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Journal of Monno Medical College (J Monno Med Coll) is a leading, open access, peer-reviewed scientific journal on medical science for rapid publication of articles published by Monno Medical College, Monno City, Gilondo, Manikgonj Bangladesh. This journal provides quick initial decisions followed by a high quality medical editing service and an excellent publishing service to its authors. This journal has been launched from June 2015 and will be continued. **J Monno Med Coll** is published 2 times per year. This journal aims to publish scientifically written, evidence-based articles from all disciplines of medical sciences and clinical practice, preventive medicine, epidemiology as well as healthcare research. There are a great scope to publish the different kinds of articles including original research papers, reviews of the specific topics, case report and short research communications. Submissions of basic and clinical research are both considered. Manuscripts should present novel findings addressing significant questions in clinical medicine research and practice, in the form of original research article, editorial, review article, short communication, case report, letter to the editor, and others. In addition to that **J Monno Med Coll** publishes studies performed by multi-center groups in the various disciplines of medicine, including clinical trials and cohort studies from large patient populations, specifically phase I, phase II, and phase III studies performed under the auspices of groups such as general clinical research centers, cooperative oncology groups, and the like. Reports of patients with common presentations or diseases, especially studies that delineate the natural history and therapy of important conditions are also published. Reviews oriented to the practicing internist and diagnostic puzzles, complete with images from a variety of specialties are also published. Careful physiological or pharmacological studies that explain normal function or the body's response to disease as well as analytic reviews such as meta-analyses and decision analyses using a formal structure to summarize an important field are acceptable to publish.

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Submission of manuscript:

- Authors should submit electronic version (Microsoft word doc) of the manuscript to the editor via e-mail **(editor.jmmc@yahoo.com)** and two hard copies of manuscript with cover letter signed by all authors of the paper
- Accepted papers will be acknowledged and processed further; if the papers are rejected, the decision will be communicated to the corresponding author but the manuscripts will not be returned.
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- The language of manuscript must be simple and explicit.
- Author's/Co-author's name or any other identification should not appear anywhere in the body of the manuscript to facilitate blind review.

Types of Manuscript

The following categories of manuscript are accepted for this journal:

a. Original Research Articles
b. Systematic Review or Meta Analysis
c. Review Article
d. Short communications
e. Case reports
f. Letter to Editor

Reporting guidelines

The guidelines listed below should be followed where appropriate. Please use these guidelines to structure your article. Completed applicable checklists, structured abstracts and flow diagrams should be uploaded with your submission; these will be published alongside the final version of your paper.

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- STARD (www.stard-statement.org/) for reporting of diagnostic accuracy studies)
- STROBE (http://www.strobe-statement.org/) for reporting of observational studies in epidemiology

a) Checklist for cohort, case-control, and cross-sectional studies (combined)
b) Checklist for cohort studies
c) Checklist for case-control studies
d) Checklist for cross-sectional studies

- PRISMA (www.prisma-statement.org/index.htm) for reporting of systematic reviews
- MOOSE for reporting of meta-analyses of observational studies
- STREGA (www.medicine.uottawa.ca/public-health-genomics/web/eng/strega.html) for reporting of gene-disease association studies.
- The Equator Network (Enhancing the Quality and Transparency Of health Research) provides a comprehensive list of reporting guidelines. The web site of it is http://www.equator-network.org/resource-centre/library of-health-research -reporting/library/

Original Research Articles:

It should be arranged into the following sections:

1. Title
2. Author(s)
3. Address

4. Structured Abstract
5. Key words
6. Introduction
7. Methodology
8. Results
9. Discussion
10. Conclusion
11. Acknowledgement
12. References
13. Tables
14. Figures

Title page

It should be paginated as page 1 of the paper. It should carry the title, authors' names and their affiliations, running title, address for correspondence including Email address & mobile number.

Title

Must be informative, specific and short and not exceed 100 words.

Authors and affiliations

The names of authors and their appropriate addresses should be given. It should be made clear which address relates to which author.

Running title

It is a short title typed in the journal at the right top corner of right hand page of the article (except the lead page). A short running title of not more than 40 characters should be given.

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The corresponding author's contact address should be given in the title page. The fax number (if available) may be mentioned. The Email ID and mobile number of the corresponding author or the contact Email ID must also be provided.

Abstract and key words

Abstract: It must start on a new page carrying the following information: (a) Title (without authors names or affiliations), (b) Abstract body, (c) Key words, (d) Running title. It should not exceed 350 words excluding the title and the key words. The abstract must be concise, clear and informative rather than indicative. New and important aspects must be emphasized. The abstract must be in a structured form consisting of background, objectives, methodology, result and conclusion briefly explaining what was intended, done, observed and concluded. Authors should state the main conclusions clearly and not in vague statements. The conclusions and recommendations not found in the text of the article should not be given in the abstract.

Key words: A list of 3-7 keywords should be provided which will help readers or indexing agencies in cross-indexing the study. The words found in title may be given as key words. All keywords should be provided according to MeSH terms at: http://www.nlm.nih.gov/mesh/MBrowser.html. Note that the preferred expression is indicated by the label "MeSH Heading" and not "Entry Term." The desired terms may then be copied from the MeSH Browser. Another way of finding appropriate headings is to search PubMed to find articles on similar topics, and review the MeSH headings assigned to those articles.

Introduction

It should start on a new page. Essentially this section must introduce the subject and briefly say how the idea for research originated. Give a concise background of the study. Do not review literature extensively but provide the most recent work that has a direct bearing on the subject. Justification for research aims and objectives must be clearly mentioned without any ambiguity. The purpose of the study should be stated at the end. It should not exceed 500 words.

Methodology

This section should deal with the materials used and the methodology - how the work was carried out. The procedure adopted should be described in sufficient detail to allow the study to be interpreted and repeated by the readers, if necessary. The number of subjects, the number of groups studied, the study design, sources of drugs with dosage regimen or instruments used, statistical methods and ethical aspects must be mentioned under the section in text format not in structured format. The methodology- the data collection procedure - must be described in sufficient detail. If a procedure is a commonly used one, giving a reference (previously published) would suffice. If a method is not well known (though previously published) it is better to describe it briefly. Give explicit descriptions of modifications or new methods so that the readers can judge their accuracy, reproducibility and reliability. The nomenclature, the source of material and equipment used, with details of the manufacturers in parentheses, should be clearly mentioned. Drugs and chemicals should be precisely identified using their non-proprietary names or generic names. If necessary, the proprietary or commercial name may be inserted once in parentheses. In case of pharmaceuticals, the first letter of the drug name should be small for generic name (e.g., dipyridamole, propranolol) but capitalized for proprietary names (e.g., Persantin, Inderal). The routes of administration may be abbreviated, e.g., intraarterial (i.a.), intracerebroventricular (i.c.v.), intra-gastric lavage (i.g.), intramuscular (i.m.), intraperitoneal (i.p.), intravenous (i.v.), per os (p.o.), subcutaneous (s.c.), transdermal (t.d.).

Statistical Methods

The details of statistical tests used and the level of significance should be stated. If more than one test is used it is important to indicate which groups and parameters have been subjected to which test.

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The results should be stated concisely without comments. It should be presented in logical sequence in the text with appropriate reference to tables and/or figures. The data given in tables or figures should not be repeated in the text. The same data should not be presented in both tabular and graphic forms. Simple data may be given in the text itself instead of figures or tables. Avoid discussions and conclusions in the results section.

Discussion

This section should deal with the interpretation, rather than recapitulation of results. It is important to discuss the new and significant observations in the light of previous work. Discuss also the weaknesses or pitfalls in the study. New hypotheses or recommendations can be put forth. Avoid unqualified statements and conclusions not completely supported by the data. Repetition of information given under Introduction and Results should be avoided.

Conclusion

Conclusions must be drawn considering the strengths and weaknesses of the study. They must be conveyed in the last paragraph under Discussion. Make sure conclusions drawn should tally with the objectives stated under Introduction.

Acknowledgements

It should be typed in a new page. Acknowledge only persons who have contributed to the scientific content or provided technical support. Sources of financial support should be mentioned.

References

It should begin on a new page. Avoid citing abstracts as references. Papers which have been submitted and accepted but not yet published may be included in the list of references with the name of the journal and indicated as “In press”. A photocopy of the acceptance letter should be submitted with the manuscript. Information from manuscript “submitted” but “not yet accepted” should not be included. Avoid using abstracts as references. The “unpublished observations” and “personal communications” may not be used as references but may be inserted (in parentheses) in the text. References are to be cited in the text by superscripted number and should be in the order in which they appear. References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification in the text of the particular table or illustration. The references must be verified by the author(s) against the original documents. The list of references should be typed double spaced following the Vancouver style. Examples are given below.

Tables

The number of table should be 3 or 4 in number. Each table must be self-explanatory and presented in such a way that they are easily understandable without referring to the text. It should be typed with double spacing and numbered consecutively with Arabic numerals. Provide a short descriptive caption above each table with foot notes and/or explanations underneath. The number of observations, subjects and the units of numerical figures must be given. It is also important to mention whether the given values are mean, median, mean±SD or mean±SEM. All significant results must be indicated using asterisks. Appropriate positions for the tables within the text may be indicated.

Check list for Table

- Units of data given?
- "n"mentioned?
- Mean ± SD or Mean ± SEM given?
- Statistical significance of groups indicated by asterisks or other markers?
- P values given?
- Rows and columns properly aligned?
- Appropriate position in the text indicated?

Figures

Each figure must be numbered and a short descriptive caption must be provided. All significant results should be indicated using asterisks. For graphs and flow charts, it is not necessary to submit the photographs. A manually prepared or computer drawn figure (with good contrast) on a good quality paper is acceptable. Identify each figure/diagrams on the back with a typed label which shows the number of the figure, the name of
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- X and Y axes titled (legend)?
- Units mentioned (if necessary)?
- Different symbols/markers for different groups given?
- SD or SEM represented (graphically)?
- Statistical significance indicated?
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Systematic Review or Meta Analysis

Authors should report systematic reviews and meta-analyses in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. For Systematic Reviews, both abstract and text of the manuscript should be subdivided into the following sequential sections:

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2) Objective: State the precise primary objective of the review. Indicate whether the review emphasizes factors such as cause, diagnosis, prognosis, therapy, or prevention and include information about the specific population, intervention, exposure, and tests or outcomes that are being reviewed.

3) Data Sources: Succinctly summarize data sources, including years searched. Include in the search the most current information possible, ideally conducting the search several months before the date of manuscript submission. Potential sources include computerized databases and published indexes, registries, abstract booklets, conference proceedings, references identified from bibliographies of pertinent articles and books, experts or research institutions active in the field, and companies or manufacturers of tests or agents being reviewed. If a bibliographic database is used, state the exact indexing terms

used for article retrieval, including any constraints (for example, English language or human subjects). If abstract space does not permit this level of detail, summarize sources in the abstract including databases and years searched, and place the remainder of the information in the "Methods" section of the text.

4) Study Selection: Describe inclusion and exclusion criteria used to select studies for detailed review from among studies identified as relevant to the topic. Under details of selection include particular populations, interventions, outcomes, or methodological designs. Specify the method used to apply these criteria (for example, blinded review, consensus, multiple reviewers). State the proportion of initially identified studies that met selection criteria.

5) Data Extraction: Describe guidelines used for abstracting data and assessing data quality and validity (such as criteria for causal inference). State the method by which the guidelines were applied (eg, independent extraction by multiple observers).

6) Results: State the main results of the review, whether qualitative or quantitative, and outline the methods used to obtain these results. For meta-analyses, state the major outcomes that were pooled and include odds ratios or effect sizes and, if possible, sensitivity analyses. Accompany numerical results by confidence intervals, if applicable, and exact levels of statistical significance. For evaluations of screening and diagnostic tests, include sensitivity, specificity, likelihood ratios, receiver operating characteristic curves, and predictive values. For assessments of prognosis, summarize survival characteristics and related variables. State the major identified sources of variation between studies, including differences in treatment protocols, protocols, co-interventions, confounders, outcome measures, length of follow-up, and dropout rates.

7) Conclusions: Clearly state the conclusions and their applications (clinical or otherwise), limiting interpretation to the domain of the review.

Systematic reviews are welcome. They should be critical assessments of current evidence covering a broad range of topics of concern to those working in the specific field of journal. Systematic reviews should be 4000-5000 words (abstracts to be structured as above).

N.B.: For advice on writing systematic reviews consult: **The Cochrane Reviewers' Handbook Meta-analysis of RCT:** A MOOSE checklist is required for meta-analysis of RCT.

Review articles:

These should contain title page, abstract (need not be structured) and key words. The text proper should be written under appropriate sub-headings. The total number of text words should not exceed 10000 and the total number of figures and tables should not be more than 7.

Short communications:

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- Name, address, telephone and fax numbers and e-mail address of corresponding author
- Running title

- Number of pages, number of figures and number of tables.
- Abstract- in structured (not in Review article, case report, short communication) form along with title, key words and running title.
- Article (double spaced)
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- Figures/photographs and legends
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- Ethical committee clearance certificate (as and whenever applicable)

Examples of References - Vancouver Style

From Uniform Requirements for Manuscripts, www.icmje.org

Articles in Journals

1. Standard journal article

List the first six authors followed by et al. (Note: NLM now lists up through 25 authors; if there are more than 25 authors, NLM lists the first 24, then the last author, then et al.)

Vega KJ, Pina I, Krevsky B. Heart transplantation is associated with an increased risk for pancreatobiliary disease. Ann Intern Med 1996 Jun 1;124(11):980-3

As an option, if a journal carries continuous pagination throughout a volume (as many medical journals do) the month and issue number may be omitted. (Note: For consistency, the option is used throughout the examples in Uniform Requirements. NLM does not use the option.)

Vega KJ, Pina I, Krevsky B. Heart transplantation is associated with an increased risk for pancreatobiliary disease. Ann Intern Med 1996;124: 980-3

More than six authors:

Parkin DM, Clayton D, Black RJ, Masuyer E, Friedl HP, Ivanov E, et al. Childhood leukaemia in Europe after Chernobyl: 5 year follow-up. Br J Cancer 1996;73:1006-12

2. Organization as author

The Cardiac Society of Australia and New Zealand. Clinical exercise stress testing. Safety and performance guidelines. Med J Aust 1996; 164: 282-4

3. No author given

Anonymous. Cancer in South Africa [editorial]. S Afr Med J 1994;84:15

4. Article not in English

(Note: NLM translates the title to English, encloses the translation in square brackets, and adds an abbreviated language designator.)

Ryder TE, Haukeland EA, Solhaug JH. Bilateral infrapatellar seneruptur hostidligere frisk kvinne. Tidsskr Nor Laegeforen 1996;116:41-2.

5. Volume with supplement

Shen HM, Zhang QF. Risk assessment of nickel carcinogenicity and occupational lung cancer. Environ Health Perspect 1994;102 Suppl 1:275-82.

6. Issue with supplement

Payne DK, Sullivan MD, Massie MJ. Women's psychological reactions to breast cancer. Semin Oncol 1996; 23(1 Suppl 2):89-97.

7. Volume with part

Ozben T, Nacitarhan S, Tuncer N. Plasma and urine sialic acid in non-insulin dependent diabetes mellitus. Ann Clin Biochem 1995;32(Pt 3):303-6.

8. Issue with part

Poole GH, Mills SM. One hundred consecutive cases of flap lacerations of the leg in ageing patients. N Z Med J 1994;107(986 Pt 1):377-8.

9. Issue with no volume

Turan I, Wredmark T, Fellander-Tsai L. Arthroscopic ankle arthrodesis in rheumatoid arthritis. Clin Orthop

1995;(320):110-4.

10. No issue or volume

Browell DA, Lennard TW. Immuno-logic status of the cancer patient and the effects of blood transfusion on antitumor responses. Curr Opin Gen Surg 1993:325-33.

11. Pagination in Roman numerals

Fisher GA, Sikic BI. Drug resistance in clinical oncology and hematology. Introduction. Hematol Oncol Clin North Am 1995 Apr;9(2):xi-xii.

12. Type of article indicated as needed

Enzensberger W, Fischer PA. Metronome in Parkinson's disease [letter]. Lancet 1996;347:1337.

Clement J, De Bock R. Hematological complications of hantavirus nephro-pathy (HVN) [abstract]. Kidney Int 1992;42:1285.

13. Article containing retraction

Garey CE, Schwarzman AL, Rise ML, Seyfried TN. Ceruloplasmin gene defect associated with epilepsy in EL mice [retraction of Garey CE, Schwarzman AL, Rise ML, Seyfried TN. In: Nat Genet 1994;6:426-31]. Nat Genet 1995;11:104.

14. Article retracted

Liou GI, Wang M, Matragoon S. Precocious IRBP gene expression during mouse development [retracted in Invest Ophthalmol Vis Sci 1994; 35:3127]. Invest Ophthalmol Vis Sci 1994;35:1083-8.

15. Article with published erratum

Hamlin JA, Kahn AM. Herniography in symptomatic patients following inguinal hernia repair [published erratum appears in West J Med 1995;162:278]. West J Med 1995;162: 28-31. Books and Other Monographs

(Note: Previous Vancouver style incorrectly had a comma rather than a semicolon between the publisher and the date.)

16. Personal author(s)

Ringsven MK, Bond D. Gerontology and leadership skills for nurses. 2nd ed. Albany (NY): Delmar Publishers; 1996.

17. Editor(s), compiler(s) as author

Norman IJ, Redfern SJ, editors. Mental health care for elderly people. New York: Churchill Livingstone; 1996.

18. Organization as author and publisher

Institute of Medicine (US). Looking at the future of the Medicaid program. Washington: The Institute; 1992.

19. Chapter in a book

Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: Pathophysiology, diagnosis, and management. 2nd ed. New York: Raven Press; 1995. p. 465-78.

20. Conference proceedings

Kimura J, Shibasaki H, editors. Recent advances in clinical neuro-physiology. Proceedings of the 10th International Congress of EMG and Clinical Neurophysiology; 1995 Oct 15-19; Kyoto, Japan. Amsterdam: Elsevier; 1996.

21. Conference paper

Bengtsson S, Solheim BG. Enforce-ment of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Infor-matics; 1992 Sep 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. p. 1561-5

22. Scientific or technical report

Issued by funding/sponsoring agency:

Smith P, Golladay K. Payment for durable medical equipment billed during skilled nursing facility stays. Final report. Dallas (TX): Dept. of Health and Human Services (US), Office of Evaluation and Inspections; 1994 Oct. Report No.: HHSI-GOEI69200860.

Issued by performing agency:

Field MJ, Tranquada RE, Feasley JC, editors. Health services research: work force and educational issues. Washington: National Academy Press; 1995. Contract No.: AHCPR282942008. Sponsored by the Agency for Health Care Policy and Research.

23. Dissertation/Thesis

Kaplan SJ. Post-hospital home health care: the elderly's access and utilization [Dissertation/Thesis]. St. Louis (MO): Washington Univ.; 1995.

24. Patent

Larsen CE, Trip R, Johnson CR, in-ventors; Novoste Corporation, assignee. Methods for procedures re-lated to the electro-

physiology of the heart. US patent 5,529,067. 1995 Jun 25.

Other Published Material

25. Newspaper article

Lee G. Hospitalizations tied to ozone pollution: study estimates 50,000 admissions annually. The Washington Post 1996 Jun 21;Sect. A:3 (col. 5).

26. Audiovisual material

HIV+/AIDS: the facts and the future [videocassette]. St. Louis (MO): Mosby-Year Book; 1995.

27. Legal material

Public law: Preventive Health Amendments of 1993, Pub. L. No. 103-183, 107 Stat. 2226 (Dec. 14, 1993). Unenacted bill: Medical Records Confidentiality Act of 1995, S. 1360, 104th Cong., 1st Sess. (1995)

Code of Federal Regulations: Informed Consent, 42 C.F.R. Sect. 441.257 (1995).

Hearing: Increased Drug Abuse: the Impact on the Nation's Emergency, Rooms: Hearings Before the Subcomm. On Human Resources and Intergovernmental Relations of the House Comm. On Government Operations, 103rd Cong., 1st Sess. (May 26, 1993).

28. Map

North Carolina. Tuberculosis rates per 100,000 population, 1990 [demo-graphic map]. Raleigh: North Carolina Dept. of Environment, Health, and Natural Resources, Div. of Epidemiology; 1991.

29. Dictionary and similar references

Stedman's medical dictionary. 26th ed. Baltimore: Williams & Wilkins; 1995. Apraxia; p. 119-20.

30. Classical material

The Winter's Tale: act 5, scene 1, lines 13-16. The complete works of William Shakespeare. London: Rex; 1973.

31. In press

(Note: NLM prefers "forthcoming" because not all items will be printed.)

Leshner AI. Molecular mechanisms of cocaine addiction. N Engl J Med. In press 1996.

Electronic Material

32. Journal article in electronic format

Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis [serial online] 1995 Jan-Mar [cited 1996 Jun 5];1(1):[24 screens].

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Checklist (to be tick marked, as applicable and one copy attached with the manuscript)

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Editorial
Journal of Monno Medical College,
June 2020, Vol. 6, No. 1, pp. 1-2
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Importance of Biomarkers in Covid 19

Naher S[1], Hoque N[2]

In December 2019, a novel coronavirus, now named as SARS-CoV-2, caused a series of acute atypical respiratory diseases termed as COVID-19 in Wuhan, Hubei Province, China. The virus is transmittable and now became pandemic, infiltrated more than 200 countries and affected almost 29.8 million confirmed people[1]. The number of death tolls also continues to rise. Countries have been forced to do social distancing and lockdown to combat the deadly situation. This pandemic is now a scientific, medical and social challenge.

As a new disease having an unpredictable course, very little is known about the biomarkers of this viral infection. Researchers around the world are in search of classical, specific and effective laboratory biomarkers of this disease that will help manage the patient promptly and stratify the patient in different risk group and the progress in this field is substantial. Identification and characterization of biomarkers is important to understand the disease pathology, to assess the disease as a whole and to develop specific drugs and/or vaccine against this havoc causing disease. SARS-CoV-2, binds with the Angiotensin converting enzyme 2 (ACE-2), expression of which is high in lung, heart, ileum, kidney and bladder. In lung, ACE-2 is highly expressed on lung epithelial cells in apical side which acts as a gateway where this virus can attaches with the cell, enters the cell and destroys the cells[2]. The pathological change that occur in lung is detected as characteristic pulmonary ground glass opacity by computed tomography (CT) scan even in asymptomatic patients. It is the CT scan of the chest that was the earliest diagnostic tool used in China. Virus-infected apoptotic epithelial cells can be phagocytized by dendritic cells (DC) and macrophages, which leads to antigen presentation to T cells. Severe COVID-19 infection is characterized by a massive pro-inflammatory response and increased plasma concentrations of pro-inflammatory cytokines, including interleukin IL-6, IL-10, granulocyte-colony stimulating factor (G-CSF), monocyte chemoattractant protein (MCP) 1-α, macrophage inflammatory protein (MIP) 1-α, and tumor necrosis factor (TNF)-α which is known as 'Cytokine Storm' that results in ARDS and multi-organ dysfunction (MODS)[2]. In fact, 'Cytokine Storm' is the exaggerated immune reaction in response to viral infection. The gold standard test for SARS-CoV-2 identification is reverse-transcriptase polymerase chain reaction (RT-PCR), a routine confirmatory test recommended by WHO. RT-PCR is designed for conserved regions of the viral genome but large number of genetic variations in viral RNA, mismatch between primers, probes, and target sequences may lead to reduced detection performance and false-negative results. Even Suspects with positive chest CT scans may show negative results for SARS-CoV-2 by RT-PCR[3]. In fact, gold standard test should be viral isolation by culture which is confined only to high-tech research laboratories.

Biomarkers identified so far include Hematological: (Leucocyte count, lymphocyte count, neutrophil count, neutrophil-lymphocyte ratio (NLR), platelet count); Inflammatory: (C-reactive protein (CRP), ESR, pro-calcitonin); Immunological : (Interleukin (IL)-6, IL-7, TNF-α, monocyte chemoattractant protein (MCP) 1-α, macrophage inflammatory protein (MIP) 1- α, granulocyte-colony stimulating factor (G-CSF) and other cytokines); and Biochemical: (D-dimer, fibrin degradation product (FDP), serum ferritin, cardiac troponin I, creatine kinase, AST, ALT, urea and creatinine). Potential new biomarkers under study include homocysteine and angiotensin-II, Ang (1-7), Ang (1-9) and almandine are gaining interest[9]. Common changes observed in hematological biomarkers are increase in leucocyte count, higher neutrophil count and lower lymphocyte count and high NLR. Thrombocytopenia is almost a consistent feature. Lower monocyte and eosinophil count also observed in in some severe cases[4]. All the biochemical markers mentioned above are found to be increased singly or in combination in the course of the disease and that depends on severity of the disease and organs involved. Inflammatory biomarkers mentioned above also found to be high in many cases separately or in combination and this depends also on severity of the disease and organs involved.

The study of SARS-CoV-2 showed that virus infected lung epithelial cells produces IL-8 in addition to IL-6. IL-8 is a well-known chemoattractant for neutrophils and T cells. Infiltration of a large number of inflammatory cells were

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observed in the lungs in severe COVID-19 patients, which are innate immune cells and adaptive immune cells. Among innate immune cells, majority are neutrophils. Neutrophils act as double-edged sword as it can induce lung injury as well[4]. The majority of infiltrating adaptive immune cells were found to be T cells, and significant reduction in circulating T cells was observed. CD8+ T cells are primary cytotoxic T cells. Severe patients also showed pathological cytotoxic T cells that also contribute to lung injury[5].

Elevated level of IL-6, the most common type of cytokine released by activated macrophages, signify severe manifestations of COVID-19. So, clinicians can use this to identify severity earlier and commence oxygen therapy sooner. Studies suggest that CRP levels also indicate the presence and severity of COVID-19 infection and reflect physiological complications[6]. Increased serum LDH hints to viral infection or lung damage, such as the pneumonia induced by SARS-CoV-2. Even significant rise in LDH levels was found among treatment failure COVID-19 patients[7].

In addition to respiratory symptoms, thrombosis and pulmonary embolism have been observed in severe diseases. Elevated D-dimer and fibrinogen levels, hallmark of thrombo-embolic process were also observed in severe diseases. D-dimer originate from the lysis of cross-linked fibrin. Activation of coagulation and fibrinolysis results in increased D-dimer and increased level of which on admission could be used to triage patients into critical care which can help clinicians monitor those who are likely to deteriorate earlier[8].

Early recognition of myocardial injury indicated by elevated hs-TnI aids in appropriate triage to a critical care area and heralds the use of appropriate medication. It is important to analyze the discriminative ability of hematologic, biochemical, inflammatory and immunological biomarkers in patient with and without the severe and fatal form of COVID-19.

Though knowledge about this deadly disease is growing very rapidly, from the scientific evidence available till date, it is clear that the levels of mentioned biomarkers specially NLR, CRP, IL-6, D-dimer, ferritin, Troponin and CK which may change according to severity of COVID-19 infection can be used as prognostic and predictive tools as well as for stratification of patient in risk category which is utmost important in clinical settings and therapeutic management[9]. Judicious use of this knowledge can reduce morbidly, mortality and ICU admission. Researchers' around the globe are very much hopeful to find out a classical biomarkers that can be targeted for drug and/or vaccine development to combat the situation. As knowledge about this devastating disease increasing rapidly around the globe, physicians involved in the management of COVID-19 patients and post COVID-19 symptoms must update themselves by seminar and symposium and training, if needed through virtual platform.

[Journal of Monno Medical College, June 2020;6(1): 1-2]

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Original Article

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Psychiatric Morbidity among Patients with Chronic Pain at a Tertiary Care Hospital in Dhaka City

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Abstract

Background: Chronic pain is a common problem among the general population and has been found to be associated with psychiatric disorders in studies based on both clinical samples and epidemiological surveys. **Objective:** The purpose of the present study was to determine the psychiatric co-morbidity in patients with chronic pain disorder in tertiary care hospital setting. **Methodology:** This descriptive cross sectional study was carried out in the department of physiotherapy in East West Medical College and Hospital,Achinagar, Uttara, Dhaka, Bangladesh from December 2017 to November 2018 for a period of around one year. Patients in the age group 18 to 65 years were interviewed face to face. We used socio demographic and clinical details by semi structured data collection sheet and DSM-V. **Results:** It was revealed that psychiatric illness in overall sample prevailed among 164(75%) cases. Among 164 patients 79(36.6%) cases were diagnosis with generalized anxiety disorder, 53(24.5%) cases of patients depressive disorder, 12(5.6%) cases of somatic symptom disorder, 10(4.6%) cases of substance related disorder, 10(4.6%)cases other psychiatric disorder. **Conclusion:** Psychiatric co-morbidity especially the prevalence of anxiety, depression and somatic symptom disorders are high amongst patients suffering from chronic pain disorder. *[J Monno Med Coll June 2020;6(1): 3-6*

Keywords: Anxiety; chronic pain; depression psychiatric co morbidity

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Introduction

Chronic pain is defined as patients present with pain for more than half of the days of at least a 90 days period[1]. Pain characterizes both medical and psychological mechanisms[2]. Chronic pain is now extensively viewed as a bio psychosocial phenomenon, in which biological, psychological, and social factors dynamically interact with one another and the psychological symptoms are produced by the patient's perception of, and reaction to the disease process and its consequences[3]. Chronic pain interferes with the quality of life and can disrupt daily routine, prevent from working or cause feelings of hopelessness and anxiety[4]. Chronic pain is a common problem among the general population. Estimates of prevalence vary depending on the methodology used and the pain conditions examined[5]. The 12-month prevalence estimates of chronic pain range from 17.0% to 29.0% cases in Europe[9]. Surveys have established the prevalence of chronic pain conditions to be 37.3% cases in developed countries and 41.1% cases in developing countries[6].

Chronic pain affects individuals' well-being, productivity and social relationships[7-8] and has been found to be associated with psychiatric disorders in studies based on clinical samples[9-10] as well as studies involving epidemiological surveys[11-12]. Depression is the most commonly reported co-morbidity in chronic pain conditions; in a literature review, Bair et al[15] found depression to be present in 5.0% to 85.0% cases depending on the study setting of patients with pain conditions. Epidemiological data have shown a strong association between generalized anxiety disorder and pain conditions[11,13] while only a few studies have shown higher odds of alcohol use disorders among individuals suffering from pain disorders[11,13].

This association has important clinical implications because patients with psychiatric disorders often present to their primary care provider with pain as the initial reason for seeking treatment and the lack of awareness of the association may lead to the under diagnosis and under treatment of the associated psychiatric disorder. Studies

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involving patients with chronic pain have shown that coexisting psychiatric disorders are associated with disability and poorer treatment outcomes[15-16] and similarly, the presence of pain in patients with major depressive disorder is associated with poorer outcomes, increased overall treatment costs, impaired productivity and poor quality of life[17-19]. The aims of the present study was to establish the prevalence, and co morbidities of chronic pain disorders among the adult population in a tertiary care hospital.

Methodology

This was a descriptive type of cross-sectional study which was conducted over a period of twelve (12) months from December 2017 to November 2018 in the Department of Physiotherapy in collaboration with Department of Psychiatry at East West Medical College and Hospital, Achinagar, Turag, Dhaka a tertiary level clinical and academic institution in Dhaka city. Patients in the age group of 18 to 65 years and who had chronic pain of more than 12 weeks duration were included in the study. Patients with severe or acute medical or neurological illness, physical disability, clinical evidence of mental retardation and those who did not consent to participate were excluded in the study. All the chronic pain patients attending the Department of physiotherapy were initially assessed by physiotherapist; a clinical diagnosis was made, and was referred for psychiatric assessment. Appropriate haematological or radiological studies were done prior to the final diagnosis. The psychiatric evaluation was done according to "The Diagnostic and Statistical Manual of Mental Disorders", Fifth Edition (DSM-5), by the first author. A semi-structured questionnaire was used to collect socio-demographic information including age, gender, marital status, educational attainment, occupation, residence and monthly income. The patients were analysed based on important socio-demographic variables, chronic pain condition and diagnoses conferred. The data was analysed by using SPSS-17.

Results

The sample consist of 216 patients with chronic pain, who attended the physiotherapy department or East West Medical College and Hospital, achinagar,Turag Dhaka, Bangladesh. The sample consists of 48.6% men and 51.4% cases women; their mean age was 39.20 years and standard deviation 13.759 years. Majorities of the cases was married in 63.9% cases and 25.0% cases was unmarried, while the rest were widow/ divorced/separated (15.2%). Education level of the responders were mostly below S.S.C level (44.0%), and a few were no academic schooling (6.5%). In this study 54.6% cases of the responders were belong to rural background while 45.4% cases were urbanities. A big proportion of responded about 39.4% cases monthly income was below 10000 taka. Among the responders 45.0% cases were low back pain; then, cervical pain was in 22.7% cases; arthritic pain was in 18.5% cases and others were in 13.4% cases (musculoskeletal pain, fasciitis pain) respectively. A huge proportion (75.9%) of chronic pain patients were co morbid psychiatric disorder. Most prevalent psychiatric disorder was generalized anxiety disorder (36.6%), then followed by major depressive disorder (24.5%). The rest of the psychiatric disorders were somatic symptom disorder (5.4%), substance related disorder (4.6%) and others (4.6%). Most prevalent psychiatric diagnosis among pain patients was 36.6% those who were suffering low back pain (Table 1).

Table1: Socio-Demographic Profile and Clinical Details of the Responded (n=216)

Variables	Frequency	Percent
Age Group		
15 to 30 Years	71	32.9
31 to 45 Years	80	37.0
46 to 60 Years	44	20.4
61 to 75 Years	21	9.7
Mean±SD	39.20±13.759	
Sex		
Male	105	48.6
Female	111	51.4
Marital status		
Married	138	63.9
Unmarried	54	25.0
Divorced	7	3.2
Separated	1	5
Widow	16	7.4
Education		
No schooling	14	6.5
Below S.S.C	95	44.0
S.S.C	41	19.0
H.S.C	35	16.2
Graduation & above	31	14.4
Occupation		
Unemployed	33	15.3
Housewife	80	37.0
Sedentary worker	50	23.1
Labour based	41	19.0
Business	12	5.6
Residence		
Rural	118	54.6
Urban	98	45.4
Monthly income		
<10,000	86	39.8
10001-20000	30	13.9
20001-30000	55	25.5
>30001	45	20.8
Chronic pain condition		
LBP	98	45.4
Arthritic pain	40	18.5
Cervical pain	49	22.7
Others	29	13.4
Psychiatric diagnosis		
MDD	53	24.5
GAD	79	36.6
SSD	12	5.6
SRD	10	4.6
Others	10	4.6
Total	**164**	**75.9**
Psychiatric Problem Absent	52	24.1

LBP=Low back pain; MDD=Major depressive disorder; GAD=Generalized anxiety disorder; SSD=Somatic symptom disorders; SRD=substance related disorders

Table 2: Psychiatric Diagnosis among Chronic Pain Patients (n=164)

Chronic Pain Patients	MDD	GAD	SSD	SRD	Others	P value
LBP	31(31.6%)	42(42.9%)	4(4.1%)	3(3.1%)	5(5.1%)	
Arthritic pain	9(22.5%)	17(42.5%)	2(5.0%)	1(2.5%)	2(5.0%)	
Cervical pain	5(10.2%)	11(22.4%)	3(6.1%)	6(12.2%)	2(4.1%)	0.003
Other pain conditions	8(27.6%)	9(31.0%)	3(10.3%)	0(0.0%)	1(3.4%)	
Total	**53(24.5%)**	**79(36.6%)**	**12(5.6%)**	**10(4.6%)**	**10(4.6%)**	

LBP=Low back pain; MDD=Major depressive disorder; GAD=Generalized anxiety disorder; SSD=Somatic symptom disorders; SRD=substance related disorders; Others: Other psychiatric disorders

Discussion

This descriptive cross-sectional study was done in the department of physiotherapy in collaboration with department of psychiatry in a tertiary level hospital to see the psychiatry morbidity in chronic pain patient. Age distribution showed most of the patient in 31 to 45 years (80, 37.0%), similar finding observed an Indian study[23]. However, in a study done in Singapore older age group was more prominent[4]. This age group is more active part in our society; so, the number is more in this study. The number of females (111, 51.4%) outweighed in this study and this was consistent with other studies[4,21-22] and a study done Rajmohon et al[23] where more male patients were present. Most of the responded were married (63.9% cases), similar finding observed in other study[4,21-23]. This present study majority of the responded come from rural area (54.6%) and monthly income mostly less than 10000 BDT (39.8%). The reason may be due to attend usually lower income people this institute as treatment cost is cheap here. In the present study 216 patients have been included; among them 75.9% patients have psychiatric diagnosis with chronic pain patient. This funding was similar to in Hong Kong study[22] 75.0% cases but little low at psychiatric disorder among chronic low back pain 81.4 to 98.0% in India and Singapore[4,21] study. Another study had shown that psychiatric morbidity in chronic pain patients was 55.0% cases[20] which was more difference than present study. Clinician often holds a dichotomous view at psychiatric disorder at chronic pain, if it was psychiatric disorder or co morbid condition. The most common psychiatric disorder in this study was generalized anxiety disorder 36.6% cases. The prevalence of generalized anxiety disorder among chronic pain patients reported 2.0 to 40.0% cases20 one study and 45.0% cases in other studies[4, 21-22]. This study result is near about the present study. Anxiety can cause people to change their behaviour and postures, change in posture especially when combined with the muscle tension causes muscle in an uncomfortable position and ultimately lead to increase pain, another issue related to anxiety causes increase sensitivity to pain sensation. Next common disorder was depression 24.5% cases which was closer the study reported 29.0% patients suffering depressive disorder in chronic pain patients[22]. Somatic symptom disorder was seen 5.6% cases of the study which was lower than the study reported 12.0% prevalence[20]. Substance related disorder is about 4.6% cases is similar about study showing prevalence 5.0 to 12.0% cases[20].

There is some limitation of this study. Being a cross-sectional study, it is difficult to say whether emotional disturbances were the cause or consequence of pain. Our study was conducted in a tertiary care set up and included only the patients referred to a particular specialty. Individual variations in clinical examination also might have influenced the diagnosis of patients.

Conclusion

Psychiatric disorders are common in chronic pain patients and that the presence of these disorders significantly reduces the efficacy of treatment for chronic pain. These findings suggest that psychiatric co-morbid disorders need to be screened for, diagnosed and treated accordingly to get the favourable response from standard treatment regimens or modalities for chronic pain disorders.

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Original Article

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Capability of Different Extracts of Garlic for the Removal of Arsenic by from Isolated Liver Tissues of Experimental Rat

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Abstract

Background: : Different extracts of garlic have many effects in the organic and inorganic matter of the body. **Objective:** The purpose of the present study was to see the ability of different extracts of garlic for the removal of arsenic from isolated liver tissues of rat. **Methodology:** This animal study was carried out on isolated liver tissues of Long Evans Norwegian adult healthy male rats weighing 160 to 200 g. The rats were 3 to 6 months of age obtained from animal house of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from 2004 to 2005. Measurements and all tasks were performed in a very careful manner. Atomic Absorption Spectrophotometer with Hydride Generator was used to measure the arsenic level. A set of freshly washed test tubes was taken. All test tubes contained 2ml tyrode solution and twenty small pieces of liver tissue maintaining ^{O}C. No arsenic was added in test tube I. 2.5 µg/ml arsenic trioxide was added rest of the test tubes. They all were incubated for 45 minutes at 37^{O}C. Then the tissues were washed properly. Different extracts of garlic were added at 20 µl/ml dose. Second incubation was also for another 45 minutes at 37^{O}C. The effects of extract of garlic (hexane and methanol) on the removal of arsenic from the arsenic loaded liver tissues of rat were analyzed. **Result:** Only twenty small pieces of liver tissues were incubated in 2 ml Tyrode solution. There was no arsenic added in both 1st and 2nd incubation. The amount of arsenic was found 7.23 ± 3.51 µg/ g (mean ± se) of protein. This value was taken as blank. In the first incubation liver tissues of rats were incubated with 2.5 µg/ ml of arsenic for 45 minutes at 37^{O}C and the amount of accumulated arsenic in the tissues was 249.02 ± 21.16 µg / g (mean ± se) of protein and this was considered as standard. The arsenic loaded tissues were incubated for the second time with hexane extract of garlic (20 µl / ml) for another 45 minutes at 37°C and the amount of arsenic was reduced to 22.83 ± 5.98 µg/ g (mean ± s.e) of protein. There was 86% removal of arsenic (P<0.001). **Conclusion:** In conclusion different extracts of garlic has the ability to remove significantly arsenic from isolated liver tissues of experimental rat. *[J Monno Med Coll June 2020;6(1): 7-10*

Keywords: Capability; Extracts of Garlic; Removal of Arsenic; Isolated Liver Tissues; Experimental Rat

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Introduction

Arsine is a hydride gas with potent hemolytic effects[1]. It is manufactured predominantly for use in the semiconductor industry; however, it may also be generated accidentally when arsenic containing ores come in contact with acidic solutions[2]. It is of historical interest that Fowler's solution, which contains 1% potassium arsenite, is widely used as a medicine for many conditions from the eighteenth century through the mid twentieth century[3]. Organic arsenicals were the first pharmaceuticals antibiotics and were widely used for the first half of the twentieth century until supplanted by penicillin and other more effective and less toxic agents[4].

Long-term exposure to inorganic arsenic has been found to give rise effects in a large number of organs[5]. Lesions in upper respiratory tract including perforation in nasal septum, laryngitis, pharyngities, and bronchitis have frequently been encountered in workers in smelting industry exposed to high level of arsenic[6]. Inorganic arsenic in trivalent state can give

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rise to skin lesion especially palmo-plantar hyperkeratosis which has a characteristic appearance. The pigmentation of chronic arsenic poisoning commonly appears in a finely freckled raindrop pattern of pigmentation or de-pigmentation that is particularly pronounced the trunk and extremities and has a bilateral symmetrical distribution[7].

High levels of arsenic in well water are causing widespread poisoning in Bangladesh[8]. In a typical aquifer in southern Bangladesh, chemical data imply that arsenic mobilization is associated recent inflow of carbon. High concentration of radio carbon young methane indicate that young carbon has driven recent biochemical process and irrigation pump is sufficient to have drawn water to depth where dissolved arsenic is at a maximum[9].

Chronic exposure to inorganic arsenic at least several hundred microgram per liter concentration may cause cancer of skin, bladder, lung and possibly several other internal organs including kidney, liver, prostate and non-cancer effects including classic cutaneous manifestations that are distinctive and characteristic of chronic arsenic poisoning like diffuse or spotted hyper pigmentation and palmo-plantar hyperkeratosis[10]. Non-cancer effects may be multisystem with some evidence of peripheral vascular, cardiovascular and cerebrovascular disease, diabetes and adverse reproductive outcome. This present study was undertaken to see the ability of different extracts of garlic for the removal of arsenic from isolated liver tissues of rat.

Methodology

This animal study was carried out on isolated liver tissues of Long Evans Norwegian adult healthy male rats weighing 160 to 200 g. The rats were 3 to 6 months of age obtained from animal house of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from 2004 to 2005. The rats were housed in standard plastic cages with a light/dark cycle 12/12 hours at room temperature in a well-ventilated room. This experiment was an in vitro study. Measurements and all tasks were performed in a very careful manner. The rats were sacrificed by inhalation anesthesia. Inhalation anesthesia is very effective in rats. Liver tissues of rat was extracted with help of a forceps and a pair of scissors and placed into Tyrode solution. The temperature of Tyrode solution was tried to be maintained at O° - 4°C. Two freshly washed test tubes containing 2 ml Tyrode solution were separated and kept into ice pieces. These would be blank as they contain no arsenic. Arsenic was added to Tyrode solution contained in a beaker from stock solution (stock solution was 2 mg/ml) to make 2.5 µg/ml concentration of arsenic. Then 2 ml of Tyrode solution of 2.5 µg/ml of arsenic concentration was transferred to each test tube from the beaker with the help of automatic micro pipette with blue tip except two test tubes which were considered as blank. All the test tubes were kept into ice pieces. Small and approximately equal pieces of liver tissues were put into the individual test tubes with the help of forceps. Approximately 20 small pieces of liver were given in each test tube. Two test tubes contained 2.5 µg/ml concentration of arsenic with no extract and these were called standard. Rest of the test tubes contained 2.5 µg/ml concentration of arsenic in first incubation and different types of extract were added in second incubation and these all were samples. Then all test tubes were incubated for the first time at 37°C for 45 minutes in water bath with shaker. After first incubation all test tubes were taken outside and again placed under ice pieces. All the open ends of the test tubes were covered with parafilm and washed with Tyrode solution properly. The test tubes were taken & shaken at a time. The tissues were washed for two times to remove loosely bound arsenic externally. Another sets of test tubes were taken containing 2 ml of Tyrode solution along with the hexane extract of garlic, 40 µl. The pieces of liver after washing properly were transferred to the respective test tubes and again incubated for 45 minutes at 37ºC in water bath with shaker. The tissues were again properly washed as before after second incubation. Then all tissues were homogenated individually by a hand tissue homogenizer. The homogenate was made up to 5 ml by adding Tyrode solution. All the time homogenizer was washed properly with deionized water. 20 µl of homogenate was separated from each test tube and kept in refrigerator with parafilm coverage for protein estimation. Rest of the homogenates were transferred to the previously marked conical flasks and digested through acid method. Then the conical flasks were left for 5 minutes to become cool and all fumes to exhaust away. The exhaust fans were always working in the laboratory to eliminate all the fumes. There were 5 tripod gas burner by which conical flasks were boiled. There was a sliding glass made wall, which separated all gas and fumes from the laboratory workers. The conical flasks were left to become cool after boiling. If the content of any flask was not clear then 2 ml perchloric acid was added and again boiled and left to be cool. 50 µl potassium iodide (KI-10%) was added to each conical flask to make all pentavalent arsenic to trivalent arsenic as the Atomic Absorption Spectrophotometer with Hydride Generator would show only trivalent arsenic. Then the clear digested solutions were diluted up to 10 ml with de-ionized water. From the diluted solutions, 1 ml was taken to another sets of test tubes as marked before. These diluted samples were run through Atomic Absorption Spectrophotometer with Hydride Generator.

Table 1: Experimental Design

Sample No	Incubation of liver tissues of rat with	
	During 1st Incubation*	During 2nd Incubation*
I	None	None
II	Arsenic 2.5 µg/ml	None-
III	Arsenic 2.5 µg/ml	+ Garlic (Hexane extract)[1]
IV	Arsenic 2.5 µg/ml	+ Garlic (Methanol extract)[2]
V	Arsenic 2.5 µg/ml	+ Garlic (Hexane + Methanol extract)[3]

Both 1st Incubation and 2nd incubation were for 45 minutes at 37°C; None means no arsenic was added; 1Hexane extract of garlic = 20 µl / ml; 2 Methanol extract of garlic = 20 µl / ml; 3Hexane+ Methanol extract of garlic =(10 µl +10 µl) /ml.

A set of freshly washed test tubes were taken. All test tubes contained 2ml tyrode solution and twenty small pieces of liver tissue maintain 0ºC. No arsenic was added in test tube I. 2.5 µg/ml arsenic trioxide was added rest of the test tubes. They all were incubated for 45 minutes of 37ºC. Then the tissues were washed properly. In second incubation, different extracts of garlic (hexane, methanol extract) were added at 20µl/ml dose. 10 µl/ml hexane extract and 10 µl/ml methanol extract were combined added to test tube V. Second incubation was also for another 45 minutes at 37ºC. There were duplicate of all test tubes.

Results

The effects of extract of garlic (hexane and methanol) on the removal of arsenic from the arsenic loaded liver tissues of rat have been shown in Table 9. Only twenty small pieces of liver tissues were incubated in 2 ml Tyrode solution. There was no arsenic added in both 1st and 2nd incubation. The amount of arsenic was found 7.23 ± 3.51 µg / g (mean ± se) of protein. This value was taken as blank. In the first incubation liver tissues of rats were incubated with 2.5 µg / ml of arsenic for 45 minutes at 37°C and the amount of accumulated arsenic in the tissues was 249.02 ± 21.16 µg/ g (mean ± se) of protein and this was considered as standard. The value already taken as blank was then deducted from the value estimated as standard to determine the value, which was considered as control. The arsenic loaded tissues were incubated for the second time with hexane extract of garlic (20 µl/ ml) for another 45 minutes at 37°C and the amount of arsenic was reduced to 22.83 ± 5.98 µg/ g (mean ± s.e) of protein. There was 86% removal of arsenic. This difference was statistically highly significant using student's 't' test (P<0.001).

The arsenic loaded tissues were also incubated with methanol extract (20 µl / ml) for 45 minutes at 37°C and the amount of arsenic was reduced to 210.60 ± 16.51 µg / g (mean ± s.e) of protein. The removal of arsenic was 12.59%. This difference was statistically not significant by student's 't' test. The second incubation of the arsenic loaded tissues was performed with the combination of hexane and methanol extract of garlic (10 µl / ml + 10 µl / ml) for 45 minutes at 37°C and the amount of arsenic was reduced to 136.40 ± 14.23 µg / g (mean ± s.e) of protein. This time removal of arsenic was only 14.81%. This difference was statistically not significant calculating through student's 't' test.

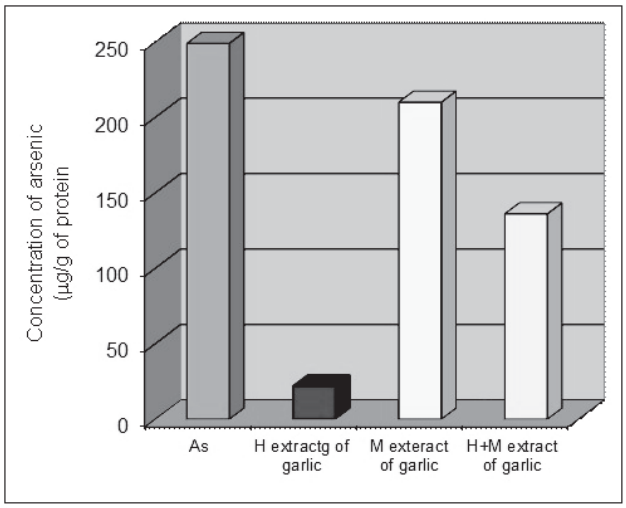

Figure I: Effects of Different Extracts of Garlic on Arsenic Loaded (2.5 g/ml) Tissues in second incubation

Discussion

Arsenic exhibit a broad range of chemical reactivity with an ability to form alloys with other elements and form covalent bond with carbon, hydrogen and oxygen[11]. It participates reacting in oxidation-reduction, methylation-demethylation and acid base reaction. It burns in air giving off an odor of garlic and dense white fumes of arsenic trioxide (As_2O_3), which is the most important commercial compound of arsenic[12]. Elemental arsenic is not soluble in water and arsenic salt exhibits wide range of solubility depending on the pH and ionic environment. The solubility of arsenic trioxide is fairly low, about 2% at 25°C and 8.2% at 98°C[10]. It is highly soluble in hydrochloric acid and alkali. An increased pH may increase the concentration of dissolved arsenic[13].

In previous experiment it was found that selenium, an essential element needed in trace amount for the biosynthesis can antagonize arsenic from tissues[13]. However, provision of arsenic free water must be ensured otherwise antagonism may be reversed into synergistic toxicity.

The present study was carried out to investigate whether the hexane and methanol extracts of garlic could remove the accumulated arsenic from isolated liver tissues of rat. This work is very important in present perspective of Bangladesh when chronic arsenicosis has been reported as the largest

Table 2: Removal of arsenic by different extracts of garlic from isolated liver tissues of rat

1st Incubation	2nd Incubation	n	Amount of arsenic µg/ g of protein (mean ± se)	% removal of arsenic	P value
None	-None-	6	7.23 ± 3.51	-	-
Arsenic2.5µg/ml	None	6	249.02 ± 21.16	-	-
Arsenic 2.5µg/ml	+Garlic (Hexane extract)[1]	6	22.80 ± 5.98	86	<0.0014
Arsenic 2.5µg/ml	+Garlic (Methanol extract)[2]	6	210.60 ± 16.51	13.23	NS5
Arsenic 2.5µg/ml	+Garlic(Hexane+ Methanol)[3] extract	6	136.40 ± 14.23	34.71	NS

Both 1st and 2nd incubation were 45 minutes at 370C; 1Garlic (Hexane extract) – 20 µl / ml; 2Garlic (Methanol extract) – 20 µl / ml; 3Garlic (Hexane extract 10 µl / ml + Methanol extract– 10 µl / ml); 4<0.001 means highly significant; 5NS = Not Significant

environmental health hazard in the world and there is no specific treatment of the disease.

Active compounds of garlic was studied in very low dose 20ml/ml in isolated liver tissues rat. The tissues were incubated with 2.5 mg / ml arsenic trioxide at 37°C for 45 minutes in water bath with shaker in first incubation. Before the second incubation extracts of garlic was added to arsenic loaded tissues at 20 ml / ml dose for 45 minutes at 37°C. The results revealed that the hexane extract of garlic at 20 ml/ml reduced accumulated arsenic from isolated liver tissues of rat and values were highly significant. In my experiment, hexane extract of garlic 20ml/ml removed accumulated arsenic from arsenic loaded liver tissues and as these experiments were repeated six times to observe reproducibility.

The chemical analysis of garlic reveals that it contains approximately 85% edible portion with moisture 62%, protein 6.3%, fat 0.1%, fibre 0.8% and other carbohydrate 29.3%, the caloric value in 142[14]. Garlic (Allicin, diallyl thio sulfinate) is moderately soluble in hexane and non-polar. The curative action of garlic has been shown for a long time. The active crystalline substances which was isolated from garlic bulbs, named Allicin[15]. Allicin was proved to be an allyl ester of thiosulphinic acid and it is formed from a biologically inactive precursor of 5-allyl cysteine sulphoxide named allin under the influence allinase, the enzyme was found in garlic tissues[13]. This substance is unstable and easily turns into a biologically inactive component diallyl disulphide.

It has been found that the sulphur compound has been found in garlic which reacts with cysteine and which involves the thiol disulphide exchange and oxidation of garlic sulphur compounds and cysteine of the animal tissue thereby brings about some changes in quantities of glycogen, lipid and protein[11]. It is suggested that synthesis of protein is increased by garlic.

Conclusion

In conclusion different extracts of garlic has the ability to remove significantly arsenic from isolated liver tissues of experimental rat. The arsenic loaded tissues has been incubated for the second time with hexane extract of garlic and the amount of arsenic has been reduced. Therefore a significant amount of arsenic has been removed from the liver tissues. Further study should be carried out in multicenter.

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Original Article

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Different Clinical Presentation of Patients with Parkinson's Disease

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Abstract

Background: Parkinson's disease is found with different clinical presentations. **Objective:** The purpose of the present study was to see the clinical features of Parkinson's disease patients. **Methodology:** This cross-sectional study was carried out in the in-patient and out-patient Department of Medicine and Neurology of Sir Salimullah Medical College and Mitford Hospital, Dhaka from July 2012 to December 2013 for a period of one and half year. All patients with Parkinson's disease who were admitted under department of Medicine and Neurology and also who visited out-patient department of Medicine and Neurology of Sir Salimullah Medical College and Mitford Hospital, Dhaka were included as study population. Patients who were diagnosed according to Brain Bank clinical criteria for diagnosis of Parkinson's disease were included in this study. The clinical findings were recorded in a semi-structured questionnaire. **Result:** This study was conducted in Sir Salimullah Medical College and Mitford Hospital with a view to see the clinical features of Parkinson's disease. The mean age was found 69.15±10.08 years. All patients had presented with a combination of complaints, among them all (100.0%) had tremor, 37(92.5%) had rigidity. However, 9(22.5%) cases had combination of tremor, hypokinesia, rigidity and postural imbalance and 10(25.0%) cases had tremor, Hypokinesia and rigidity. **Conclusion:** In conclusion most of the Parkinson's disease patients are presented with tremor and rigidity or both. *[J Monno Med Coll June 2020;6(1): 11-13*

Keywords: Clinical Presentation; Parkinson's disease; clinical features

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Introduction

Parkinson's disease is the second commonest neurodegenerative disease[1]. Clinically Parkinson's disease is characterized by rest tremor, rigidity, bradykinesia, and gait impairment[2]; however, pathologically, there are degeneration of dopaminergic neurons in the substantia nigra pars compacta with the reduction of striatal dopamine, and intracytoplasmic proteinaceous inclusions[3].

PD symptoms include rigidity, postural instability, tremor at rest, and slowness or absence of voluntary movement, and even neuropsychiatric symptoms[4]. The pathological hallmarks of PD include progressive degeneration of dopamine neurons, as well as accumulation of α-synuclein positive Lewy bodies in afflicted brain regions[5]. The diagnosis of PD in living patients is mainly based on the clinical presence of bradykinesia and one other motor feature (rest tremor or cogwheel rigidity), which have been outlined in the United Kingdom Brain Bank criteria[6]. However, diagnosis of all PD patients accurately is difficult only using these strict criteria. What is worsen, making a diagnosis may be too late until the motor symptoms developed, especially if we want to intervene early in the course of the disease[7]. Hence, developing reliable diagnostic markers and therapeutic goals of early PD is necessary.

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Most Parkinson's disease occurs sporadically and are of unknown cause[8]. Environmental factors play more important role in patients older than 50 years, with genetic factors being more important in younger patients[8]. Epidemiologic studies suggest increased risk with exposure to pesticides, rural living, and drinking well water and reduced risk with cigarette smoking and caffeine[9]. About 10 to 15% of cases are familial in origin and associated of multiple specific gene mutations among which mutation in Parkin gene are associated with early onset inherited and sporadic early onset Parkinson's disease[10] (Rappor & Samuels 2009). This present study was undertaken to see the clinical features of Parkinson's disease patients.

Methodology

This cross-sectional study was carried out in the in-patient and out-patient Department of Medicine and Neurology of Sir Salimullah Medical College and Mitford Hospital, Dhaka from July 2012 to December 2013 for a period of one and half year. All patients with Parkinson's disease who were admitted under department of Medicine and Neurology and also who visited out-patient department of Medicine and Neurology of Sir Salimullah Medical College and Mitford Hospital, Dhaka were taken as study population. Patients who were diagnosed according to Brain Bank clinical criteria for diagnosis of Parkinson's disease were included in this study. The different clinical features were recorded in a semi-structured questionnaire. Respondents were selected by non-probability purposive sampling method on the basis of willingness of the patients, attendants. Before data collection, informed written consent was taken from patient himself/herself or his/her attendant. A semi-structured questionnaire and checklist was prepared for each patient. The interview schedule was made in Bengali which included questions related to the objects of the study. Data was collected by researcher himself. All the data were checked and edited after collection. Then the data were entered into computer and statistical analysis of the result was obtained by using Windows based computer software devised with statistical packages for Social Sciences (SPSS-16). The statistical terms includes in this study are mean, standard deviation, percentage. After collection, all data were checked for inadequacy, irrelevancy and inconsistency. All irrelevant and inconsistent data were corrected or discarded methodically. Prior to the commencement of this study, the research protocol was approved by the thesis committee of Sir Salimullah Medical College and Mitford Hospital, Dhaka.

Results

This study was conducted in Sir Salimullah Medical College and Mitford Hospital with a view to see the socio-demographic characteristics of Parkinson's disease. All socio-demographic characteristics were noted. It was observed that 15(37.5%) patients belonged to age 71 to 80 years and their mean age was found 69.15±10.08 years (Table 1).

Table 1: Distribution of the study population by age (n=40)

Age Group	Frequency	Percent
Less than 60 Years	10	25.0
61 to 70 Years	13	32.5
More than 71 Years	17	42.5
Total	**40**	**100.0**
Mean±SD (Range)	69.15±10.08 (48 to 100)	

Table 2 shows multiple responds for presenting complaints of the patients. It was observed that all patients had presented with a combination of complaints, among them all had tremor, 37(92.5%) had rigidity, 19(47.5%) had hypokinesia and 12(30.0%) had postural instability.

Table 2: Distribution of the study patients by presenting complaints (n=40)

Presenting complaints	Frequency	Percent
Tremor	40	100.0
Rigidity	37	92.5
Hypokinesia	19	47.5
Postural Instability	12	30.0

*Multiple response analysis was performed

It was observed that 9(22.5%) had combination of tremor, hypokinesia, rigidity and postural imbalance, 10(25.0%) had tremor, Hypokinesia and rigidity and 21(52.5%) had tremor and rigidity (Table 3).

Table 3: Distribution of the study patients by presenting complaints in combinations (n=40)

Presenting complaints	Frequency	Percent
Tremor+ Hypokinesia +Rigidity+ Postural imbalance	9	22.5
Tremor+ Hypokinesia +Rigidity	10	25
Tremor+ Rigidity	21	52.5

Discussion

Parkinson's disease (PD) is one of many progressive neurodegenerative disorders[3]. Despite the availability of symptomatic treatment, it remains a debilitating and incurable disease[8]. During the study period a total of 40 patients diagnosed as Parkinson's disease by Neurologist and Medicine specialist by clinical criteria admitted under Department of Medicine and Neurology and also visited outpatient Department of Medicine and Neurology of Sir Salimullah Medical College and Mitford Hospital, Dhaka were included.

In this study it was observed that in case group 37.5% patients were in 8th decade and their mean age was 69.15±10.08 years, varied 48 - 100 years. In control, 38.6% patients were in 6th decade and their mean age was 67.14±10.25 years, varied 50 to 90 years. The mean age was almost alike between two groups. Iranmanesh et al[9] showed the mean age of male patients was 64.7±6.4 years and the mean age of the female patients was 63.2±5.6 years. 20.0%

of patients are under 60 years, 18.0% between 61 to 65 years, 28.0% patients are between 66 to 70 years and 34.0% patients are more than 70 years old, which is consistent with the current study. Findley[10] mentioned in his study that one in seven patients with PD is under the age of 50 years, and there is an increase in prevalence with increasing age. In this study only 5.0% of patients are 50 years or below which is much lower than that of previous study[5].

Regarding the clinical presentation of the patients it was observed in this study that patients usually presented with various combinations of symptoms among those all patients had tremor, 37(92.5%) had rigidity, 19(47.5%) had hypokinesia and 12(30.0%) had postural instability. Analysing the combinations of presentation, it is shown that 9(22.5%) have presented with combinations of tremor, hypokinesia, rigidity and postural imbalance; however, 10(25.0%) patients with tremor, hypokinesia and rigidity and 21(52.5%) patients with tremor and rigidity. O'Sullivan et al[11] found tremor in 76.3% cases, rigidity in 78.2% cases, Postural instability in 7.8% cases with "motor symptoms" at presentation, which are a little differ from the current study and that may be due to the lake of awareness and scarcity of available of health care facilities in our community which failed to detect the disease in early stage. Jankovic[1] has reported that there are four cardinal features of PD that can be grouped under the acronym TRAP which stands for tremor at rest, rigidity, akinesia (or bradykinesia) and postural instability. In addition, flexed posture and freezing (motor blocks) have been included among classic features of parkinsonism, with PD as the most common form. Because of the diverse profiles and lifestyles of those affected by PD, motor and nonmotor impairments should be evaluated in the context of each patient's needs and goals[12].

In this study the most common presenting symptoms is tremor. This rest tremor is the most common and easily recognised symptom of PD[1]. Tremors are unilateral, occur at a frequency between 4 and 6 Hz, and almost always are prominent in the distal part of an extremity[11]. Hand tremors are described as supination–pronation (''pill-rolling'') tremors that spread from one hand to the other. Rest tremor in patients with PD can also involve the lips, chin, jaw and legs but, unlike essential tremor, rarely involves the neck/head or voice[13]. Thus a patient who presents with head tremor most likely has essential tremor, cervical dystonia, or both, rather than PD[11]. Characteristically, rest tremor disappears with action and during sleep[14]. Some patients also report an ''internal'' shaking that is not associated with a visible tremor[15]. The tremor of PD is differentiated from essential tremor.

Conclusion

In conclusion all patients have presented with a combination of complaints. The most of the Parkinson's disease patients are presented with tremor and rigidity or both. Among them all have tremor. Furthermore, combination of tremor, hypokinesia, rigidity and postural imbalance are also reported in this study. In addition to that the combination of tremor, hypokinesia and rigidity are also found in a significant number of Parkinson's patients. tremor and rigidity. Further large scale multicentre study should be conducted to see the reflection of majority of the patients.

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Original Article

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Long Term Outcome of Bile Duct Injury following Laparoscopic Cholecystectomy

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Abstract

Background: Bile duct injuries are the most common and dreadful complications following laparoscopic cholecystectomy despite advancement of training and technology. It's a great challenge to the surgeons and also the patient. **Objective:** The purpose of the present study was to assess outcome of bile duct injury following laparoscopic cholecystectomy. **Methodology:** This prospective cohort study was performed in the Department of Surgery at Shaheed Suhrawardy Medical College and Hospital, Dhaka, Bangladesh from January 2015 to December 2017 for a period of two (02) years. The patients were included this study. Data collected in data collection sheet regarding demographic data, risk factors, classification of bile duct injury, different therapeutic approaches after injury and outcome of patients which were analyzed. **Results:** Total 40 patients were included in this study with the age ranged from 20 to 60 years. Females were 31(77.5%) cases and males were 9(22.5%) cases. Common risk factor encountered acute cholecystitis (25.0%). Injury or leakage from cystic duct was more (50.0%). Most common therapeutic procedure were hepatichojejunostomy (65.0%) and intra-abdominal drainage (17.5%). Most of the patients were good (55.0%); however, wound infection (20.0%), leakage (7.5%), septicemia (5.0%), stricture (10.0%) and death (2.5%) were also reported. **Conclusion:** Most of the injuries following cholecystectomies are related to the cystic duct which can be treated withdraining procedures. A considerable number of patients following hepaticojejunostomylater on develops a stricture. *[J Monno Med Coll June 2020;6(1): 14-16*

Keywords: Laparoscopic cholecystectomy; bile duct injuries; stricture; hepatichojejunostomy

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Introduction

Laparoscopic cholecystectomy is one of the most commonly performed surgical procedures since its introduction by Erich Muhein. The incidence of bile duct injuries are now decreasing due to improvement in the equipment and improved training in laparoscopy. Most of the bile duct injury are recognized in the early post-operative period and less than half of these are during operation[1]. A bile duct injury even after repair adversely affects the quality of life and can be financial disaster for the patient and a legal one for the surgeon[2-3].

The treatment of bile duct injuries has changed since the introduction of laparoscopic surgery. Most bile leaks are now treated with endoscopic procedures like stents and endoscopic sphincterotomy, whereas the more severe cases will still need a repair of the common bile duct[4]. Despite this a rather high proportion of the patients will still have strictures and episodes of cholangitis[5]. The aim of this study was to evaluate the outcome of bile duct injury following laparoscopic cholecystectomy.

Methodology

This prospective cohort study was carried out in the Department of Surgery at Shaheed Suhrawardy Medical

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College Hospital, Dhaka, Bangladesh in between January 2015 to December 2017. Total 40 diagnosed cases of bile duct injury following laparoscopic cholecystectomy those admitted in the surgery department and underwent laparoscopic cholecystectomy of this hospital were enrolled in this study. All patients (males and females) in the age group 20 to 60 years who presented with injury per-operatively and biliary leakage following cholecystectomy were included in this study. There were no ethical problems as before study procedure conducted, verbal consent of each patient was taken. Relevant information according to questionnaire were taken from the patients. Patients were observed for injury during or after laparoscopic cholecystectomy and managed accordingly. They were observed for last one year of study period. All data were collected and analyzed manually in view of the study. Then the results were established in a tabulated form.

Results

A total number of 40 cases were recorded for this study. In this study bile injury was more common in female because females were suffered from more cholelithiasis. Females were 31(77.5%) cases and males were 9(22.5%) cases (Table 1).

Table 1: Demographic Background of Patient (n=40)

Gender	Frequency	Percent
Female	31	77.5
Male	9	22.5

Age Range: 20 to 60 years

The common risk factors for developing bile duct injury were acute cholecystitis. Here acute cholecystitis were 10(25%) cases, previous laparotomy in 3(7.5%) cases, pancreatitis 3(7.5%) cases, diabetes 4(10%) cases (Table2).

Table 2: Risk Factors among Study Population (n=40)

Risk Factors	Frequency	Percent
Acute Cholecystitis	10	25
Previous Laparotomy	3	7.5
Pancreatitis	3	7.5
Diabetes	4	10
None	20	50

According to Strasberg classification of bile duct injury, more common injury Type A. Cystic duct leak or leaks from small ducts in liver bed were 20(50%), Type C. Leak from an aberrant RHD were 4(10%), Type D. lateral injury to CBD were 2(5%), Type E2. E2. CHD stricture, stump less than 2 cmwere 12(30%) and Type E3. Hilar stricture with preserved biliary confluence were 2(5%) (Table3).

The common therapeutic procedure after bile duct injury were hepatic-jejunostomy 26(65%) cases, T-Tube insertion were 5(12.5%) cases, removal of clips and drain were 2(5%) cases and intra-abdominal drainage were 7(17.5%) cases (Table 4).

The outcome of bile duct injury management were uncomplicated in 22(55%) patients. The wound infection were in 8(20.0%) cases; leakage was in 3(7.5%) cases; septicaemia was in 2(5%) cases; stricture was in 4(10.0%) cases and death was in 1(2.5%) case (Table 5).

Table 3: Classification of bile duct injuries in 40 patients according to Strasberg

Types of injury	Frequency	Percent
A.Cystic Duct Leak or Leaks From Small Ducts In Liver Bed	20	50
C. Leak from an Aberrant RHD	4	10
D. Lateral Injury to CBD	2	5
E_2. CHD Stricture, Stump Less than 2 cm	12	30
E_3. Hilar Stricture with Preserved Biliary Confluence	2	5

Table 4: Therapeutic Procedure after Injury (n=40)

Therapeutic Procedure	Common Bile Ducts	
	Frequency	Percent
Hepaticojejunostomy	26	65
T-Tube insertion	5	12.5
Removal of clips and drain	2	5
Intra-abdominal drain	7	17.5

Table 5: Post-Operative Outcome among Study Population (n=40)

Outcome	Frequency	Percent
Uncomplicated	22	55
Wound infection	8	20
Leakage	3	7.5
Septicaemia	2	5
Stricture	4	10
Death	1	2.5

Discussion

Gallstone disease is common all over the world. Laparoscopic cholecystectomy which has become the gold standard of management of gall stone diseases is associated with 2 to 4 time's higher (0.5%) risk of bile duct injury than open cholecystectomy[6].

Total forty patients were included in this study. Age range was 20-60 years. Females were more common about 77.5% than males (22.5%). Ahsan and Ahmad[7] showed that female and male bile duct injury 70% and 30 % respectively which were more prominent in females. In this study common risk factor for bile duct injury were acute cholecystitis (25%). In acute cholecystitis gall bladder remained oedematous so identification sometimes to be difficult for managing injury. Risk factors for bile duct injuries (BDIs) are assumed to be related to age, sex, acute cholecystitis, and impacted gallstone within the Hartmann's pouch. Anomalies and anatomical variations of biliary ducts or vascular system are not uncommon and represent operative challenges and looming sources for operative complications[8].

The main findings in this study were that 50.0% of bile duct

injuries or leaks following cholecystectomy were related to the cystic duct or aberrant bile ducts in the liver bed of the gall bladder. This is in the same order as was found in an extensive American study comprising 83000 patients where about 60.0% of the leaks were related to the cystic duct[9].

In addition, most of the open procedures were performed in the first years of the study period. The reported frequency of bile duct injuries varies considerably in published studies[10-12]. Iatrogenic injuries to the common hepatic duct or right hepatic duct with side branches were normally severe requiring operative management. Following complete division of the common bile duct, there were mainly two options for repair: direct anastomosis between the cut ends or hepaticojejunostomy with a Roux-en-Y limb (65%) in this study. T-tube insertion were (12.5%) and another common options were intra-abdominal drain (17.5%). Most authors consider the last option as the most appropriate method[8,13]. This was also the main policy at our department. The outcome after hepaticojejunostomy was generally fair, with strictures as the most severe long-term challenge.

Recurrent cholangitis as a consequence of postoperative strictures is commonly found following surgical repair of the common bile ducts[14]. In addition to a well-timed planned preparation, there might be several reasons for the development of strictures, like technical failures during reconstruction, unawareness of constrained blood supply, or extensive damage making anastomoses difficult. In this series stricture were(10%), wound infection were (20%). Treatment of postoperative strictures should also be individualized, and balloon dilatation might be a good option for many patients[15]. In general, it is found that the long-term quality of life is reduced following bile duct injuries compared to all patients undergoing laparoscopic cholecystectomy[16].

As one of our patients in this small series died in the course of bile duct injuries, this should focused on the severity of these lesions. This was especially relevant in elderly patients who didn't tolerate postoperative sepsis and reoperations. It was important to act immediately when bile leaks occur (7.5%). Whether drainage was performed endoscopically the most of the patients could be treated with endoscopic procedures, which was also the conclusion in a paper by Pitt et al[17].

Conclusion

As bile duct injury is associated with health and financial disaster, more attention needs to be paid both to prevent and management such injury cautiously. After recognition of injury this type of injury should be managed by experienced hand for the betterment of the patient.

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Original Article

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Rapid Detection of *Mycobacterium tuberculosis* by Gene Xpert® Method at a Tertiary Care Hospital in Dhaka City

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Abstract

Background: *Mycobacterium tuberculosis* is an acid fast bacilus cause's tuberculosis which kills more people than any other infectious disease. **Objective:** The aim of this study was to identify the M. TB DNA and resistance to rifampicin from different samples. **Methodology:** This cross-sectional study was carried out in the department of Microbiology, Dhaka National Medical College & Hospital, Dhaka, Bangladesh, from January 2019 to December 2019. Samples were collected from suspected cases of tuberculosis from in-patient and out-patient of Dhaka National Medical College & Hospital. Samples were collected from both sexes and different age groups. Identification was done by GeneXpert® Method. **Results:** A total of 1536 samples from the suspected patients of tuberculosis were collected from Dhaka National Medical College & Hospital, Dhaka, Bangladesh. Among, them sputum 1521, pus 10 and Ascitic fluid 05 were respectively. **Conclusion:** In conclusion a large number of *Mycobacterium tuberculosis* is detected in the specimen by GeneXpert® among the tuberculosis patients. *[J Monno Med Coll June 2020;6(1): 17-19*

Keywords: M. tuberculosis; GeneXpert; tuberculosis; sputum; MDR

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Introduction

Mycobacterium tuberculosis is the causative agent of tuberculosis mainly causing pulmonary tuberculosis. About one third of the world population has been infected with M.tuberculosis[1-2]. According to the World Health Organization (WHO) report, there is 8-10 million new cases of tuberculosis are diagnosed in the world annually and 1.4 million tuberculosis deaths worldwide annually[3].

National TB Control Program (NTP), in Bangladesh has begun for implementing DOTS since 1993 and DOTS has already been proved with a high cure rate. However, with proper treatment almost all TB cases are curable[4]. The success of tuberculosis control programs depends not only on successful completion of treatment but also on early diagnosis, steady monitoring, and response to treatment, because incomplete treatment carries a risk of development of resistance, increases disease transmission and increases morbidity and mortality[5].

Tuberculosis is one of the most emerging infection world-wide which posing medical and social problem and causing high morbidity and mortality especially in the developing countries[5]. Therefore, early and rapid detected of *Mycobacterium tuberculosis* (MTB) is very important for better treatment of the patients and prevent resistance, also complications. Now a days, easily detect MTB and drug resistance can be detected such as rifampicin and INH by GeneXpert® Method within two hour[6].

In order to overcome conventional methods, low sensitivity and diagnostic delays, Xpert MTB/RIF, a fully automated molecular test has been introduced. It can detect the presence of *Mycobacterium tuberculosis* (MTB) complex DNA and mutations associated with rifampicin (RIF) resistance directly from sputum in less than 2 hours, and it minimizes staff manipulation and biosafety risk[7]. It is very important to

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identify M. tuberculosis as early as possible to avoid any long term complications to reduce the risk of morbidity and proper treatment.

Methodology

This cross-sectional study was carried out in the Department of Microbiology at Dhaka National Medical College & Hospital, Dhaka, Bangladesh from January 2019 to December 2019 for a period of one year. Different specimens were collected from suspected cases of tuberculosis from in-patient and out-patient department of Dhaka National Medical College & Hospital, Dhaka. Samples were collected from both sexes and different age groups. Identification was done by GeneXpert® Method3-5. The GeneXpert® was a small machine, about the size of micro-wave oven. The machine was used for the DNA specific to TB bacterium. The GeneXpert® was used to test for resistance to one of the most common TB drugs rifampicin. The test procedure was very quick and it was taken only about 2 hours which was much faster than the other TB test, which usually took at least a few days.

Results

A total of 1536 samples from suspected patients of tuberculosis were included in this study. There were 850(55.34%) cases male and 686(44.66%) cases females patients (Table 1).

Table 1: Sex distribution of tested patients (n=1536)

Gender	Frequency	Percent
Male	850	56.34
Female	686	44.66
Total	**1536**	**100.0**

Among them, sputum 1521, pus 10 and Ascitic fluid 05, were respectively. The sputum, pus and Ascitic fluid were 1536 (100%) cases. Total detected MTB were 139(9.05%) cases. Among, them Mycobacterium tuberculosis were detected from different samples, such as sputum 136 (97.84%), pus (1.44%) and ascitic fluid 1(0.72%) (Table 2).

Table 2: Distribution of detected MTB from different samples (n=1536)

Samples	*Mycobacterium tuberculosis*		Total
	Detected	Not Detected	
Sputum	136(97.84%)	1385(99.1%)	1521(99.02%)
Pus	2(1.44%)	8(0.6%)	10(0.65%)
Ascitic fluid	1(0.72%	4(0.3%)	5 (0.33%)
Total	**139(100%)**	**1397(100.0%)**	**1536(100.0%)**

Detection of MTB from different samples from male and female. In male seventy five 75 (54%), MTB were detected from different samples and in female 64 (46.04%), MTB were detected only from sputum samples (Table 3).

MTB resistance to rifampicin were also detected. There were 3(2.16%) in number only from sputum samples from male patients (Table 4).

Table 3: Distribution of detected MTB from Male and Female (n=139)

Samples	Detected MTB
Male	
Sputum	72 (51.8%)
Pus	02 (1.44%)
Ascitic	01 (0.72%)
Female	
Sputum	64 (46.04%
Male and Female	139 (100%)

Table 4: Detected MTB, Resistant to Rifampicin

Samples	MTB Resistant to Rifampicin
Male	
Sputum	3(2.16%)
Pus	Nil
Ascitic	Nil
Female	
Sputum, Pus and Ascitic fluid	Nil

Discussion

Mycobacterium tuberculosis is an aerobic acid fast bacilli/rods that causing infection primarily in human[6]. Tuberculosis patients are increasing throughout the world. The prevalence of tuberculosis varies in different areas, age groups and socio-economic groups[7]. HIV infection[8], intravenous drugs use, immuno-suppression, alcoholism, malnutrition, poverty, transplantation, immigration, homelessness and over crowding are the predisposing factors for tuberculosis. The Gene Xpert is a new test for tuberculosis. It can find out if a person is infected with TB and also if the TB bacterium of the person has resistance to one of the common drugs rifampicin. If there are MTB in the samples, the machine will detect their DNA. This test is very quick and only takes about two hours, much faster than other MTB tests, which usually take a few days.

Rapid diagnosis of mycobacterial disease is critical, and attempts to shorten the time to detection of such organisms deserve attention[7]. Smear examination is a rapid method for detection of mycobacteria in a clinical specimen, especially sputum but the limitations are low sensitivity and inability to diagnose rifampicin sensitivity pattern. Increased prevalence of drug resistant tuberculosis in Bangladesh and other developing countries is a growing threat to tuberculosis control. So, early detection of MDR TB is crucial both for the patient management and infection control in TB positive cases[9].

In this study sputum was 1521 cases; pus was 10 cases and Ascitic fluid was 5 cases. The sputum, pus and Ascitic fluid were 1536(100%) cases. Total detected MTB were 139(9.05%) cases. Among, them *Mycobacterium tuberculosis* were detected from different samples, such as sputum 136 (97.84%), pus (1.44%) and ascitic fluid 1(0.72%). Similar to this present study Laskar et al[9] have reported that among 107 clinically suspected pulmonary

tuberculosis cases 64 (59.81%) cases are male and 43 (40.19%) cases are female and male female ratio is 2:1.34 which is consistent with the present study result. Torrea et al[10] have reported that out of 247 pulmonary tuberculosis patients, 160 (64.78%) cases are male and 87 (35.22%) cases are female with male female ratio 1.83:1. This is almost similar to the present study. The reason of higher male tuberculosis cases than female cases might be explained by the fact that males are actively populated in the community and may come in contact with TB infected persons more frequently[9]. Furthermore, female members in Bangladesh still reside at home and therefore the chance of exposure is comparatively less[11].

In the present study, total 139 MTB were detected from different samples especially in sputum samples. Among them, 75(54%) MTB were detected from male patients and 64 (46.04%) were detected from female patients. The GeneXpert® is more sensitive than most other TB test up to 98%. MTB showed resistance to rifampicin only 03 (2.16%) from sputum samples in male patients. This is good indicator that the patient might have multi drug resistant MDR TB.

Conclusion

In conclusion a large number of *Mycobacterium tuberculosis* is detected in the specimen by GeneXpert among the tuberculosis patients. Male is predominant than female. Sputum is most commonly collected specimen and majority of the *Mycobacterium tuberculosis* is detected by GeneXpert®. Further large scale study should be conducted countrywide.

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Original Article

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Characteristic of Pain among the Prolapse Lumbar Intervertebral Disc Patients

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Abstract

Background: Prolapse lumbar intervertebral disc is presented with varied characteristics of pain. **Objective:** The purpose of the present study was to see the different characteristics of pain among the patients presented with prolapse lumbar intervertebral disc. **Methodology:** This cross-sectional study was carried out in the department of Neurosurgery at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from March 2006 to October 2007 for a period of one and half year. Prolapse lumbar intervertebral disc (PLID) patients who were admitted in the Department Neurosurgery at BSMMU, Dhaka, Bangladesh after clinical and radiological evaluation were selected as study population. Different characteristics of pain were recorded. **Result:** A total of 59 hospital-admitted cases of PLID were included in the study. The mean age of the patients was 40.8±11.9 years. In this study 95.0% of the patients had low back pain. Over one-quarter (28.8%) of patients complained of radiation of pain to the right lower limb and 30.5% to the left lower limb. Distribution of patients by site of radiation of pain shows that about two-third (66.1%) of the patients' pain was distributed over the back of the thigh, calf muscle and sole of the feet, while 27.1% cases of the patients had distribution of pain on the lateral aspect of thigh leg and foot. **Conclusion:** In conclusion majority of the PLID patients have given the complaints of pain which is mostly radiated to lower limbs. *[J Monno Med Coll June 2020;6(1): 20-23*

Keywords: Characteristic; pain; prolapse lumbar intervertebral disc

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Introduction

Low back pain is the second most common complaint encountered by primary care physicians[1]. In Thailand, 62.0% of complicated cases that the provincial social security officers consulted the Medical Committee of the Compensation Fund were musculoskeletal causes[2]. Among these, 25.0% were occupational back pain and 7.0% were occupational lumbar disc herniation[3].

The syndrome of low back pain with or without sciatica is one of the more common diagnostic problems that the orthopaedist faces in his daily practice[4]. Mixter and Barr[5] described the syndrome of the ruptured intervertebral disc and showed that the condition could, if necessary, be treated by operation; then the surgeon has searched for accurate methods of definite diagnosis prior to surgery. Following the concepts of Walter Dandy it was the practice on the Orthopaedic Surgery Service at Barnes Hospital not to employ the myelogram in those patients operated on for disc lesions in the lumbosacral spine, since it was believed that an accurate diagnosis and localization of the lesion could be made by history and physical examination[6].

However, patients with low back pain in the hope that this could improve the results in their diagnosis and treatment. It has been later found that the pain characteristics are varied among the PLID patients. This may be due to the different life style and their occupation. Some of the patients have reported that the pain is radiated from the site of the disc prolapse. The radiation may involve one limb which may be right or left limb. However, both lower limb involvement is also reported. Therefore it is essential to know the pain

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characteristics to get the real picture of PLID. Ford and Key have reported to the American Orthopaedic Association their experience with myelography in 253 patients, of whom 206 cases had surgical exploration of the lumbosacral canal[7]. They found and positive correlation in 72.3 percent and felt that the myelogram was a valuable aid in diagnosis and may be a decisive factor in borderline cases. At that time they felt that not every patient having signs and symptoms referable to a lumbar disc should be subjected to a lumbar myelogram but that it should be reserved for those patients in whom the diagnosis or the location of the lesion was not sufficiently clear to enable the surgeon to operate with confidence[8]. The purpose of the present study was to see the different characteristics of pain among the patients presented with prolapse lumbar intervertebral disc.

Methodology

This was a cross-sectional study. This study was carried out in the Department of Neurosurgery at Banghabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from March 2006 to October 2007 one and half year. PLID patients who were admitted in the Department Neurosurgery at BSMMU, Dhaka, Bangladesh after clinical and radiological evaluation. Patients who were clinical diagnosis of PLID and MRI done for confirmation were selected as study population. Clinical diagnosis of PLID patients but refuse MRI for confirmation were excluded from this study. Clinical features of low back pain with its characteristics were recorded. The research protocol was approved by the Department of Neurosurgery at BSMMU. One admission, detailed history of the patients was taken and thorough general and neurological examinations were performed by the researcher. Relevant image findings of X-ray of lumbosacral spine and MRI of lumbosacral spines were studied carefully and necessary information were recorded. Then the data collection sheet was filled accordingly. Data were processed and analyzed using SPPS (Statistical Package for Social Sciences) version 11.5. The test statistics used to analyze the data were descriptive.

Results

A total of 59 hospital-admitted cases of PLID were included in the study. Of the 59 patients 20.3% cases were below 30 years; 8.5% cases were in between 30 to 35 years; 15.3% cases were in 35 to 40 years; another 15.3% cases were in 40 to 45 years and 40.7% cases were 45 or above 45 years of age. The mean age of the patients was 40.8±11.9 years and the lowest and highest ages were 21 and 65 years respectively (Table 1).

In this study 95.0% of the patients had low back pain and remaining 5.0% did not have such complain (Figure I).

Out of 59 patients, 16(27.1%) cases had the disease of 3 or less than 3 months duration and another 16(27.1%) cases had 4 to 6 months duration. Over 13.0% patients had been suffering from the disease for 7 to 12 months, 25.4% cases 13 to 24 months and 6.8% cases over 24 months. The median duration of suffering was 6 months with lowest and highest durations of sufferings being 1 month and 7 years respectively (Table 2).

Table 1: General Characteristics of the Patients (n = 59)

Age Group	Frequency	Percent
Less Than 20 Years	0	0.0
20 to 25 Years	4	6.7
25 to 30 Years	8	13.5
30 to 35 Years	05	8.5
35 to 40 Years	09	15.3
40 to 45 Years	09	15.3
More Than 45 Years	24	40.7
Total	**59**	**100.0**

* Mean age = (40.8 ± 11.9) years; range = (21 - 65) years

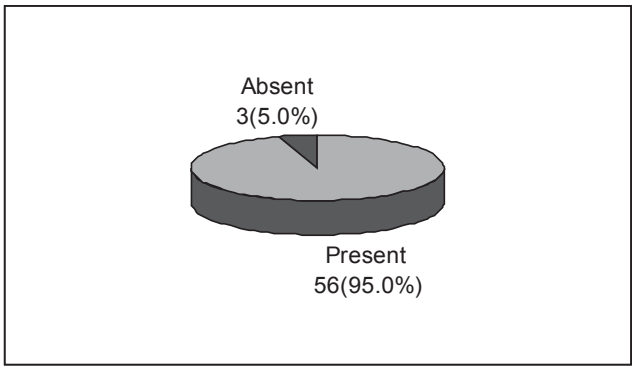

Figure I: Showing the Distribution of Patients by Low Back Pain (n = 59)

Table 2: Distribution of Patients by Duration of Lumbago-sciatica (n=59)

Duration of Sciatica	Frequency	Percent
Less than or Equal to 3 months	16	27.1
4 to 6 months	16	27.1
7 to 12 months	08	13.6
13 to 24 months	15	25.4
More than 24 months	04	6.8

*Median(range) duration of suffering = 6(1 – 84) months

Over one-quarter (28.8%) of patients complained of radiation of pain to the right lower limb, 30.5% to the left lower limb and 39% to both lower limbs. Only 1 patient did not complain of any radiation of pain (Table 3).

Table 3: Distribution of Patients by Radiation of Pain (n=59)

Radiation of Pain	Frequency	Percent
Right lower limb	17	28.8
Left lower limb	18	30.5
Both lower limbs	23	39.0
Absent	01	1.7
Total	**59**	**100.0**

Distribution of patients by site of radiation of pain shows that about two-third (66.1%) of the patients' pain was distributed over the back of the thigh, calf muscle and sole of the feet, while 27.1% of the patients had distribution of pain on the lateral aspect

of thigh leg and foot. Only 6.8% patients had pain sensation over the front of the thigh and leg (Table 4).

Table 4: Distribution of Patients by Distribution of Pain (n=59)

Distribution of Pain	Frequency	Percent
Front of the thigh and leg	4	6.8
Lateral side of thigh, leg and foot	16	27.1
Back of thigh, calf and down to sole	39	66.1

Discussion

Usually sciatica affects one side of the body[8]. The pain may be dull, sharp, burning, or accompanied by intermittent shocks of shooting pain beginning in the bullock radiating downward to the back or side of the thigh and or leg. Herniated discs are the most common cause of sciatica in the lumbar spine. Lumbar spinal stenosis and spondylolithesis may cause sciatica[9].

The present study showed that the mean age of the PLID cases was 40.8 years with lowest and highest ages were 21 and 65 years respectively which is consistent with the findings two other studies where mean ages of the study patients were 42.9 years and 41.6 years respectively[10]. Lumbar disc herniation in childhood and adolescence is a relatively rare condition. Only 1 to 3% of lumbar disc herniation occurs in individuals under 21 years of age[11].

Over one-quarter (28.8%) of patients complained of radiation of pain to the right lower limb, 30.5% to the left lower limb and 39% to both lower limbs. Only 1 patient did not complain of any radiation of pain. The present study demonstrated 95% of patients with low back pain which bears consistency with the findings of Zhang et al[12]. They observed that the patients with lumbar disc herniation present with complain of low back pain and sciatica (90.8%), low back pain only (3.3%) and sciatica only (5.9%). Leg pain is a common finding in lumbar disc herniation. While hip and buttock pain are frequent complaints, their presence rarely helps to localize the problem. Pain that is primarily localized to the hip in particular, must be differentiated from hip joint pathology, especially if there is radiation to the groin[13].

Distribution of patients by site of radiation of pain shows that about two-third (66.1%) of the patients' pain was distributed over the back of the thigh, calf muscle and sole of the feet, while 27.1% of the patients had distribution of pain on the lateral aspect of thigh leg and foot. Only 6.8% patients had pain sensation over the front of the thigh and leg. A study conducted by Kelsey et al[14] shows that projection of pain was localized to right lower limb in 51%, to the left lower limb in 43.0% and to both lower limbs in 6.0% of the prolapsed discs. In this study projection of pain to the right lower limb was 29.0%, to the left lower limb 31% and to the both lower limbs in remaining 39.0% cases.

The onset of low back pain is usually sudden, in the form of a ''catch'' after lifting a weight or after bending forwards to pick up annulus object, or it may have annulus insidious onset and progress slowly. Often the backache is mild and intermittent, brought on by exertion and relief by rest. This pain may be felt over the spine, sacroiliac joints for the iliac crest or occasionally even in the groin, and this is due to the stretching of the annulus and the posterior longitudinal ligaments. Tender area may be felt over the sacral or the gluteral region, but tenderness of the sciatic nerve is uncommon in the disc lesions[14].

Pain that is localized to the lower back and gluteal area often is associated with disk disease. Pain associated with nerve root involvement commonly radiates down the leg, particularly below the level of the knee. Pain with flexion, rotation, or prolonged sitting or standing, and sharp (rather than dull) pain are suggestive of disk disease[15].

The character of back pain may give some clue as to the underlying disease process. Pain improved by back flexion suggests a component of lumbar spinal stenosis, while pain exacerbated by back flexion suggests instability or advanced disc degeneration. In contrast, pain with simulated axial loading, pain with simulated notation, and other non-organic physical signs suggest that the patient is showing psychological distress out of proportion to the organic back disorder[16]. The most common type of radicular leg pain is "sciatica," a deep, occasionally stabbing pain felt in the posterior thighs and calves. This pain tends to be worse when standing or walking and best when the patient is lying down with the legs elevated and the knees bent. More severe radicular pain is generally better localized, and may be accompanied by numbness in and identifiable nerve root distribution. It is this type, which is of most value is localizing the problem. Leg pain exacerbated by coughing or the Valsalva maneuver is also suggestive of radiculopathy[16].

Conclusion

In conclusion majority of the PLID patients have given the history of pain. The patients also complaint about radiation of pain which is mostly radiated to lower limbs. Furthermore, a large number of patients have given the history of radiation of pain in both lower limbs simultaneously. Few patients also mention that the pain is radiated to back of the thigh, calf muscle and sole of the feet.

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Review Article

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Virological Aspects of Mumps: A Review

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Abstract

Mumps virus is a member of the paramyxoviridae family. The mumps viruses contain a non-segmented, negative-strand RNA genome. The entire replication cycle of mumps virus takes place in the cell cytoplasm. Messenger RNA transcripts are made by the viral RNA polymerase. Mumps viruses attach to host cells via the hemagglutinin glycoprotein (HN, H or G Protein). The replication of the respiratory pathogens is limited to the respiratory epithelia, and but mumps become disseminated to target tissues of the salivary glands and central nervous system, throughout the body and produced generalized disease. Mumps mostly colonizes and replicates along the upper respiratory tract in the midst of a symptomatic infection. After entering the respiratory system, the virus locally replicates and has a marked tropism for glandular tissues which explains the great diversity of this virus. In this review summarize the current state of knowledge on the virus, its origin and nomenclature, its replication and its pathogenesis. *[J Monno Med Coll June 2020;6(1): 24-27*

Keywords: Mumps virus; virology; tropism; hemagglutinin-neuralminidase

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Introduction

Mumps is an acute contagious viral disease caused by Mumps virus and is a type of acute respiratory infectious disease that is prevalent worldwide[1]. The inflammation and swelling of the parotid glands are the main clinical features of Mumps Virus infection. The virus can also damage many internal organs and the central nervous system and cause the emergence of a variety of clinical manifestations, including pancreatitis, orchitis, oophoritis, deafness, aseptic meningitis, encephalitis, and other complication[1]. Outbreaks occur where crowding favors dissemination of the virus. Cases appear throughout the year in hot climates and peak in the winter and spring in temperate climates. The overall mortality rate for mumps is low (one death per 10,000 cases in the United States), mostly caused by encephalitis[1]. The incidence of mumps and associated complications has declined markedly since introduction of the live-virus vaccine. In 1967, the year mumps vaccine was licensed however in 2009, a mumps outbreak occurred in the states of New York and New Jersey in which 88% of those affected had been vaccinated[2]. A surveillance system for mumps virus infections at the national and international levels is organized, particularly at the molecular level.

History

The mumps virus (MuV) has long been responsible for one of the most common infections in children. The vernacular name "mumps" appeared at the end of 16th century. It comes from the old English verb "to mump", which means to speak in a low in distinct manner as a typical consequence of the characteristic infection of the parotid glands causing a submaxillary swelling moving back from the jaw to the ear. One first description of an epidemic of mumps would be the work of (Hippocrates) in the 5th century BC. In 1934, Johnson and Goodpasture demonstrated the viral origin of mumps. Then, in a second study, the following year, they validate the postulate of Koch by causing mumps in young children by inoculation of a parotid filtrate of infected monkeys[3].

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Origin and Nomenclature

The MuV belongs to the order Mononegavirales, the family Paramyxoviridae, the subfamily Paramyxovirinae and the genus Rubulavirus. The closest known virus of MuV is a bat virus, the MuV-like bat virus described in 2009[4]. The virus is strictly human, and there is only one serotype, but a multitude of wild genotypes circulating on the surface of the globe are described. Under certain conditions, it is possible to infect laboratory animals, notably rhesus macaque and hamster, but also rats, marmosets, mice or ferrets. WHO proposed a revision of the MuV nomenclature in 2012, and described 12 different genotypes (A to D, F to L and N) based on analysis of the small hydrophobic (SH) and hemagglutinin-neuraminidase (HN) genes[5]. The number of MuV sequences available in GenBank is very limited, since it was only in 2015 that sequences from the 12 geno types have been available[6].

Taxonomic Classification

Mumps virus is a member of the paramyxoviridae family. All the members of paramyxoviridae family initiate infection via the respiratory tract. Whereas replication of the respiratory pathogens is limited to the respiratory epithelia, and measles and mumps become disseminated throughout the body and produced generalized disease. The paramyxoviridae family is divided into two subfamilies: paramyxovirinae and pneumovirinae. Belongs to paramyxovirinae there are four genera: Respirovirus, Rubulavirus, Morbilivirus, Henipavirus, and in pneumovirinae there are two genera: Pneumovirus and Metapneumovirus. The genus Rubulavirus contains two species: Parainfluenza viruses and Mumps viruses. Most of the members are monotypic. They consist of a single serotype. All are antigenically stable. Members with in a genus share common antigenic determinants. Although the viruses can be distinguished antigenically using well defined reagents, hyper immunization stimulates cross-reactive antibody that react with all four Parainfluenza virus (1-4), Mumps virus, Newcastle disease virus. Such heterotypic antibody responses, which includes antibodies directed against both internal and surface proteins in older people. This phenomenon makes it difficult to determine by serodiagnosis, the most likely infected type. All members of the genus Rubulavirus possess hemagglutinating and neuraminidase activities, both carried by the HN glycoprotein, as well as membrane fusion and hemolysis properties; both function of the F protein[7].

Scientific classification

- Order - Mononegavirales
- Family - Paramyxoviridae
- Subfamily - Paramyxovirinae
- Genus - Rubula virus
- Species - Mumps virus

Morphology

The morphology of mumps virus is pleomorphic. The size range is 100-600 nm. The mumps virus is single-stranded, negative-sense, RNA virus covered by a glycoprotein envelop. There are spikes of two different transmembrane glycoproteins on the RNA envelope: one is the larger glycoprotein, regulates hemagglutinin-neuralminidase activity and the other is F protein, responsible for attachment to the lipid membrane of a host cell.

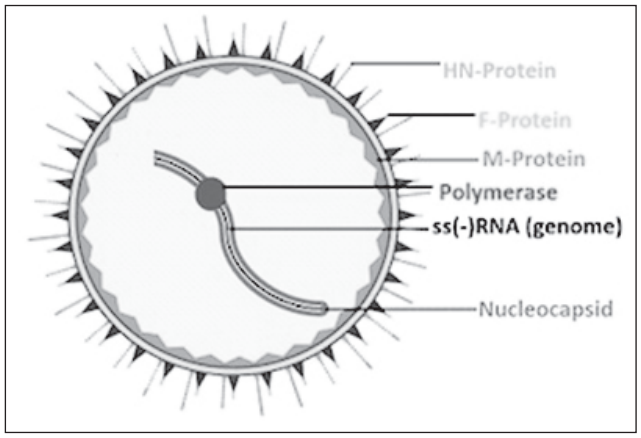

Figure I: Schematic representation of the mumps virus particle (Source: Study.com 2017)

Genome

Within the structure, the long, coiled, electron dense ribonucleoprotein (RNP) containing the mumps virus genome. The mumps virus genome is a non-segmented RNA strand that contains 15,384 nucleotides. It encodes seven tandemly linked transcription units: The nucleo (N), V/phosphor-/I (V/P/I), matrix (M), fusion (F), small hydrophobic (SH), hemagglutinin-neuraminidase (HN) and large (L) proteins. Among them, the degree of variation of the SH gene is the largest in the entire genome and is therefore generally used as the basis for genotyping. Mumps virus has been shown to have 12 genotypes (A –N, excluding E and M) circulating in the world, among which there is large diversity[8].

Replication

The entire replication cycle of mumps virus takes place in the cell cytoplasm. The typical replication cycle is illustrated as virus attachment, penetration and uncoating, transcription, translation and RNA replication and maturation.

Virus Attachment, Penetration and Uncoating: The proteins on the surface of the virion attach to specific receptor proteins on the cell surface through weak, non-covalent bonding. Mumps viruses attach to host cells via the hemagglutinin glycoprotein (HN, H or G Protein). Next the virion envelops fuses with the cell membrane by the action of the fusion glycoprotein F1 cleavage product. The F1 protein undergoes complex refolding during the process of

viral and cellular membrane fusion. If the F0 precursor is not cleaved, it has no fusion activity. Virion penetration does not occur and the virus particle is unable to initiate infection. Fusion by F1 occurs at the neutral PH of the extracellular environment, allowing release of the viral nucleocapsid directly into cell. Thus the mumps viruses are able to bypass internalization through endosomes.

Transcription, Translation and RNA Replication: The mumps viruses contain a non-segmented, negative-strand RNA genome. Messenger RNA transcripts are made in the cell cytoplasm by the viral RNA polymerase. The mRNA are represents a single gene. Transcriptional regulatory sequences at gene boundaries signal transcriptional start and termination. The position of a gene relative to the 3/ end of the genome correlates with transcription efficiency. The most abundant class of transcripts produced by an infected cell is from the N gene, located nearest the 3/ end of the genome, the least abundant is from the L gene, located at the 5/ end.
Viral proteins are synthesized in the cytoplasm. Viral glycoproteins are synthesized and glycosylated in the secretory pathway. The viral polymerase protein complex (P and L proteins) is also responsible for viral genome replication. A positive strand anti-genome is synthesized as intermediate template, full length progeny genomes are copied from the anti-genome template[9].

Maturation: The virus matures by budding from the cell surface. Progeny nucleocapsids form in the cytoplasm and migrate to the cell surface. They are attracted to sites on the plasma membrane that are studded with viral HN and F0 glycoprotein spikes. The M protein is essential for partical formation, serving to link the viral envelope to the nucleocapsid. During budding, most host proteins are excluded from the membrane. The neuraminidase activity of the HN protein of mumps virus presumably functions to prevent self-aggregation of virus particle[7].

Infectious Dose, Incubation and Colonization
The incubation period of mumps ranges from 2 to 4 weeks, but is typically about 14 to18 days[7]. Fever can last for three to four days, and if parotitis occurs, usually lasts seven to ten days. A person is considered most infectious from one to two days before and five days after the symptoms of parotitis. Mumps mostly colonizes and replicates along the upper respiratory tract in the midst of a symptomatic infection.

After entering the respiratory system, the virus locally replicates. To target tissues of the salivary glands and central nervous system, viremic dissemination occurs. The virus replicates at target organs leading to a secondary phase of viremia before the immune response occurs[10].

Virulence Factors
The double layered envelope surrounding the mumps virus is one of the highest contributing factors to its virulence, working through a series of protein. The M protein contributes to viral budding from infected cells. The HN and F proteins on the outer surface work in tandem to induce fusion of the host cell membrane and virion membrane to create cell-to-cell fusion after infection. To circumvent the IFN-mediated antiviral responses, the V protein limits IFN production and block IFN signaling. The small hydrophobic protein (SH) also contributes to the evasion of the host antiviral response by blocking the TNF-α mediated apoptotic signaling pathway. Both the F and HN proteins within the mumps genome have been identified as the primary virulence factors. Antibodies that target the F and HN proteins have provided definitive evidence of the neutralization of the infectivity of the virus in vitro and provide protection in vivo[11].

Pathogenesis
Mumps is transmitted by droplet spread or by direct contact. Primary replication occurs in nasal or upper respiratory tract epithelial cells. The virus quickly spreads to the local lymphoid tissue and a primary viraemia occurs and Viremia then disseminates the virus to the salivary glands and other major organ systems; thereby the virus spreads to distant sites in the body. Alternatively, the virus may ascend from the buccal mucosa up Stensen's duct to the parotid gland[10]. A few days after the onset of illness, virus can again be isolated from the blood, indicating that virus multiplication in target organs leads to a secondary viraemia. Parotitis is the most frequent presentation, occurring in 95% of those with clinical symptoms and also occurs on the CNS, testis or epididymis, pancreas and ovary. Occasionally, meningitis may precede parotitis by a week[11]. The central nervous system is also commonly infected and may be involved in the absence of parotitis. Viral invasion of the CNS presumably occurs across the choroid plexus. Blood-borne infected mononuclear cells may cross the fenestrated endothelium of the choroid plexus stroma and serve as a source for subsequent infection of the

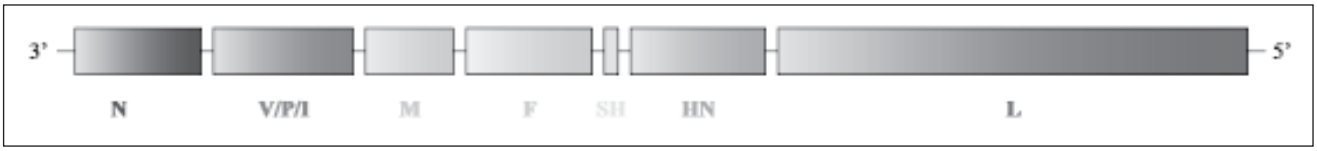

Figure II: Schematic representation of the RNA genome of the mumps virus. Each rectangle represents an independent transcription unit frame. (Source: Virologie. 2017). N=Capsomer Unit; V=Counteracts the interferon response; P=Transcription complex element; I=Unknown role; M=Confers its structure to the virus particle; F=Induces fusion of the envelope and the cellular Membrane; SH=Unknown Role; HN=Recognises the host cell and binds to its receptor;L=Transcription complex element.

choroidal epithelium. Maturation of virus from the ventricular surfaces of choroidal cells provides progeny virions that are widely distributed through ventricular pathways and the subarachnoid space by CSF. Termination of viral excretion in saliva correlates with the local appearance of virus-specific secretory IgA. Virus-specific IgM antibodies are also present early in saliva. A cell-mediated immune response also develops. Interferon is induced early in mumps infection[12]. Virus frequently infects the kidneys and can be detected in the urine of most patients.

Conclusion

As a re-emerging disease, mumps is now a major issue globally. elucidation of mechanisms of MuV pathogenesis is of paramount importance, as this information will help direct the development of improved vaccines. These include the elucidation of the target cell tropism throughout an infection, the mechanisms by which MuV establishes a systemic infection and the basis of neurotropism. The utilization of existing reverse genetic systems alongside the generation of new, clinically relevant systems for other aspects of the disease will allow a more complete understanding of disease. This review has summarized our current understanding of MuV clinical disease, pathology, and how this relates to viral pathogenesis.

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