot has evolved over many million years to attain the human type. It has 28 bones and 31 articulations to support daily biomechanical loads of up to three to seven times the body weight.The bones of the foot are essential for supporting the body's axial load. One of the key bones supporting the body weight is the calcaneus[1].

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Calcaneus, also called as the "Heel Bone" is the largest and strongest tarsal bone in humans. It projects posterior to the tibia and fibula as a short lever for muscles of the calf attached to its posterior surface.It is the first bone of the foot to ossify. It acts as the posterior pillar of the longitudinal arches of foot for the transmission of body weight[2].It articulates with the talus to provide support for the ankle jointof the foot. The calcaneus is acrucial bone in the formation of the subtalar and joint, which is essential for the inversion and eversion movements of the foot[3].

The calcaneus is so configured that it forms an angle when a person stands erect and this angle is called Bohler's angle[2].It is a geometric angle resulting from three points of reference on the calcaneus. Bohler's angle is formed by the intersection of a line joining the highest point of the calcaneal tuberosity to the

highest point of the posterior facet and a line joining from the highest point of the anterior process to the highest point of the posterior facet of the calcaneus[4]. Since all the reference points are on the calcaneus, any distortion of the calcaneus will cause a change in the Bohler's angle. Additionally, it has long been accepted practice in ankle fracture reconstruction to restore the Bohler's angle. To reflect ethnic particular anthropometry, it is therefore required to evaluate Bohler's angle in various populations[5].

The introduction of Bohler's angle in 1931 by surgeon Dr. Lorenz Bohler is considered to be milestone in the management of Calcaneal fractures[6]. Bohler's angle is also known as Calcaneal angle, Tuber joint angle or Salient angle. The range of the normal values in adults, without presence of fractures, is from 25° to 40°, but this value varies depending on the examined population. The range of normal Bohler's angle varies depending on the gender, age and the ethnicity of the observed population[7].

Sex determination is considered as the first and most important step in the biological identification process of skeletal remains[8]. Skeletal remains in forensic cases are often poorly preserved and fragmentary which makes analysis complicated or impossible[9]. Calcaneus is often recovered in forensic and archaeological contexts[10].By virtue of its anatomical position, it can resists putrifaction better than other bones[11].

Measurement of Bohler's angle of the calcaneus provide an additional reliable method for sex estimation via discriminant function analysis[12]. Numerous researchers have confirmed the Bohler's angle in Caucasians and it does not exhibit sexual dimorphism[2]. Studies among African, Malawian, and Ugandan populations found that Bohler's angle had sexual dimorphism. Khoshhal[13] researched sexual dimorphism ofBohler's angle in Asian populations and reported that there was no discernible sex difference in the Bohler's angle[5].

The majority of the body's axial weight is transferred to the calcaneus, as it is the largesttarsal bone and the most inferior bone in the body[14]. The calcaneus is repeatedly subjected to static and dynamic stresses, especially in the weight-bearing positions during walking, working or running[15]. Calcaneus is most commonly fractured after a fall from a height road traffic accidents in which axial loads exceed its support capacity[16].

Calcaneal fractures are the most common tarsal fractures following a foot-ankle trauma. Calcaneal fractures severely restrict mobility, which significantly impact the patient's ability to perform activities of daily living while the patient heals or develops complications[14]. These fractures have very variable patterns; can be divided into intra-articular and extra-articular fractures.Fractures of the calcaneus is account for 75% of all foot fractures and about 1-2%of all fractures.A displacedcalcaneal fracture results in asignificant reduction of the value of theBohler's angle[17].

Bohler's angle is the important landmarks in assessing calcaneal fractures. Calcaneal height and joint depression are represented by Bohler's angle[18]. In a fractured calcaneus, a decrease in Bohler's angle indicates that the posterior facet of the calcaneus has collapsed and hence shifting the body weight anteriorly[19].

The evaluation of Bohler's angle is crucial for the diagnosis, treatment and prognosis of calcaneal fractures. A Bohler's angle of 15 degrees or less is an indicator that the fracture should be surgically reduced[1]. During the surgical procedure the displaced fragment is reduced in such a way that the normalvalue of Bohler's angle is restored. Additionally, it has been demonstrated that theBohler's angle has a significant prognostic value in determining morbidity and outcomes following calcaneus fractures[3].

The present study was aimed to determine the normal range and means of Bohler's angle in Bangladeshi population. Therefore, the results of the present study may be useful to radiologists, orthopedic, and reconstructive surgeons to achieve accurate diagnosis, deliver appropriate treatment and make a better assessment of prognosis. In forensic medicine and archeology, the morphometric measurement of the Bohler's angle can be used toestablish the sexual dimorphism of fully ossified dry calcaneus bones.

Materials and methods:

The present study was carried out in the Department of Anatomy, Dhaka Medical College, Dhaka from January 2018 to December 2018. A total two hundred (200) dry adult human left calcaneus of unknown sex were collected from the Department of Anatomy and also from the MBBS students of Dhaka Medical College (DMC) Dhaka, Dhaka National Medical College (DNMC) Dhaka, Dr. Sirajul Islam Medical College (Dr. SIMC) Dhaka & Dhaka Community Medical College (DCMC) Dhaka. By discrimination function analysis technique[8] and also with the help of various morphological criteria used by different authors[8,10], the sex was determined and the grouping was done.

Procedure of measurement of Bohler's angle:

Bohler's angle was measured with the help of goniometer (Figure-1). Measurement of goniometer was recorded in degree (°). Measurements were taken three times and then the average values were taken for each measurement[20].

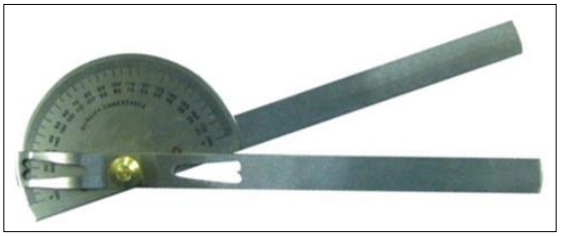


Figure 1: Goniometer

Bohler's angle:

Figure-1 displays BA which represents the Bohler's angle. To measure the Bohler's angle, a red dot was given on the anterior most point of the calcaneus and the blue dot was given on the superior most point of the posterior articular facet. Another green dot was given on the superior most point of the calcaneal tuberosity.The fixed jaw of the goniometer was placed along the line connecting the red and the blue dots.

The rotating jaw was placed along the line connecting the green and the blue dots. Line between the green and the blue dots was extended and an acute angle was formed. The resultant acute angle was identified as Bohler's angle. Then the angle was measured by using the goniometer and was represented by BA (Bohler's angle)[20].

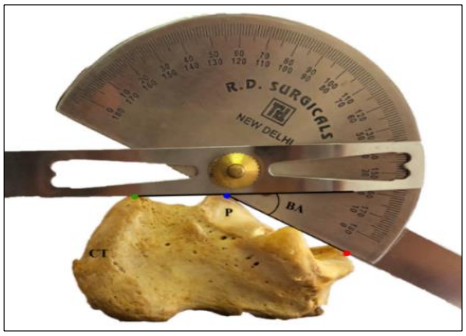


Figure 2: showing the measurement of the Bohler's angle (BA) by the goniometer. Red dot indicates anterior most point of the calcaneus, blue dot indicates the superior most point of the posterior articular facet and green dot indicates the superior most point of the calcaneal tuberosity. CT represents the calcaneal tuberosity and P represents the posterior articular facet.

Statistical analysis:

The data collected from morphological studies were processed to get mean values, standard deviations and percentage values as applicable. Then the calculation of mean and standard deviation (SD) with minimum measurements between male and female were done by using an unpaired Student's 't' test. Statistical significance was accepted at p value equal to or less than 0.01 ($p<0.01$) [2 tailed]. All statistical analyses were performed using Computer based Software, Statistical Package for Social Science (SPSS) Version 20.0.Data were expressed as mean ± SD with minimum and maximum values.

Results:

Among the total 200 dry adult human left calcaneus, majority (103) were found to be male sample which is determined by discrimination function analysis technique and also with the help of various morphological criteria[8,9]as shown in Table-I.

From Table-II and Figure 3, it is evident that in male, the mean ± SD of Bohler's angle was 32.26°±2.65. The Bohler's angle ranged from 25.57° to 39.20° in male. In the female, the mean ± SD of Bohler's angle was 31.64°±2.42. The Bohler's angle ranged from 26.15° to 36.87° in female.

The finding of the present study revealed that the mean ± SD Bohler's angle was greater in the male than in the female and when compared between male and female, it was found to be statistically insignificant (p=0.087).(Figure 3).

Table I: Grouping of the sample.

Sex	Number of study sample
Male	103
Female	97

Table II: Bohler's angle of left calcaneus in male and female (N = 200).

Variables	Male n= 103 Mean ± SD	Female n= 97 Mean ± SD	p value
Bohler's Angle in degree	32.26±2.65 (25.5739.20)	31.64±2.42 (26.15-36.87)	0.087[ns]

Figure in parentheses indicate range

Comparison between sex was done by unpaired Students' test

ns= not significant

n= sample size

SD = Standard Deviation

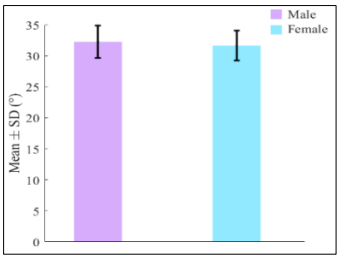


Figure 3: Bar diagram showing Bohler's angle in male and female

Discussion:

Calcaneus is the largest tarsal bone, it is designed to support the body and endure great degree of pressure. It is the most vulnerable bone of the ankle region[21].The Bohler's angle is a parameter used in assessing the integrity of the calcaneus in the foot. It is commonly assessed when evaluating patients with calcaneal fractures. Traumatic alteration of this angle can be used to measure the fracture severity. The restoration of Bohler's angle to normal values is one of the objectives of surgical management of fracture. It is essential to understand the acceptable range of Bohler's angle in order to assess the degree of deformity in calcaneus fractures and to predict morbidity after reduction[4].

The Bohler'sangle issignificant in anthropometric studies because osteometric variations in humans have been utilized to identify the sex and ethnic group of individual skeletons, an important tool in archaeology and forensic medicine.Numerous investigations have been done on **Bohler's angle on different races**[3].

Although the Bohler's angle has garnered a lot of attention, little research has been done to ascertain its range of values in Bangladesh. Few investigations have been carried out with dry calcaneus bones in Bangladesh, despite the fact that Bohler's angle studies utilizing radiographic methods are quite popular.The goal of the current study was to determine the Bohler's angle on the calcaneus of an adult human and to offer baseline data for future investigations in Bangladesh.

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The Bohler's angle of the present study in both male and female was almost similar ($p>0.05$) with that of Kim[22], et al. from Korea and Rokaya[23], et al. from Nepal. It might be due to use of different measurement techniques. Kim[22] used Korean cadaver and Rokaya[23] used radiographic calcaneus instead of dry ossified calcaneus.

In 2013, Udoaka and Didia[24] carried out a study on the population of Nigeria. The mean male value of Bohler's angle was almost similar ($p>0.05$) to thatof the present study but mean female value was dissimilar ($p<0.001$) to the findings of the present study. However the variation in sex could not be explained.

In 2009, Seyahi[25], et al., worked on the Turkish population andZakaria and Mohammed[26] studied on the Egyptian population in 2010.The findings of their study were significantly higher ($p<0.001$) than the findings of the present study.This divergence might be due to variation in race and ethnicity.While Egyptians are a mixture of Nubian and African tribal races, Turkish people are all Caucasiansby race.

Kim[22], et al. Rokaya[23], et al. Udoaka and Didia[24] Seyahi[25], et al. and Zakaria and Mohammed[26] all noticed that the mean Bohler's angle was greater in the male than in the female but when compared the difference was found to be non significant ($p=0.56$, $p=0.55$, $p=0.68$, $p=0.17$ and $p=0.23$).

Conclusion and recommendation:

Calcaneus, the weight bearing bone of the lower limb handles the stresses of the upright human posture. Fracture of this bone leads to hindrance in day today activities. Morphometric measurements of Bohler's angle of the calcaneus is relevant parameters in diagnosis of calcaneal fractures, its intra operative reduction, fixation and assessment of prognosis.Further studies can be done on radiograph of living calcaneus bones and compare them with the fully ossified dry calcaneus bones are recommended. Newer advanced technology like computed tomography scans, MRI etc. are suggested.

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Original Article

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Correlation of Serum Zinc with HbA1c in Type 2 Diabetes Mellitus Patients

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Abstract:

Background and objectives: Diabetes mellitus is one of the greatest medical problems threatening the world. Zinc is an essential trace element and its abnormal metabolism has been suggested to play a role in the pathogenesis of diabetes and its complications. The present study was aimed to evaluate the correlation of serum zinc with HbA1c in type 2 diabetes mellitus patients. Materials and methods: This cross sectional study was conducted in the department of Biochemistry, Dhaka Medical College, Dhaka from July 2016 to June 2017. A total number of 100 individuals both diabetic and healthy individuals were included in this study. HbA1c was measured by high performance liquid chromatography and estimation of serum zinc was done by using Automatic Biochemistry Analyzer. Results: A total of 100 individuals were enrolled of which 50 diagnosed patients of type2 DM were selected as group A and same number of age and sex matched apparently healthy individuals were selected for comparison as group B. Mean serum zinc in group A and group B were 45.7 ± 12.3 µg/dl and 77.4 ± 10.4 µg/dl respectively. There was statistically significant decreases in serum zinc concentration in group A compared to group B. Serum zinc levels showed significant negative correlations with HbA1c (r= -0.482, p<0.001). Conclusion: Patients with type2 DM showed significant negative correlation between serum zinc with HbA1c. Routine screening along with supplementation of zinc may be beneficial for them.

Keywords: Type 2 diabetes mellitus, serum zinc, HbA1c.

Introduction:

Diabetes is one of the largest health emergencies of the 21st century. Each year more and more people suffering from this condition, which can result in life-changing complications[1]. Type 2 diabetes mellitus is a major health problem affecting nearly about 170 million people all over the World[2]. Type 2 diabetes mellitus accounts for 90–95% of all diabetes.It encompasses individuals who have insulin resistance and usually relative (rather than absolute) insulin deficiency[3].

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In diabetes mellitus, the metabolism of several minerals have been reported to alter and they have specific role in the pathogenesis and progress of the disease. Among these, the trace elements like magnesium, zinc and copper are important for the normal growth and biological functions[4]. Zinc (Zn) is an essential trace element that is directly involved in the synthesis, storage and secretion of insulin, as well as conformational integrity of insulin[5]. It is regulated through uptake from the intestinal mucosa in processes that depends on intracellular Zn binding proteins. Human zinc deficiency is mainly caused by low zinc in the diet; high fibre content decreases the availability of Zn for intestinal absorption. The main clinical features of zinc deficiency include growth retardation, delay in skeletal maturation, testicular atrophy, hepato- splenomegaly, susceptibility to infection, impaired wound healing, scaly dermatitis and diarrhea[6].

Recent studies revealed that serum zinc levels are decreased in diabetic patients may be due to

increased urinary excretion due to reduction in renal function associated with disease, gastrointestinal malabsorption, genetic factors or signs of infection during which zinc acts as a defense mechanism. However, abnormal zinc metabolism has been suggested to play a role in the pathogenesis of diabetes and its complications[7]. Decreased plasma level of zinc adversely affects the ability of islet cells to produce and secrete insulin[8]. For this, hypozincemia and hyperzincuria are developed in patients of diabetes mellitus[9].

Considering all these, the study was aimed to correlate serum zinc with HbA1c in type 2 DM patients attending in the OPD of Department of Endocrinology & Metabolism, Dhaka Medical College Hospital.

Materials and methods:

***Study Population and place*:** This cross sectional study was conducted from July 2016 to June 2017 after receiving Institutional Review Board approval. Informed written consent was taken. By convenient and purposive sampling a total of 100 subjects were selected according to the selection criteria. Among them, 50 diagnosed patients of type2 DM attending in the OPD of Department of Endocrinology & Metabolism, Dhaka Medical College Hospital were selected as group A and same number of age and sex matched apparently healthy individuals were selected for comparison as group B. According to ADA (2016) diagnostic criteria of diabetes mellitus are fasting blood glucose ≥7.0 mmol/L and/or 2 hour after 75gm glucose ≥11.1mmol/L and/or HbA_{1C} ≥6.5%. The subjects with type 1 Diabetes mellitus or acute complications of diabetes mellitus, history of hypertension, chronic and debilitating diseases like malignancy, chronic liver disease, chronic kidney disease, acute illness, pregnant and lactating women, recent history of acute infection and diarrheal disease were excluded from this study.

Collection of blood sample:

With all aseptic precautions, blood samples were collected from each subject. Fasting plasma glucose was estimated enzymatic ally by glucose oxidase method. Plasma HbA1c was measured by high performance liquid chromatography. Normal level of HbA1c:<5.7%, pre-diabetes: (5.7- 6.4)% and diabetes: ≥6.5%.[3] Estimation of serum zinc was done by using Automatic Biochemistry Analyzer. Normal level of Serum Zinc is 66-110 µg/dl[10].

Data analysis:

All data were recorded in a predesigned data collection sheet. Continuous variables were expressed as mean ± SD and were compared between groups of patients by unpaired Student's 't' test. Categorical variables were compared using chi-square test. Pearson's correlation coefficient was used to test the relationship between the parameters. The quantitative observations were indicated by absolute frequencies. The result was considered as statistically significant when p value was less than 0.05 at the level of 95% confidence interval.

Results:

This study was aimed to correlate serum Zn with HbA1c (%) in type2 diabetes mellitus patients. Table I shows mean ± SD of age, sex, systolic BP, diastolic BP and Body Mass Index of study subjects. P value < 0.05 was significant. There were no significant difference between them in terms of such parameters. Table II shows Fasting plasma glucose and HbA1c levels were significantly higher and serum zinc levels were significantly lower in T2DM patients than healthy individuals. Table III shows out of 50 Group-A cases, 43 (86%) had lower serum zinc level than the normal reference range (66-110 µg/dl) while all the Group A cases were within the normal range.

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Table I: Baseline parameters of the study subjects in both groups (N=100).

Parameters	Groups		p value
	Group A (n=50)	Group B (n=50)	
Age (years)	50.5 ± 6.0	50.4 ± 5.1	0.943[a]
Male	32 (64.0)	30 (60.0)	0.680[b]
Female	18 (36.0)	20 (40.0)	
Systolic BP (mmHg)	115.4 ± 5.8	115.0 ± 6.1	0.736[a]
Diastolic BP (mmHg)	75.5 ± 5.7	75.5 ± 5.3	1.000[a]
BMI (kg/m^2)	19.9 ± 2.8	19.0 ± 4.0	0.219[a]

Here, type 2 DM as group A and healthy individuals as group B. Chi-square test was done to measure the level of significance.

Table II: Biochemical parameters of the study subjects in both groups (N=100).

Parameters	Groups		p value
	Group A (n=50)	Group B (n=50)	
Fasting plasma glucose (mmol/l)	8.8 ± 1.7	5.2 ± 0.9	<0.001*
HbA1c (%)	7.1 ± 1.1	4.9 ± 0.6	<0.001*
Serum Zinc (µg/dl)	45.7 ± 12.3	77.4 ± 10.4	<0.001*

Unpaired Student's t test was done.

Table III: Distribution of T2DM patients according to level of serum zinc (n=50).

Biochemical Parameter	(n=50)	Percentage
Serum Zinc (µg/dl) <66	43	86%
66-110	7	14%

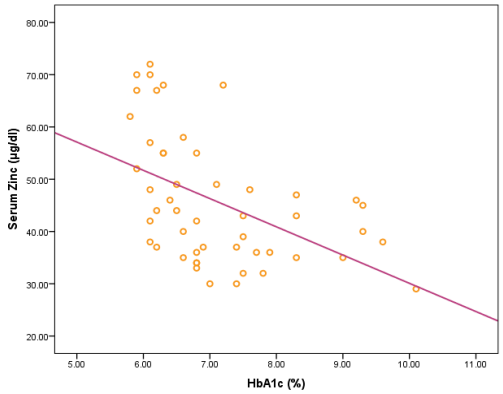


Figure 1: Correlation of HbA1c with serum zinc in group A.

Serum Zn was correlated with HbA1c by Pearson's correlation test to observe the association among parameters. It revealed that there was significant negative correlation between serum zn(µg/dl) with HbA1c (r=-0.482 and p=0.05) (Figure 1).

Discussion:

This cross sectional study was aimed to evaluate correlation of serum zinc with HbA1c in type 2 Diabetes Mellitus patients and age and sex matched healthy individuals. We also measured serum zinc and HbA1c level. Serum zinc concentration was significantly lower in type 2 DM patients (p<0.001) compared to healthy individuals. These results of our study were in agreement with the other studies[11-14]. The possible explanation of hypozincemia seen in the diabetic population due to low gastrointestinal absorption and high urinary excretion of zinc in diabetic patients.

Correlation of serum zinc with HbA1c was done. Serum zinc levels showed negative correlation with HbA1c. The correlation coefficient was r = -0.482 and p < 0.001. These results were in harmony with the reported study[2, 11]. So, we found that serum zinc level was decreased in type2 DM patients comparison with healthy individuals. Concentration of serum zinc was inversely correlating with HbA1c in patients with type 2 diabetes mellitus.

Conclusion:

It is concluded that serum zinc levels were decreased in type 2 diabetes mellitus patients and these levels were negatively correlated with HbA1c. So, regular assessment of these parameters might be helpful to prevent the complications of DM related with hypozincemia.

Acknowledgement:

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Conflict of interest:

The authors declare no conflict of interest.

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Original Article

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Health Problems of Garment Workers During Natal Period

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Abstract:

Background: Bangladesh is the tenth most densely populated country in the world, with one of the fastest growing global economies.A major contributor of this economic boom has been the readymade garment (RMG) and textile manufacturing (TM) industries.This industry has provided 4 million people, of whom 80% are female to participate in income-earning activities. Working in this industry has made women economically independent and empowered. Objective: The objective of this study is to explore the major health problems of garment workers during natal period from July 2019-June 2020. Methodology: A descriptive cross sectional study was performed among 380 puerperal mothers working in garment industry of Dhaka and Chittagong district who were selected by simple random sampling. Data were collected using semi – structured questionnaire by face to face interview and record review from puerperal mothers at their own household. Results: The finding more than three four of the female workers were married within 11-17 years which indicate the asperity of early marriage among female garment workers and more than three fourth of them had their first child before their mature age. Among the respondents, unplanned pregnancies constitute more than two fifth and history of MR given by three fifth of the respondents. A total of 78.1% of respondents took ANC from garment doctor. More than two fifth (65.8%) of the respondents did not hear about warning signs of pregnancy. The findings also showed that due to unfavorable environmental situations the workers faced headache, eye strain, fatigue, swelling of feet, leg pin, back pain, abdominal pain etc. Problems due to excess working hours were faced by almost three fourth of respondents. Conclusion: The findings from this study showed that special care need to be given to the pregnant workers in order to have a healthy baby who are our future generation. So, it can be recommended that health issue of pregnant garment worker should be highly prioritized to provide all medical facilities and easy access to their medical center for complete health service of garment workers during natal period.

Keywords: Garment workers, natal period, anti natal care

The ready-made garment (RMG) industry is a mainstay of economic success. Bangladesh is today one of the world's largest garment exporters, with the RMG sector accounting for 84 percent of Bangladesh's exports. Garment workers in Bangladesh work around 9-12 hours a day, often 7 days a week, in confined and unhealthy environments without adequate rest and food.Overtime work is compulsory and forceful[1]. The environment wherethey work is not suitable for working hours after hours with suffocating heat inside. Most of the health problems occurred from the occupational health hazards that include long working hours, absence of leave facilities, over-crowded working conditions, absence of health facilities and safety measures, absence of staff amenities, etc[2] .Tremendous work pressure, lack of sufficient light and ventilation, pure drinking water and toilets for the workers causes the condition much more worse.

Workplace risk assessments during pregnancy are especially important. For any workers, sitting 8 to 10 hours a day behind a sewing table can lead to back

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and neck injuries, stiff muscles and joints, poor circulation, worker's fatigue and more[3]. Despite there being doctors available, the workers do not have opportunity for regular medical examinations to check their health status[4]. Long working hours with excessive overtime is a common practice in garment factories. The female workers are destitute women with very poor economic background and in the factories; the promotion prospects are strongly associated with working time. So a significant portion of the workers are unable to seek healthcare services and commodities from the formal providers[5].

The garment owners do not want to give job or reluctant to continue the job of female workers when they become pregnant or came to know of having their baby. For this reason, when a female worker became pregnant she do abortion to retain job that results in poor health condition. The rate of miscarriage among garments workers is very high and most of them experience abortions more than once. Most of the female workers are unaware of the importance of antenatal care during pregnancy[6].

RMG factory managers appear to view pregnant workers as inefficient. As supervisors and managers do not want to cut production targets, they sometimes pressure pregnant women to quit their jobs. If women become slower at completing tasks during pregnancy, supervisors intentionally subject them to verbal abuse to prompt them to quit. As a result, pregnant women suffer in silence – much to the detriment of their own, and their child's, health and well-being[7].

Female workers can access factory clinics for health care services. The women need to meet a production quota of one hundred pieces per hour. If they lag behind the quota due to their pregnancy, their supervisors will encourage them to leave the job.

The women reported that they do not visit the factory doctor for an ante-natal check-up. They only go to the factory clinic for a check-up during pregnancy when their pregnancy becomes visible[8].

Ergonomic factors represent the major occupational constraint of working women. The increasing number of women continuing their professional activity during pregnancy makes it important to assess the effect of ergonomic factors on the outcome of pregnancy. The workers were aware about antenatal but had very limited knowledge on maternal danger signs[9].

Materials and method:

It was a descriptive type of cross-sectional study conducted among puerperal mothers. The study was conducted in four selected garments in Dhaka and Chattogram city from July 2019 to June 2020. The study population were puerperal mothers who had ANC card or valid document worked in garment industry. They were in their home for maternity leave. A purposive sampling method was followed to select 380 respondents for the study. Data collection instrument were pre-tested by semi- structured questionnaire. Data were collected by face to face interview, record review and observation from household of the respondents. Data entry, cleaning, and analysis were done by using SPSS 24 version.

Results:

This cross-sectional descriptive study was conducted among 380 respondents and their mean age was 23.3 ± 4.52 years. Most of the respondents (36.3%) were aged between 20-24years. The majority of the respondents (52.37%) completed education up to class V. A total of 28.2% of respondents had their monthly income ranging from BDT 5001-6000 (Table 01).

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Table 01: Sociodemographic characteristics of the respondents.

Variable	Frequency	Percentage
Age group		
< 20	100	26.3
20-24	138	36.3
25-29	102	26.8
30-34	34	8.9
> 35	6	1.6
Mean ± SD	23.3 ± 4.52	
Educational Status		
Able to put signature only	128	33.68
Class I-V	199	52.37
Class VI to VIII	41	10.79
Class IX to X	12	3.16
Religion		
Muslim	369	97.1
Hindu	11	2.9
Monthly Income		
4000-5000	33	8.7
5001-6000	107	28.2
6001-7000	94	24.7
7001-8000	74	19.5
8001-9000	47	12.4
9001-10000	22	5.8
10001-11000	3	0.8
Mean ± SD	771.30±1368.75	

Most of the respondents (87.4%) were married within 11-17 years. A total of 80.3% of respondents became pregnant for first time before they each maturity. More than two fifth (46.8%) of the respondents had unplanned pregnancies. History of MR was given by more than two third (60.3%) of respondents. (Table 02).

Table 02: Behavior of the respondents.

Variable	Frequency	Percentage
Age at first marriage		
11-13	63	14.6
14-17	292	72.8
18 and above	25	12.6
Mean ± SD	16.1 ± 1.58	
Age at birth of first child		
13-15	35	9.2
16-18	270	71.1
19-21	67	17.6
22 and above	8	2.1
Intention about last pregnancy		
Planned	127	33.4
Unplanned	178	46.8
Accidental	75	19.7
History of MR		
Present	229	60.3
Absent	151	39.7

A total of (78.1%) of respondents took ANC from garment doctor. More than two fifth (65.8%) of the respondents did not hear about warning signs of pregnancy.Maternity leave was given with payment to 45.5% of respondents. (Table 03).

Table -03. Information regarding antenatal care

Variable	Frequency	Percentage
Place from where ANC is taken		
Garment doctor	297	78.1
Other place	83	21.8
Hearing about warning signs of pregnancy		
Yes	130	34.2
No	250	65.8
Maternity leave with payment		
Yes	173	45.5
No	207	54.5

About 43.4% of respondents reported ofhaving headache due to poor illumination. More than three fourth (78.2%) of respondents complained of problems due to poor working positions. More than half of the respondents had headache due to excessive noise. Nearly three fourth (71.2%) of respondents had faced problems for overtime.

Table04: Information regarding working environment

Variable	Frequency	P
Problems faced due to insufficient light(n=53)		
Eye strain	14	26.4
Headache	23	43.4
Lacrimation	16	30.2
Complications for working positions (n=380)		
Yes	297	78.2
No	83	21.8
Problems faced due to working positions(n=297) (Multiple responses)		
Swelling of feet	62	20.8
Abdominal pain	49	16.5
Leg pain	78	26.3
Back pain	119	40.1
Fatigue	26	8.7
Adverse effect due to excessive noise (n= 178) (Multiple responses)		
Earache	65	36.7
Headache	93	52.5
Tingling sensation	28	15.8
Tinnitus	21	11.9
Excess Working hours		
Yes	264	69.5
No	116	30.5
Problems faced for excess working hour (n=264)		
Yes	188	71.2
No	76	28.8

Discussion:

The study revealed that most of the respondents were poorly paid. A study conducted in Bangladesh shows similar results[10]. A total of 80.3% of respondents became pregnant for first time before they each maturity. A study carried out in Dhaka city also found similar type of findings[9]. History of MR was given by more than two third (60.3%) of respondents. This result has similarity with a study carried out in a garment in Dhaka city[11]. Most of the respondents received ANC from garment doctor (78.1%) which has similar findings with a study carried out in different garment factories in Bangladesh8 (Akhter et al,). The present study reveals headache and back pain as the common health problems among the respondents due to the physical environmental hazard. Similar type of findings were seen in different studies done by Azad et al[12], Begum et al[10] and Mahmud et al[13]. About two third (71.2%) of respondents faced problems due to long working hours.

Conclusion:

The findings from the study revealed that most of the respondents received antenatal care from garment doctors. They received maternity leave with payment but those received maternity leave without payment due to being new in job with duration less than 6 months. Due to unfavorable environmental conditions the respondents suffered from headache, earache, weakness, vertigo, back pain, swelling of feet. They had to work for a long time in the factory due to overtime for which they also faced problems. From these findings, it can be recommended that awareness among the pregnant workers should be increased and improvement of working environment is necessary. Ensure full time doctor in the factory and easy access to medical facility by the respondents.

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Review Article

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A Review on Management of Fungal Urinary Tract Infection

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Abstract:

Summary: In fungal urinary tract infection almost always the organisms are Candida.The important risk factors for fungal UTI are older age, female sex, antibiotic use, intensive care unit (ICU) patients and urinary drainage devices.Symptoms are indistinguishable from those in bacterial infections. Differentiating fungal colonization from invasive fungal infection is a major issue. In patients without indwelling catheters, renal infection is documented with colony counts of 10^4 yeast cfu/ml. In patients with indwelling catheters, colony counts of 2×10^4 to 10^5 yeast cfu/ml is noted. Most patients with candiduria do not need treatment with an antifungal agent. For asymptomatic patients, treatment should be given to those who are at high risk of systemic candidemia or in whom the candiduriais likely due to disseminated fungal infection. Oral fluconazole is the drug of choice. Intravenous amphotericin B is reserved for patients with upper UTI or fluconazole-resistant patients.

Keywords: Urinary tract infection, candida, fluconazole.

Introduction:

Fungi in urine are a frequent finding in hospitalized patients. Almost always the organisms are Candida[1]. Practically, most patients with candiduria are asymptomatic and have colonization only.

Risk factors for candiduria:

The important risk factors are older age, female sex, use of broad-spectrum antibiotics, urinary drainage devices (e.g. bladder catheter, percutaneous nephrostomy (PCN), DJ stents), uncontrolled diabetes mellitus (DM), neutropenic hosts, central venous catheter (CVC), parenteral nutrition, hemo- and peritoneal dialysis (HD, PD), recent surgical procedures.

Pathogenesis:

- Candida can cause urinary tract disease by either the hematogenous or the ascending route.
- After hematogenous seeding of Candida to the kidney, multiple microabscesses develop throughout the cortex, with penetration through the glomeruli into the proximal tubules. Then they are shed into the urine. However, the immunocompromised hosts cannot clear the fungi and get fungal UTI.
- Candida are common inhabitants of the perineum but are not found in urine in healthy people. A variety of predisposing factors favor these commensals to grow in the urine, to invade the bladder or the upper urinary tract, resulting in infection.
- These factors are more frequently encountered in the intensive care unit (ICU) patients. For ascending infection, obstruction is an important factor in many patients. Virulence factors of Candida, such as those that control adherence and biofilm formation, are also likely relevant.
- A clinical condition seen early after kidney transplantation is graft site candidiasis. This results from contamination of the donor kidney during the harvest procedure. Most patients lose the graft, and mortality is high.

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Microbiology:

C. albicans accounts for up to 70% of all candiduria, and **C. glabrata** for about 20%.[1]. Older patients frequently have C. glabrata in urine. In a prospective survey of candiduria in renal transplant patients, C. glabrata was isolated in 53% and C. albicans in 35% cases[2].

Clinical manifestations:

Most patients with candiduria are asymptomatic, and do not have infection. Less than 5% of patients with candiduria had any symptoms of UTI. Symptoms of fungal cystitis or pyelonephritis are indistinguishable from those in bacterial infections. Cystitis is manifested by dysuria, frequency, urgency, and suprapubic discomfort. Patients with pyelonephritis can manifest with fever with chills and rigor, and flank pain. Urinary tract obstruction may occur from formation of fungal ball. In candidemia with seeding of the renal parenchyma, patients manifest the clinical features of invasive candidiasis and not the UTI. Fever with chills and rigor, hypotension, and other manifestations of sepsis are often noted in patients with candidemia.

Diagnosis of fungal UTI:

- Pyuria is not often helpful for diagnosis of infection in patients with candiduria. Concomitant bacteriuria with candiduria may be responsible for pyuria.
- In patients with an indwelling bladder catheter, pyuria is routinely observed, whether infection is present or not. In patients without an indwelling bladder catheter or bacteriuria, pyuria is helpful for diagnosis of fungal UTI.
- Anyhow, differentiating contamination of a urine specimen with fungal colonization from invasive fungal infection is a major issue.
- Contamination is most easily differentiated by repeating the urine culture 1 to 2 days later to determine persisting candiduria. If the repeated culture yields no fungi (yeasts), no further diagnostic studies or therapeutic interventions are needed.
- The second urine specimen should be obtained by sterile bladder catheterization if the patient is unable to collect a clean-catch urine. In patients with an indwelling bladder catheter, a second urine specimen should be collected on the next day of replacing the catheter.
- In bacterial UTIs, the diagnosis is based on appropriate symptoms plus pyuria (>10 pus cells/hpf) plus quantitative bacterial counts on C/S. But in fungal UTI, no studies have established the quantitative fungal counts on cultures or pyuria for the diagnosis.
- In patients without indwelling catheters, renal infection is documented with colony counts of 10^4 yeast colony-forming units per milliliter (cfu/ml). In patients with indwelling catheters, colony counts of $2\times10^4$to 10^5 cfu/ml is noted. Ahematogenous renal candidiasis, renal involvement can be seen with any concentration of Candida in the urine[3].
- The techniques routinely used for the detection of bacteria, also detect Candida in urine. However, C. glabrata grows more slowly than other species and colonies may not appear for 48 hours.
- Abdominal ultrasound and computed tomography (CT) are essential to see obstruction at any level in the urinary tract and determine fungus balls in bladder or kidney. In some patients, cystoscopy and biopsy of the bladder wall is helpful to diagnose inflammation and extent of invasion.

Treatment with antifungal medicine:

- Most patients with candiduria do not need treatment with an antifungal agent. For asymptomatic patients, treatment should be given to those who are at high risk of systemic candidemia or in whom the candiduriais likely due to disseminated fungal infection[4].

- Infectious Diseases Society of America (IDSA) recommended treatment of candiduria with antifungal drugs for patients with urologic procedures (e.g. urethrocystoscopy, DJ stenting, etc), infants with very LBW and neutropenic hosts, due to high risk of disseminated candidiasis**.**

- Asymptomatic candiduria in the renal transplant patient does not need systemic antifungal treatment unless obstruction is present or symptoms of local or systemic infection develop.

- In low-risk patients with asymptomatic candiduria, removal of an indwelling urinary catheter will eradicate candiduria in many patients. If catheter is necessary, replacing the existingcatheter with a new one should be done. This may eradicate candiduria transiently, but the organisms will return within a short time. For eradication of Candida from the urinary tract, removal of obstruction in essential.

- Patients with symptoms of cystitis or pyelonephritis, and in whom bacteria as well as Candida are found in the urine culture, should be treated with antibacterial drug initially. If no bacteria are present, treatment with an antifungal drug is appropriate. Eradication of the organism is more likely after removing the indwelling catheter[5].

- **Oral fluconazole (200 mg capsule) is the drug of choice.** It is excreted as active drug in the urine. A loading dose of 400 mg should be given, followed by 200 mg daily for 14 days. For systemic candidiasis IV infusion of fluconazole (Injection Fluconazole 200 mg/100 ml) is necessary. Many C. glabrata infections do not respond to fluconazole.

- Renal dose: If CrCl is <50 mi/min and patient is not on dialysis, dose should be reduced to 50% of usual dose. If patient is on maintenance hemodialysis, usual dose should be given after each session.

- The possibility of drug-drug interactions should be kept in mind. Cyclosporine or tacrolimus (resulting in CNI toxicity and high serum creatinine), sulfonylurea anti-diabetic drugs (resulting in hypoglycemia), phenytoin (resulting in phenytoin toxicities, e.g. tremor), warfarin (resulting in increased prothrombin time and hemorrhage), benzodiazepine (resulting in deep and prolong sleep), rifampicin (resulting in reduced fluconazole level with therapeutic failure) etc may cause drug-drug interaction with fluconazole. The other available azole agents, e.g. itraconazole, voriconazole, posaconazole are not excreted into the urine as active drug, which may or may not be effective in fungal UTI[6].

- Intravenous amphotericin B is also effective in treating Candida UTIs but should be reserved for patients with upper UTI or fluconazole-resistant patients, particularly in C. glabrata infection. Due to its nephrotoxicity, the drug must be used judiciously in patients with renal impairment. The recommended dosage is 0.3 to 0.6 mg/kg/day for 1 to 7 days, which may be extended to 14 days for complicated upper UTI**.**

- Lipid formulations of amphotericin B are not recommended for fungal UTIs due to failure to achieve adequate levels in the urinary tract[6].

- Flucytosine is excreted into the urine in high concentrations as active drug, should be used only when fluconazole is not tolerated or the organism is fluconazole resistant.

- The echinocandins (caspofungin, micafungin, and anidulafungin) have minimal or no excretion into the urine as active drug. Therefore echinocandins are not recommended for the treatment of Candida UTIs[7]. But they can be used in invasive candidiasis, candidemia with intra-abdominal abscess and peritonitis which may result in fungal UTI (e.g. Anidulafungin infusion 100 mg 2 vials IV slowly, followed by 1 vial IV for14 days after having the last positive C/S report).

Local antifungal administration:

- Continuous bladder irrigation with amphotericin B 50 mg in 1 liter of sterile water through a triple-lumen catheter is sometimes used to treat Candida bladder infection. This clears candiduria more quickly than systemic antifungal agents. However, the effect is brief, and recolonization occurs within 1 to 2 weeks.

- In the patient with urinary tract obstruction with a fungus ball, irrigation through a PCN tube with amphotericin B is recommended, in addition to systemic antifungal treatment with fluconazole. Absorption of amphotericin B does not occur. Endoscopic removal of the fungus ball is essential to eradicate the infection.

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Case Report

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Vitamin D Resistant Osteomalacia TYPE –I: A Case Report

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Abstract:

Osteomalacia is a bone disorder characterized by decreased mineralization of newly formed osteoid at sites of bone turnover. It is caused by different processes leading to decreased available mineral or enzymeatic alterations. Signs and symptoms include diffuse bone, muscle weakness and characteristic feature patteren, often referred to as pseudofractures, involving ribs, scapulae, pubic rami, proximal femurs and codfish-type vertebrae. Our patient, a 55 years old lady from Dakha City presented with diffuse body pain, LBP, difficulty in standing from sitting position, pain in both achilis tendons, feet and along both inguinal regions with wadling gait and almost in bedridden condition. She was finally diagnosed as a case of Vitamin D Resistant Osteomalacia Type I and was treated with active Vitamin D (Calcitriol) supplemented with calcium and phosphate. With in couple of months she recovered and came to normal life.

Keywords: Active vitamin D deficiency, osteomalacia.

Introduction:

Osteomalacia is a metabolic bone disease characterised by incomplete mineralisation of mature organic bone matrix following growth plate closure in adult[1]. Most common cause is vitamin D deficiency, but can also occur as a result of inherited defects in renal phosphate excretion, inherited defect in vitamin D receptor (Vitamin D Resistant Osteomalacia / Ricket Type II) and in the pathway of vitamin D activation. Other causes include defects in phosphate and phyrophosphate metabolism, iotrogenic, excess fluorine in water and chronic kidney disease [2]. Overall prevalence of biochemical ostemalacia was 10%, girls suffered more than boys (14.7 %vs 3.6%, p< 0.001) in a study carried on Arab adolescents[3]. But Incidence of Vitamin D resistant Type I Ostemalacia is uncommon. 1,25 dihydroxy vitamin D3 is one of the principal hormone regulator of calcium and phosphate metabolism in the body. Vitamin D depended rickets type 1 is a autosomal recessive disorder caused by mutation of 1 alpha hydroxylase gene resulting in deficiency or absenceof 1 alpha hydroxilase enzyme, which is responsible for activation of 25(OH)D to $1,25(OH)_2D$, the active form of vitamin D in the kidney. This is characterized by laboratory findings of hypocalcaemia, increase concentration of serum parathormone, low or undetectable level of $1,25\ (OH)_2D$ despite increased or normal concentration of 25(OH)D. Physiological dose of active vitamin D induce clinical and biochemical recovery[4].

Case report:

A post menopausal hypertensive, diabetic lady presented with diffuse bone and muscle pain throughout the body, LBP, pain in both Achillis tendons, feet and along both inguinal regions for 4 years. She is almost bedridden for the last 6 month. For her condition she took consultation from different specialist at home and abroad. Her previous investigations showed low serum calcium, phosphate, high alkaline phosphatase, normal 25 (OH) D, negative RA and Anti CCP, normal CRP, CBC, uric acid, mild disc bulge at L3-4, L4-5, L5-S1 and

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generalised osteopenia in MRI of lumbar spine, mild tenosynovitis of right perineal tendons and degenerative change in right tenonavicular joint in USG of right ankle and feet, unremarkable SI joints in MRI,and normal X-ray chest PA view and USG. With these investigations she was being treated with NSAID, Vitamin D and physiotherapy but her condition is deteriorating.

On examination by the present investigators, there were bony and muscle tenderness in different parts of the body but no features of inflammatory arthritis. She found extreme difficulty in walking and could not stand from sitting position. Her gait was wadling. She was well nourished, not anaemic and no other notable sign in general and systemic examination. Her blood pressure and diabetes under control with drugs.

On investigation RA, ANA were negative, serum Alkaline phosphatase (560 U/L, normal range-91-218 U/L), serum parathormon (206.80ngm/ml, normal range-15–58 ngm/L) were significantly high, serum calcium (7.5 mgm/ml, normal range- 8.0- 10.0 mgm/ml) and phosphate (1.90 mgm/ml, normal range- 2.5-5.0 mgm) were significantly low. Vitamin D [25(OH) D] level was normal but active vitamin D [1,25 $(OH)_2$] was significantly low (20-30 pmol/ L, normal range-47.76-190.32 p mol/L). Her serum CPK, CRP, uric acid, creatinine, thyroid function, X ray chest, USG whole abdomen and X-ray of SI join normal were normal. X-ray pelvis showed pseudo fracture in left iliopelvic eminence and X-ray right foot and ankle revealed pseudo fractures in the right 5th metatarsal bone and lower end of right tibia and degenerative change in right tenonavicular joint. Her BMD showed osteoporosis in both femoral necks and low bone mass in left fore arm.

With the above clinical, laboratory and imaging findings she was diagnosed as a case of Type I Vitamin D Resistant Osteomalacia with concominent Osteoporosis. She was then treated with active vitamin D with calcium and phosphate supplements and with denosumab for osteoporosis and within couple of months she recovered and returned to normal life.





Discussion:

This 55 years old lady was suffering from complaints mentioned above for long 4 years. Initially she was thought to be suffering from seronegative spondyoarthopathy, but it was excuded by normal MRI of SI joints, negative HLA B27 and normal CRP, CBC. Rheumatoid Arthritis and SLE were excluded clinically and with normal CRP, CBC and negative RA, ANA, Anti CCP. Her previous investigations showed low serum calcium and phosphate, high serum parathormon and alkaline phosphatase level that favoured diagnosis of osteomalacia but **normal vitamin D [25(OH)D] level**. That suggest that this Ostemalacia was not due to deficiency of 25 (OH) D. That's why replacement with this vitamin did not work.

All the Investigations for osteomalacia were repeated by the present investigators. The results were similar. **Then level of 1, 25 $(OH)_2$ D was done, which were significantly low.** This favours diagnosis of Vitamin D Resistant Osteomalacia Type I [2]. In addition her BMD report showed osteoporosis in both femoral necks and low bone mass in left fore arm. Then she was treated with active vitamin D- cacitriol, phosphate and calcium supplements and with denosumab for osteoporosis. The patient completely recovered biochemically and clinically within couple of months. Minwang et al reported a 59 years old lady with similar presentations except osteoporosis who was treated similarly except denosumab and she also recovered[5].

Chan Tong Kim M.D. also reported three women with Vitamin D Deficiency OstemalaciaType l with similar clinical presentations, similal way of diagnosis and treatment except denosumab.

Conclusion:

In any case of Ostemalacia with normal vitamin D level should be investigated for Vitamin D Resistant Ostemalacia as well for other rare causes.

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Medical Quiz

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Medical Quiz: Images

Mamun KAA[1]

53 yearold male presented with 2 months history of headache and visual disturbances. In the past 2weeks ,his headache became severe that was not relieved by analgesia and his vision was getting worse. He reported change in shoe size . On examination he was found to have bitemporal hemianopia. MRI Brain was done.

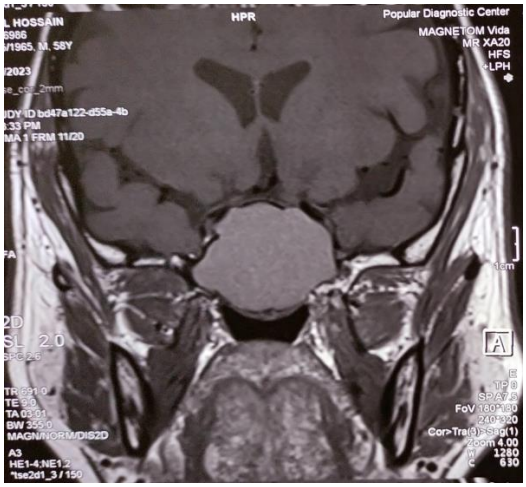


Figure 1: MRI Brain T 1 image Coronal view

- **Q1**. Mention the abnormal findings in MRI brain.
- **Q2**. What is the diagnosis? What will be the differential diagnosis?
- **Q3**. What further investigations should be done ?
- **Q4**. What is the treatment option?

Answer to Medical Quiz: Images

- ✓ MRI brain shows large stronglyenhachinglobuled mass with sellar and .suprasellerextenision
- ✓ Pituitary macroedema. D/D Craniopharygioma
- ✓ Serum prolactin , Growth hormone, ACTH, Serum TSH, Cortisol and Testosterone.
- ✓ Surgery

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Discussion:

Pituitary adenomas are benign tumors of the pituitary gland[1]. Most are located in the anterior lobe of the gland.About 1 in 15 people will develop a pituitary adenoma in their lifetime[2].Some pituitary adenomas secrete one or more hormones in excess. Even when they are small in size, these endocrine-active pituitary tumors can cause hormonal imbalances that affect body functions[3]. People can develop pituitary adenomas at any age[4].The key clinical signs and symptoms of a pituitary adenoma include: bitemporal hemianopia, reduced visual acuity, difficulty in reading, headache, photophobia, abnormal colour vision (red-green defect), optic atrophy and ocular palsies[5].

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