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TMSS Medical College Journal (TMCJ)

INFORMATION FOR AUTHORS

Submission of Manuscripts

Papers are accepted for publication with an understanding that they are submitted solely to the journal of 'TMSS Medical College Journal' and are subject to peer review and editorial revision. The statement, views and opinions expressed in the articles are those of the author(s) and are not necessarily those of the editor or publisher. Manuscripts should be accompanied by a cover letter from the author who will be responsible for correspondence. In case of multiple authors, the cover letter should contain a statement that the manuscript has been seen and approved by all the authors. Two copies of the manuscript should be sent to Executive Editor, TMSS Medical College Journal.

General Instructions

- Article must be within 5 years of research work.
- Authors of research work should be of relevent fields.
- Type manuscripts double-spaced, on a good quality A4 sized paper, including references, figures with legends and tables on one side of the page only.
- Use Times New Roman 11 sized font.
- Leave a margin of 1-inch on all sides of the page. Beginning with abstract page, all the pages (including pages containing tables, figures and references) will contain page numbers at the lower right hand corner.
- Cite each reference in text in numerical order and list in the reference section.
- Begin each component of the manuscript with a new page in the sequence of (i) Title page with author information, name of the department(s) and institutions to which the work should be attributed, name md address of the author with post code responsible for correspondence and requests for reprints (ii) Acknowledgements (iii) Abstract page (iv) Text (v) References (vi) Tables (vii) Figures with legends, for illustrations.
- Present the text in the sequence of Introduction, Methods & Materials, Results and Discussion.
- Use SI units of measurements (for blood pressure use mm of Hg).
- Define Statistical methods in method section of the paper.
- Use standard abbreviations, the full forms of which should precede in its first use in the text
- As a general rule, articles should not exceed 10-12 pages. Too much large volume manuscripts will not be accepted for publication
- With two copies of manuscript (hard copy), submit an electronic version (soft copy) composed in Microsoft Word 97-2007 format in a CD.

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Text page must include:

- Full title of the article not exceeding 50 characters with three to five key words for use as indexing terms and as running title for use on top of the text pages
- Author's names, highest academic degree, affiliations, and complete address for correspondence including Fax number, telephone number, and E-mail address.

The acknowledgments pages (Second page, but do not number)

- List all sources of funding for the research, plus substantive contributions of individuals. (Note: If the article is published, this section will be printed at the end of the text).

Abstract page (First numbered page)

- Do not cite references in the abstract. Be concise (250 words, maximum).
- Limit use of acronyms and abbreviations. Abbreviations must be defined at the first mention.

- The abstract should be a total of about 250 words maximum. Abstract should cover Background and Purpose (description of rationale for study); Methods (brief description of methods); Results (presentation of significant results); and Conclusion (succinct statement of data interpretation) in separate headings.

The Text

The following are typical main headings:

Introduction, Materials and Methods, Results, Discussion and Conclusion

- **Introduction:** Summarize the rationale for the study with pertinent references. The purpose(s) of the study should be clearly stated.
- **Materials and Methods:** Identify type of study and describe the study subjects and methods used. Provide methods of statistical analysis, Cite reference(s) for standard study and statistical methods. Describe new or modified methods. Identify apparatus (with name and address of manufacturer) used. Generic names of drugs must be given. Manuscripts that describe studies on humans must indicate that the study was approved by an Institutional Ethical Committee and that the subjects gave informed consent. Add statistical analysis.
- **Results:** Present only important results/observations in logical sequence in the text, tables or illustrations with relevant statistics.
- **Discussion:** Emphasize new and important results and the conclusions that follow including implications and limitations. Relate observations to other relevant studies.
- **References:** Accuracy of reference data is the author's responsibility. Verify all entries against original sources, especially journal titles, inclusive page numbers, publication dates. All authors must be listed if less than six. Use et al, if more. Personal communications, unpublished observations, and submitted manuscripts must be cited in the text as "([Name(s)], unpublished data, 20XX)." Abstracts may be cited only if they are the sole source and must be identified in the references as "Abstract". "In press" citations must have been accepted for publication and add the name of the journal or book including publisher. Use Vancouver style, for example.

1. World Health Organization: WHO Recommendations: Obesity: Preventing and Managing the Global Epidemic. Geneva, World Health Org., 2000 (Tech. Rep. Sen, no. 894).
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Tables

- Each table must be typed on a separate sheet and double-spaced. The table number should be Roman, followed by a brief informative title. Place explanatory matter in footnotes. For footnotes use symbol in this sequence. *, **, t, tt" etc.

Figures

- Line drawings, photomicrographs, colour prints and halftones should be camera ready, good quality glossy prints (highest quality reproduction with 300 dpi or higher). Submit only originals of laser prints, not photocopies. A set of original figures must be submitted. Indicate figure number, short figure title on top of figure lightly in pencil. Any abbreviations or symbols used in the figures must be defined in the figure or figure legend. Legends or captions for figures should be listed on a separate page, double spaced. Keep an extra set of original figures for your records.

Editorial

Postgraduate Medical Education: a 'Pipeline' to Competence

Dr. DM Arifur Rahman, Assistant Professor, Department of Pathology, TMSS Medical College, Bogura.

Postgraduate medical education (PGME) contains training after graduation (MBBS) from a medical college before a physician is thought to be competent for independent practice. The establishment of outcome (competency) based education is now a key feature in curriculum planning in both undergraduate and PGME. The concept of outcome-based education (OBE) was promoted by Spady as 'a way of designing, developing, delivering and documenting instruction in terms of its intended goals and outcomes'.[1] The competency based approach highlights the competencies achieved by the learner, rather than how they were trained. The learning outcomes/ competencies expected at the end of training and at the end of each phase of training are clearly stated, and communicated to all concerned including teachers, students and other stakeholders, such as employers in the health service.

In addition to being a learners, Postgraduate medical trainees are unique in that way, they are simultaneously both workers and learners.[2] The postgraduate trainees perform a part of the patient care in teaching hospitals and other healthcare institutions, under the supervision of postgraduate trainers. A postgraduate trainee has got many roles apart from a learners and clinical practitioner including teaching the undergraduate medical students, and a researcher.[3]

Contemporary postgraduate education was based on trainees rotating through various basic, para-clinical and clinical departments for a defined period of time. Competency based learning in PGME creates an unique environment, with its emphasis on work-based learning, clinical supervision as a predominant method of training, performance-based assessment, and the challenge of simultaneously delivering education, training and service.[4] In PGME, much of the learning occurs in a workplace predominantly in small group setting, while the trainees are concurrently caring for a patient or performing other clinical tasks. The trainee's clinical supervisors may coach, direct and teach informally. 'Informal learning' is described as unintended, opportunistic and unconstructed since it occurs in surroundings of an unstructured curriculum.[5] Role-modelling is an important educational strategy that occurs at every level of education but is particularly important in PGME.[6] As well as work-based learning, trainee education may occur in non-clinical settings through problem based learning activities, workshops, lectures, journal clubs, case-based discussions and in simulation contexts.[3]

As part of work-based learning, trainees undergo ongoing assessment, both formative and summative. The common assessment strategies are direct observation of trainee performance, Learning portfolios (e.g. records of performance achievements), Logbooks (e.g. records of activities or procedures etc.)

There are a number of controversial issues in PGME. The duty hours of the trainees, the length of training period, appropriate residence allocation, allowance during training period, and problem of managing deputation for government service holders are the main obstacles in the way of PGME competency in Bangladesh. Moreover, most clinical supervisors are practicing physicians who have trained in clinical medicine but do not necessarily have any training in teaching, assessment or supervisory skills. Without addressing these issues, competency based PGME can't be obtained!

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(TMSS Medical College Journal 2023; 20(1): 5-6)

Original Article

Antimicrobial Sensitivity Pattern of Salmonella Typhi Isolated from Blood Samples of Enteric Fever Patients at a Tertiary Care Hospital in Bangladesh

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Abstract

Background: Enteric fever is an important multisystem infectious disease caused by Salmonella typhi. It is a major public health problem in developing countries including Bangladesh. A changing antimicrobial sensitivity pattern of Salmonella typhi and emergence of resistance has increased to a great concern. **Objective:** To investigate the antimicrobial sensitivity pattern of Salmonella typhi and selection of appropriate antimicrobial therapy to avoid multidrug-resistance. **Materials and Methods:** This cross-sectional descriptive study was conducted at MH Samorita Hospital and Medical College, Dhaka, Bangladesh from January 2021 to December 2021. Blood culture samples were collected aseptically and cultured in Microbiology laboratory. A total of 100 laboratory reports were collected during this period. Simple random sampling technique was applied for selection of culture positive Salmonella typhi patients laboratory reports. Specimens from the blood culture were identified by standard procedures as needed. Antimicrobial sensitivity testing was performed by disk diffusion method according to 'The Clinical Laboratory Standard Institute' guidelines. **Results:** Among the culture positive cases, Salmonella typhi was sensitive to ceftriaxone and gentamicin 100% followed by Ceftazidime 99%,Imipenem 98%, Cefixime 93%, Cotrimoxazole 79%, and least sensitive antibiotic was azithromycin 21% and Ciprofloxacin 23%. The incidence rate was high in male 63% and the age group 0-10 years 35%. **Conclusion:** The antimicrobial sensitivity testing showed that the Salmonella typhi were highly sensitive (>88%) to most of the drugs used in this study, whereas azithromycin showed only 21% sensitivity. So this study indicates that Ceftriaxone, Gentamicin, Ceftazidime, Imipenem and Cefixime can be used as a first line therapy and Azithromycin, Ciprofloxacin should be avoided for treatment.

Key words: Enteric fever, Salmonella typhi, Multidrug resistant, Antimicrobial sensitivity testing.

Introduction

Enteric fever is a febrile illness caused by infection with the Gram-negative bacterium Salmonella enterica serovar Typhi (S. Typhi).[1] It is an endemic disease in many developing countries including Bangladesh.[2] World Health Organization (WHO) estimates the global enteric fever disease burden roughly 21.6 million people annually, resulting in about 223,000 deaths per year.[3] The pathogens are transmitted by the faeco oral route with poor hygienic practices resulting in high morbidity and mortality. More than 90% of this morbidity and mortality occurred in Asia.[4] Antimicrobial therapy is the mainstay of managing enteric fever. If not treated properly, enteric fever carries a mortality rate of 30 %. Prompt institution of appropriate antimicrobial therapy can reduce the mortality and morbidity of this illness.[5]

Since 1948, chloramphenicol had been the mainstay of treatment of enteric fever until 1972. Then chloramphenicol resistant enteric fever became a problem. Extensive and irrational use of antimicrobial

drugs have led to the emergence and spread of drug-resistance, often referred as multidrug resistance (MDR) in the pathogenic strains of Salmonella.[6] The early emergence of drug resistance among Salmonella isolates dates back to late 1980s when the traditional first-line drugs (chloramphenicol, ampicillin and co-trimoxazole) became ineffective due to antibiotic resistance, which compelled clinicians to rely upon fluoroquinolones, especially ciprofloxacin.[7] Recent global surge in resistance to fluoroquinolones could lead to a disastrous increase in global infectious diseases.[8] However, several findings suggest the increasing burden of nalidixic acid resistant S. typhi (NARST) strains with reduced susceptibilities to fluoroquinolones, which subsequently has led to the introduction of third generation cephalosporins like Cefixime, Ceftazidime, Ceftriaxone and Macrolieds like Azithromycin.[9] But with their increasing usage in clinical settings the resistance against these antibiotics is increasing reported. Multidrug-resistance (MDR) has been emerging rapidly and consistently in enteric fever pathogens driven by selection pressure due to irrational drug therapy. This has resulted in treatment failures leading to extended hospital stay, health complications and leading to rise in morbidity and mortality.[10]

The study of antimicrobial sensitivity pattern of S. typhi isolates is crucial in prompt and appropriate therapy of enteric fever in prevention and control of the disease. Continual consistent surveillance and monitoring of local antimicrobial resistance trends is a pre-requisite for implementing rational measures and to update the therapeutic guidelines.[11]

In light of above facts, the present cross sectional descriptive study was under taken to evaluate the antimicrobial sensitivity pattern of S. typhi isolated from blood cultures proven enteric fever in a tertiary care hospital in Dhaka, Bangladesh.

Materials and Methods

The blood samples for culture were collected from Microbiology laboratory of MH Samorita Hospital, Dhaka, Bangladesh. A total of 100 laboratory reports were collected during the period of January 2021 to December 2021. Simple random sampling technique was applied for selection of culture positive Salmonella typhi patients laboratory reports. Venous blood samples (10 ml from adults and 5 ml from children) were drawn aseptically by venipuncture from clinically suspected cases of enteric fever before starting any antimicrobial therapy. The specimens were Cultured and antimicrobial sensitivity tests were performed according to standards microbiological techniques. Brain-Heart infusion (BHI) broth was used for culture. Subcultures into blood agar, Mac-Conkeys agar were done as per standard methods. Non-lactose fermenting colonies were identified by biochemical reactions and confirmed by group and type specific Salmonella antisera. Antimicrobial sensitivity was performed by Kirby- Bauer Disc- diffusion methods on Muller Hinton agar plates. Antimicrobial disc used in this study were, Amoxicillin, Azithromycin, Cefepime, Cefixime, Ceftazidime, Ceftriaxone, Cefuroxime, Ciprofloxacin, Co-trimoxazole, Gentamicin and Imipenem. Interpretation was done in accordance with the National Committee for Clinical Laboratory Standards (NCCL) and data were entered in Microsoft Excel. This study was approved by ethics Committee of MH Samorita Hospital and Medical College.

Results

In this study total 100 S. typhi were obtained by blood culture from the suspected cases of enteric fever. The age of the patients range from 02 to 60 years.

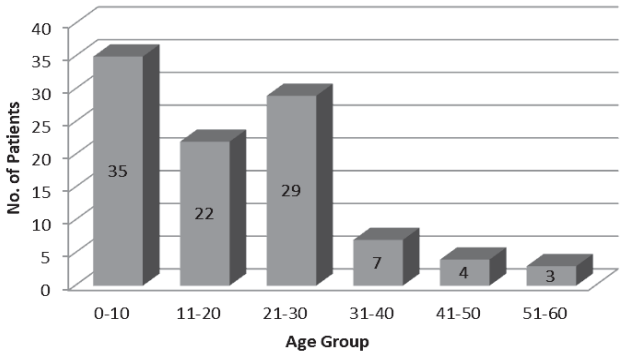

Figure 1. Age wise distribution of Salmonella typhi.

Figure 1 Shows the age wise distibution of Salmonella typhi isolates. The Majority cases of enteric fever were in 0-10 years age group and least from 51-60 years age groups.

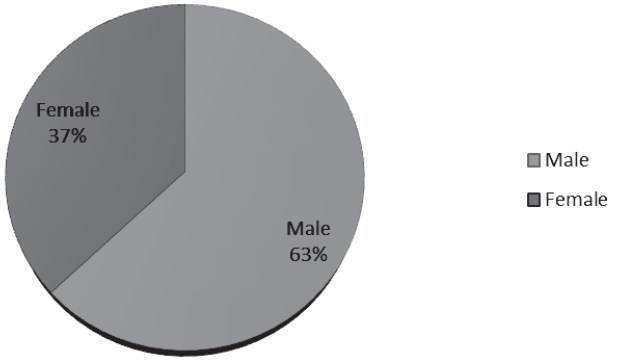

Figure 2. Gender wise distribution of Salmonella typhi.

The gender wise distribution of patients is shown in figure 2, here male were 63% and female were 37%. In this study make preponderance was observed in Enteric fever cases with male: female ratio=1.70:1 for all Salmonella typhi isolates.

Table I: Antimicrobial sensitivity pattern of Salmonella typhi by kirby-bauer disc diffusion method

Antibiotic	Serotype typhi (N = 100)		
	Sensitive (%)	Intermediate (%)	Resistant (%)
Amoxycillin	81(81)	-	19(19)
Azithromycin	21(21)	1(1)	78(78)
Cefepime	96(96)	4(4)	-
Cefixime	93(93)	3(3)	4(4)
Ceftazidime	99(99)	-	1(1)
Ceftriaxone	100(100)	-	-
Cefuroxime	41(41)	59(59)	-
Ciprofloxacin	23(23)	-	77(77)
Co-trimoxazole	79(79)	13(13)	8(8)
Gentamicin	100(100)	-	-
Imipenem	98(98)	2(2)	-

The antimicrobial sensitivity pattern of S. typhi as depicted in Table I, showed very high sensitivity towards Gentamicin and Ceftriaxone (100%) followed by Ceftazidime (99%) and Imipenem (98%). S. typhi isolates were least sensitive towards Azithromycin (21%). However, sensitivity to conventional antibiotics like Amoxicillin (81%) and Co-trimoxzole were (79%) respectively. S. typhi isolates were mostly resistant to Azithromycin (78%)) and Ciprofloxacin (77%).

Discussion

Enteric fever is an endemic disease in the tropic and subtopic regions of the world. It has become a major public health problem in low-to-middle-income countries (LMICs) like Bangladesh. The occurrence of enteric fever was higher in summer month, but now a day it spreads highly among the community in all seasons of the year. The presence of densely populated urban areas with reduced access to safe drinking water and sanitation, lowered socio-economic status, lack of effective surveillance and poor infection control are some of the driving factors for the high endemicity of the diseases in these countries. Poverty and lack of proper health care facilities incite disease burden in Bangladesh.[12] Global burden for Salmonella typhi is 80% seen in the Asian and African countries. Proper sanitation, public health education and vaccination are long term preventive measures that would improve this situation. The emergence of antibiotic resistant strains of bacteria is closely linked to the irrational use of antibiotics.[13]

In the present study 23% of the isolates were susceptible to Ciprofloxacin in disc-diffusion test. This is concurrent with the findings from other studies.[14] It needs higher concentration for disc diffusion test. The requirement for higher concentrations of Ciprofloxacin for the inhibition of S. typhi could be due to the overuse of Ciprofloxacin in the treatment of enteric fever and other unrelated infections. Over-the-counter (OTC) availability of antibiotics and incomplete treatment due to many reasons in a developing country like ours may also be the factors contributing to the development of resistance.[15]

Our study showed 100% sensitivity of Salmonella typhi against Ceftriaxone and Gentamicin. Similar results were reported from studies done in India, Pakistan and neighboring countries.[16, 17, 18] Emphasis is laid on the sparing use of this drug. If we do not make any limitation of its use then it became resistant to these first line drugs very soon. S. typhi were found to be 21% susceptible towards Azithromycin. The emerging resistant of Azithromycin has also been reported in India.[19] This may be the result of misuse of

Azithromycin that has been propelled due to its oral route of administration, as well as broad-spectrum antimicrobial activity with minimal side effect and interactions.[20] Conventional first line drugs are not used for a long period in enteric fever because of the high resistance rate, so they are regaining their sensitivity. From this study we observed that Co-trimoxazole is still a little bit sensitive of Salmonella typhi (79%). Now a days Co-trimoxazole is the second cost effective drug used to treat S. typhi.[21]

In this study we male were more affected than female and male: female ratio =1.70:1. The highest prevalence rate was observed in children whose age was between 0 to 10 years (37%) due to less development of immune power and poor personal hygiene. Children cannot maintain proper hygiene by themselves. These findings were in agreement with the findings of other studies.[22, 23, 24]

Conclusion

The findings of the present study indicated that MDR strains prevail in Bangladesh. Co-trimoxazole and Amoxicillin resistant by Salmonella typhi were found to be minimal, so these drugs may still have a role in the treatment of enteric fever. However Gentamicin and Ceftriaxone showed cent percent sensitivity followed by Ceftazidime (99%), Imipenem (98%), Cefepime (96%), Cefixime (93%). Hence Cephalosporin groups are the choice of drugs to treat enteric fever. Antibiotics are unnecessarily prescribed for common cold, cough, any febrile illness and diarrhea in Bangladesh. Physicians, therefore should always be aware of the antibiotic sensitivity /resistance profile of the organism for the rational use of antibiotics. Therefore it might be recommended that blood/stool/ urine culture should be sent to diagnostic center for characteristics of a particular pathogen before prescribing antibiotics in suspected enteric fever patients to prevent further resistance. Improvement in sanitation and water supply systems has been suggested as a method to control epidemics of enteric fever in Bangladesh as these factors are the tip of the iceberg.

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Original Article

Clinical Response of Analgesics to Patients- A Hospital Based Study

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Abstract

Introduction: Pain is the crucial reason patients seek medical assistance. Pain has sensory and emotional constituents and is often classified as acute or chronic. Doctors should assess the cause, severity, and nature of the pain and its effects on function focusing on daily events, mood, cognition and sleep. Analgesics are a class of medications designed specially to relieve pain without causing a loss of consciousness and can constrain the sensation of pain by preventing transmission of non-nociceptive impulses along primary afferents (local anesthetics) or by altering the perception of pain (opioids). **Materials and Methods**: A prospective study was carried out in the Department of Surgery, TMSS Medical College and Rafatullah Community Hospital, Bogura, Bangladesh from January 2022 to June 2022. A total of 86 patients with proper documentation were confirmed as the study population. Ethical clearance was taken from the hospital. Verbal consent was taken from all the participants before starting data collection. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 25.0. **Results:** Among the study population (N= 86), the majority of the people (30, 34.9%) were between 41-60 years old. Analgesics were administered in IV/IM route. The maximum number of patients (79, 91.9%) were given both opioid and non-opioid drugs. Based on Post-operative day (POD), In case of 1st POD, the majority of patients (53,61.6%) felt moderate pain, thirteen patients (13,15.1%) felt severe pain and in the case of 2nd POD, most of the patients (56,65.1%) felt moderate pain, and only four (4,4.7%) felt severe pain. There was an observed improvement in the case of the 3rd, 4th and 5th POD. Early discharge was noticed in most of the patients (52,60.5%) and late discharge was noticed in one-fifths of the patients (18,21.0%) who were given both opioid and non-opioid drugs. Late discharge was noticed in only one non-opioid groups (1,1.2%). There was no significant relationship between given analgesics and discharge of the patients (p=.634). **Conclusion**: The range of diverse experimental pain models allows pain and analgesia in humans to be studied under precise labs. In this present findings, clinical outcomes, claims and evaluations of the patients improved after suggesting both opioid and non-opioid groups.

Keywords: Pain, Drags, Analgesics Post-operative day (POD)

Introduction

Pain is the most common reason patients seek medical urgency. Pain has sensory and emotional components and is often classified as acute or chronic.[1] Physicians should assess the reason, severity, and nature of the pain and its effects on function focusing on daily activities, mood, cognition and sleep. Evaluation of the causes of acute pain differs from that of chronic pain.[2] acute pain is frequently associated with anxiety and hyperactivity of the sympathetic nervous system (tachycardia, increased respiratory rate and blood pressure, diaphoresis, and dilated pupils). Chronic pain does not involve sympathetic hyperactivity but may be associated with vegetative signs (fatigue, loss of appetite).[3] Analgesics are a class of medications designed specially to relieve pain without causing a loss of consciousness.[4] The word analgesics derives from the Greek a (without) and algein (pain) and it works on the peripheral and nervous systems without blocking the conduction of nerve impulses.[5,6] Analgesics can inhibit the sensation of pain by inhibiting the transmission of non-nociceptive impulses

along primary afferents (local anesthetics) or by altering the perception of pain (opioids).[7] Analgesics drugs can be classified into three groups; such as non-opioid drugs, opioid drugs, and analgesic drugs also known as adjuvants.[8] Medications used to manage pain should be carefully chosen based on the sort of pain the resident is undergoing and the selection of medications should also take into consideration the impact of old age and frailty.[9,10] To enhance pain relief and minimize side effects, consideration can be given to combining analgesics with distinct modes of action. The 1st and perhaps the most evident is that the pain is reduced, resulting in the patient feeling improved. Using a combination of drugs makes them act more efficiently in alleviating pain and the more effective analgesics are, the minimum pain the patients feel.[11] There is another great advantage to the patient that if an amalgamation of painkillers is taken, then the patients will be able to take lower levels of any one particular type of analgesic and this means that they do not experience many of the unpleasant side effects that may result from high doses of one specific analgesics.[12] Antagonistic trials arise such as drowsiness, respiratory depression, nausea, vomiting and constipation for the opioid medications and drowsiness, dizziness, nausea and headache for the non-steroidal anti-inflammatory drugs.[13] The current analysis intended to evaluate the clinical response of analgesics to patients.

Objective

- To evaluate the clinical response of analgesics to patients.

Materials and Methods

A prospective study carried out in the Department of Surgery, TMSS Medical College and Rafatullah Community Hospital, Bogura, Bangladesh from January 2022 to June 2022. A total of 86 patients with proper documentation were confirmed as the study population. Randomized sampling techniques were followed. Data were collected using the predesigned semi-structured questionnaire. Ethical clearance was taken from the hospital. Verbal consent was taken from all the participants before starting data collection.

Inclusion criteria

a. Patients who agree to participate in the study.

b. Patients suffering from cholelithiasis, appendicitis, hernia, perianal abscess.

c. HPR-Duct Cell Carcinoma.

Exclusion Criteria

a. Medically unfit patients.

b. Patients who showed unwillingness to participate in the study.

c. Patients with incomplete data.

Pain Measurement

The visual analogue scale (VAS) and numeric rating scale (NRS) are the most frequently used to determine the current intensity of acute pain. They are consistent, sensitive to change, and feasible to apply for the measurement of the severity of pain. A dolorimeter is an instrument used to measure pain threshold and pain tolerance scientifically. Measurement by the subjective report is by far the most common type of procedure for quantifying pain. Patients may indicate pain levels verbally, mark simple scales, or fill out complex questionnaires. In all cases, the patient determines data.[14] The most common multidimensional pain scales are the McGill Pain Questionnaire, and the Brief Pain Inventory. This scale uses to assess a ‘problem’ list that does not just include pain intensity, moods, behavior, thoughts, beliefs, psychological effects, and interaction with each other.[15]

McGill Pain Questionnaire

Melzack and his team at McGill University designed the questionnaire in the early 1970s redeveloped it in 1950. The prior 11 words describe the sensory dimension and the next four are the affective dimension.[15]

Data analysis

The study coordinators performed random checks to verify data collection processes. Completed data forms were reviewed, edited, and processed for computer data entry. Frequencies, percentages, and cross-tabulations were used for descriptive analysis.

The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 25.0. The significance level of 0.05 was considered for all tests.

Results

Most of the patients were suffering from cholelithiasis, appendicitis, hernia, and perianal abscess. They were prescribed to take analgesics. In our study, among the study population (N = 86), the majority of the people (30,34.9%) were between 41-60 years old, and around one-third of the people (25,29.1%) were included between 21-40 years of age, & only five (5,5.8%) were of 80 or more than 80 years old Table I**.** Analgesics were administered in IV/IM route. The maximum number of patients (79,91.9%) were given both opioid & non-opioid drugs, two patients (2,2.3%) were given opioid drugs, five patients (5,5.8%) were given non-opioid drugs Table II**.** Based on postoperative day (POD), in the case of 1st POD, the majority of patients (53,61.6%) felt moderate pain, and thirteen patients (13,15.1%) felt severe pain. In the case of the 2nd POD, most of the patients (56,65.1%) felt moderate pain, and only four (4,4.7%) felt severe pain. There was an observed improvement in the case of the 3rd, 4th & 5th POD. No one felt severe pain in the case of the 3rd,4th & 5th POD. In terms of the 3rd POD, around half of the patients (45,52.3%) felt mild pain, and fourteen (14,16.3%)felt no pain. In the 4th POD, around one-third of the patients felt no pain & only seven (7,8.1%) had moderate pain. In the 5th POD, most of the patients (62,72.9%) had no pain and only around a fourth of them (24,27.9%) felt mild pain Table III**.** Based on outcome, ambulation was done spontaneously in the majority of both opioid & non-opioid drugs group**s** (46,53.5%), ambulation was done with help in most of the opioid groups (5,5.8%). The relationship between given analgesics with ambulation was non-significant (p=.230). Early discharge was noticed in most of the patients (52,60.5%) & late discharge was noticed in one-fifths of the patients (18,21.0%) who were given both opioid & non-opioid drugs. Late discharge was noticed in only one non-opioid groups (1,1.2%). There was no significant relationship between given analgesics and discharge of the patients (p=.634) Table IV

Table I: Distribution of study population according to age groups (N=86)

Age	(N,%)
≤20	11, 12.8
21- 40	25,29.1
41- 60	30,34.9
61- 80	15,17.4
≥80	5,5.8

Table 1: Most of the patients aged from 41-60 (30),

Table II: Distribution of study population according to Types of analgesic was given (N=86)

Analgesic	(N,%)
Opioid drugs	9,10.5
Opioid and Non-opioid drugs	70,81.4
Non-opioid drugs	7,8.1

Table-II: Most of the patients treated with opioid and non-opioid (70), only opioid used in 9 patients & non-opioid used in 7 patients.

Table III: Distribution of study population based on severity of pain on different Postoperative day (POD) (N=86)

POD	No pain (N,%)	Mild pain (N,%)	Moderate pain (N,%)	Severe pain (N,%)
1st POD	1,1.2	19,22.1	53,61.6	13,15.1
2nd POD	1,1.2	25,29.1	56,65.1	4,4.7
3rd POD	14,16.3	45,52.3	27,31.4	0,0.0
4th POD	25,29.1	54,62.8	7,8.1	0,0.0
5th PoD	62,72.9	24,27.9	0,0.0	0,0.0

Table-III: Most of the patient feeled moderate pain on 1st and 2nd POD (53, 56)

Table IV: Distribution of study population based on Outcome of different types of analgesics (N=86)

Analgesics	Opioid drugs, (N, %)	Opioid and non-opioid drugs, (N, %)	Non opioid drugs (N, %)	p-value
Ambulation				
Spontaneously	4,4.7	46,53.5	3,3.5	.230 ns
Done with help	5, 5.8	24,28.0	4,4.7	
Discharge				
Early	7,8.1	52,60.5	6,7.0	.634ns
Late	2,2.3	18,21.0	1,1.2	

Table-IV: With opioid and non-opioid spontaneous ambulation occurred in 46 patients and done with help in 24 patients, p-value is .230ns. Again early discharged patients were 52 in case of opioid and non-opioid use and late discharged in 18 patients, p-value is .634ns.

*t-test was performed

*p-value <.05s

Discussion

The choice of analgesics is determined by the type of pain; for neuropathic pain, traditional analgesics are less effective, and there is a frequent advantage from classes of drugs that are not usually considered analgesics, such as tricyclic antidepressants and anticonvulsants.[16]

In this current analysis, among the study population (N=86), the majority of the people (30,34.9%) were between 41-60 years old and only five (5,5.8%) were 80 or more than 80 years old. Another study depicted that the mean age of the patients was 49.5 years and about half of the patients (53.1%) were female.[17] A related article published in an Indian journal found that 40 American females 20 to 55 years of age were provided postoperative analgesics.[18] Another study carried out in the United States and Canada found that patients of age between 60 to 70 years old were prescribed analgesics.[19] Another related article showed that the mean age of the patients was 34.2 years who were prescribed to take analgesics.[20] A similar study based in Australia found that ages between 45 and 54 years of age were 1.7 times higher to take analgesics compared to others age groups.[21]

In this present study, the maximum number of patients (79,91.9%) were given both opioid & non-opioid drugs, two patients (2,2.3%) were given opioid drugs and five patients (5,5.8%) were given non-opioid drugs. A study based on HIV cases found that rates of opioid use were around 2.5 times greater among those with HIV than their counterparts, while rates of non-opioid analgesics use were around twice the maximum.[22] The data from 2015 to 2017 based on National Hospital Ambulatory Medical Care Survey showed that around 14.3% of emergency department visits received opioid analgesics, 23.4% received non-opioid and 8.8% both opioid and non-opioid analgesics.[23] Another randomized trial found that pain intensity was considerably better in the non-opioid groups and the adverse medication-related syndrome was more common in the opioid groups.[24] A systematic review indicated that pain scores did not significantly vary between patients who received opioid analgesics and those who received non-opioid drugs.[25] Another similar series depicted that, the most commonly prescribed clinical guideline-concordant non-opioid pain medications among individuals with a cancer diagnosis were antidepressants.[26]

This current study represented that based on postoperative day (POD), in the case of 1st POD, the majority of patients (53, 61.6%) felt moderate pain, and thirteen patients (13,15.1%) felt severe pain. In the case of the 2nd POD, most of the patients (56,65.1%) felt moderate pain, and only four (4,4.7%) felt severe pain. There was observed an advancement in the case of 3rd,4th and 5th POD. A similar study carried out in Berlin showed that after taking analgesics patients were declared to be ready for discharge.[27] Another observation found that multimodal analgesics mitigate the risk factors and could potentially prevent postoperative delirium in high-risk patients undergoing surgery.[28] In another study, the pain was relieved quickly after analgesics were administered to the patients and the 2nd outcome was the patients who received analgesics experienced less postoperative delirium.[29] A systematic review found that the threat of delirium appeared to be lower with hydromorphone or fentanyl, in contrast with other opioids.[30]

A doctor's clinical knowledge, attitudes and consciousness about analgesics will be help to the shape their prescribing practices and treatment. Effective knowledge requires to be dependent on the types of skills that clinicians would feel competent to prescribe analgesics. It is essential to allow them to recognize and address risk good, effective, engaging and balanced analgesics use for the management of pain.[31]

In our study, most of the patients were given combination drugs (opioid and non-opioid drugs) and early discharge was noticed in most of the patients. Only few were given either opioid or non-opioid drugs so, there was no significant relationship was found due to small sample size.

Conclusion

Pain is an unpleasant signal in the nervous system of the brain. The medical influence of pain is such that essential determination is being applied to enhance novel analgesic drugs directed towards new targets and to investigate the analgesic efficacy of known drugs. The diversity of distinct experimental pain models allows pain and analgesia in humans to be studied under controlled labs. In this current finding, clinical outcomes, claims and evaluations of the patients improved after suggesting both opioid and non-opioid analgesics.

Recommendations

The study population was selected from one selected hospital, so that the results of the study may not reflect the exact picture of the country. The present study was conducted at a very short period of time. Small sample size was a limitation of the present study. Therefore, in future further study may be under taken with large sample size. There is a necessity for setting a screening docket to cover all age groups for early detection of severity of pain. Furthermore, strategies should be implemented to accelerate government programs to understand different types of analgesics. To get robust data, multicenter studies are in great need of policymakers to interpret the demonstrable scenario and to take necessary steps towards mitigating this problem.

Conflict of interest: None declared

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Original Article

Histopathological and Clinical Differences between Right and Left Sided Colorectal Carcinoma (CRC) in a Group of Patients

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Abstract

Introduction: Colorectal cancer (CRC) is the third most common cancer and the second for mortality over the world. Some researchers suggest that cancers located in the right vs. the left side of the colon are different and they can be regarded as distinct disease entities. The aim of this study was to analyze differences in clinical, epidemiological and pathological features of patients with right-sided (RCC) and left-sided (LCC) colon cancer. **Materials and Methods:** A cross sectional observational study on a group of 50 patients of resected colon cancer was included from different hospitals of Dhaka and Kishoregonj. Parameters studied included age, sex, location of the tumour, histopathological subtype, grade, stage and lymphovascular (LVI) between LCC and RCC. **Results:** The age range was from 19 years to 84 years with mean age of 46.6 ± 14.8 years. Per rectal bleeding was the commonest symptom at the time of diagnosis. Male patients were presented more with left sided colon cancer. Left sided cancer tended to be more poorly differentiated and higher stage compared to right side colon cancer. Mucinous adenocarcinoma was seen in 6 (12%) cases. Rectum was the most common tumour subsite involved. **Conclusion:** Cancers of the right and left side of the colon vary according to clinical and pathological features. In our study, cancer of the left side of the colon (LCC) was more advanced stage and grade at diagnosis.

Keywords: Colorectal carcinoma (CRC), Stage, Grade, Right sided colon cancer, Left sided colon cancer.

Introduction

Colorectal cancer (CRC) is the third most common cancer in the world and the second leading cause of cancer related death.[1] The lifetime risk of developing CRC is about 6% or one in 18. Over 95% of these CRC is adenocarcinoma.[2] In 2040, the global cancer burden is anticipated to reach 28.4 million cases, and developing low-income countries are anticipated to register 64-95% of all these cases.[3] The incidence of colorectal cancer in Bangladesh is not exactly known, it appears to be common and occur in younger age group with slight male preponderance. Average age at diagnosis is 10 years less than the developed countries.[4] Researchers divides CRC into two groups based on the localization of the primary tumor into right-sided colon cancer (RCC) and left-sided colon cancer (LCC). Both of them have different embryological, genetic, and clinical characteristics leading to differences in prognosis and in the outcome. Anatomically, the right colon includes the caecum, ascending colon, liver flexure, and transverse colon and the left colon includes the splenic flexure, descending colon, sigmoid colon and rectum. The proximal colon arises from the midgut and receives its major blood supply through the superior mesenteric artery. The distal colon arises from the hindgut and is supplied by the inferior mesenteric artery.[5] Clinically, patients with RCC are older and more likely to be women. RCC clinically appears early with more advanced and poorly differentiated tumor grade and stages.[6] Studies have reported that outcome of colon cancer are different according to the location of the tumor. However, some studies have suggested no difference between RCC and LCC.[7] Two meta-analyses showed that survival is worse for patients with right-sided colon cancer.[8]

The aim of our study was to analyze differences in clinical, epidemiological and pathological features of patients with adenocarcinoma located in the right and left side of the colon and rectum.

Materials and Methods

It was a cross sectional observational study. A total of 50 cases of colorectal carcinoma surgically resected specimen were collected for study. 28 cases were collected from Bangabandhu Sheikh Mujib Medical University (BSMMU) during the period of 2009 to 2011 and 32 cases were from Jahurul Islam Medical College hospital from 2018 to 2022. The right sided colon cancer included all tumours located proximal to splenic flexure and those distal to it were part of left side colon cancer including rectosigmoid cancers. Variables included in study were: age, laterality, stage, histology type, histological grade and Lymphovascular Invasion (LVI). Clinical information was obtained by taking history and recorded in clinical proforma. Data was analyzed using Microsoft Excel and SPSS software.

Inclusion criteria

a. Confirmed cases of adenocarcinoma of the colon.
b. Cases with complete clinical information.
c. Availability of fresh unfixed colorectal cancer specimen.

Exclusion criteria

a. Clinically suspected colorectal carcinoma subsequently proved to be non-malignant lesions after histological examination.
b. Non Hodgkin lymphoma and other non epithelial tumors of the colon.
c. Cases without clinical data.

Results

The age range was from 19 to 84 years with mean age of 46.6 ± 14.8 years. The patients were divided into 8 groups on the basis of decades. Out of 50 cases maximum number 12 (24%) of patients belonged to the age group 50-59 years. 29 (58%) patients were male and 21 (42%) were female with male to female ratio of 1.4:1. Figure I show age distribution of colorectal cancer.

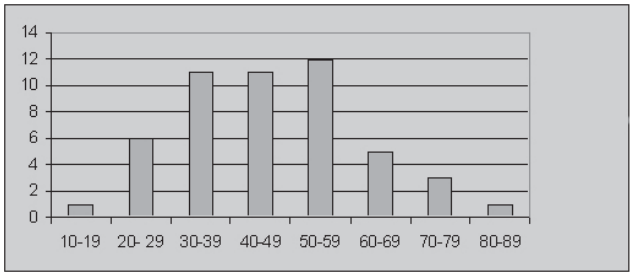

Figure I: Bar diagram showing age distribution of colorectal cancer.

At the time of first consultation, majority of the patients 20(40%) had per-rectal bleeding, 8(16%) had lower abdominal pain, 7(14%) had altered bowel habit, 6(12%) had generalized weakness, anorexia and pallor, 6(12%) had combined per rectal bleeding and abdominal pain and 3(6%) had palpable abdominal mass. Per rectal bleeding was commonest symptom in left sided colon and lower abdominal pain was in right sided colon cancer patient. Table I shows clinical presentation of colorectal cancer cases.

Table I: Clinical presentation with tumour location of colorectal cancer cases (n=50)

Symptoms	Cases N=50(%)	Site distribution	
		Right colon	Left colon
Per rectal bleeding	20 (40)	1	19
Lower abdominal pain	8 (16)	6	2
Altered bowel habit	7 (14)	4	3
Generalized weakness, anorexia and pallor	6(12)	4	2
Per rectal bleeding and abdominal pain	6(12)	4	2
Palpable abdominal mass	3(6)	2	1

Among the 50 cases, 33 (66%) case were in rectum, 6 (12%) were in the ascending colon, 3 (6%) in hepatic flexure of colon, 2 (4%) each in caecum, descending colon, sigmoid colon and in the transverse colon (Table II). Thirty seven (74%) patients were in the left colon (splenic flexure to rectum) and 13 (26%) patients were in the right colon (caecum to splenic flexure). In 29 male patients, 17 (34%) in rectum, 4 (8%) in ascending colon, 2 (4%) each in transverse colon, hepatic flexure of colon and caecum and one (2%)

each in sigmoid colon and descending colon. In 21 female cases, 16 (32%) cases were in rectum, 2 (4%) cases in ascending colon, one (2%) case each in sigmoid colon, descending colon and hepatic flexure of colon.

Table II: Site distribution of CRC from distal to proximal.

Variable	N=50	Male (%)	Female (%)
Rectum	33	17(34)	16(32)
Sigmoid colon	2	1(2)	1(2)
Descending colon	2	1(2)	1(2)
Transverse colon	2	2(4)	-
Hepatic flexure of colon	3	2(4)	1(2)
Ascending colon	6	4(8)	2(4)
Caecum	2	2(4)	-

of the 50 colorectal cancer cases, 39(78%) cases were moderately differentiated and 11(22%) cases were poorly differentiated. In this present study no well differentiated adenocarcinoma was observed. Male predominance was observed in both moderately differentiated and poorly differentiated cases. Among the 39 moderately differentiated cases, 22 cases were seen in male and 17 cases in female and of 11 poorly differentiated cases, 7 cases were seen in male and 4 in female. Of thirty nine moderately differentiated cases, 10(20%) cases originated in right colon and 29 (58%) cases in the left colon. Of 11 poorly differentiated carcinomas, 4(8%) cases were in the right colon and 7(14%) cases were in the left colon. Table III shows histological grade of colorectal cancer in 50 cases with location and sex distribution.

Table III: Histological grading of colorectal cancer cases with gender and location

Tumour differentiation	Number (%)	Male (%)	Female (%)	Right colon (%)	Left colon (%)
Moderately differentiated	39(78)	22(44)	17(34)	10(20)	29(58)
Poorly differentiated	11(22)	7(14)	4(8)	4(8)	7(14)

Staging of colonic cancer were done in all the cases. It was done on the basis of TNM system.[9] The maximum number of cases 22 (44%) were in stage III, 14 (28%) cases were in stage II, 13 (26%) cases in stage I and 1 (2%) case in stage IV. Out of 22 stage III cases, 11(22%) cases were male and 11(22%) cases were female. In 14(28%) cases of stage II, 9(18%) cases were male and 5(10%) cases were female. In stage I cases, 8(16%) cases were male and 5(10%) cases were female. Among the total 23 cases of combined stage III and IV cases right colon were 9 (39%) cases and left colorectum were 14 (61%) cases. Table IV shows TNM stage in 50 colorectal cancer cases with sex distribution and location.

Table IV: TNM (Tumour, Node, Metastasis) stage with gender and location (n=50)

TNM stage	No. of cases (%)	Male (%)	Female (%)	Right colon (%)	Left colon (%)
Stage I	13(26)	8(16)	5(10)	2(4)	11(22)
Stage II	14(28)	9(18)	5(10)	6(12)	8(16)
Stage III	22(44)	11(22)	11(22)	8(16)	14(28)
Stage IV	1(2)	1(2)	-	1(2)	-

Lymphovascular invasion (LVI) and perinureal invasion (PNI) and tumour border configurations were examined microscopically. LVI was seen in 18 cases and were absent in 32 cases. Among the 18 cases, 12 were cases were in left sided and 6 were in right sided colon cancer. Perinureal invasion is seen in 6 cases of left sided and 3 cases of right sided colon cancer patients.

Discussion

The mean age of the 50 cases was 47±14.8 years. The age range was from 19-84 years with male and female ratio of 1.4:1. 58% of the cases were below the age of 50 years. The mean age of colorectal cancer in this present study indicate that colorectal carcinoma is relatively common in lower age group in our country. Our population present mostly before 50 years of age, suggesting a possible hereditary etiology or earlier and persistent exposures to known risk factors like physical inactivity, improper diet and smoking. [10] Male predominance was seen in our study with more females with left sided cancer than right sided, consistent with the other international reports.[11] However, Keating *et al* found equal gender distribution in their study.[12]

Rectal bleeding was the commonest presentation (40% cases) at the time of first consultation followed by abdominal pain (16% cases). Per rectal bleeding was observed in 17(85%) cases of left colon cancer. Most of the cases with per rectal bleeding, tumour were present in rectum which explains partly that per rectal bleeding may be most common symptoms in rectal cancer.

Abdominal pain was the commonest symptom in a study done in Saudi Arabia.[13] In our study, 8(16%) cases had this feature possibly due to negligence on the part of the patient and frequent use of analgesics.

The sub site distribution of colorectal cancer in this study shows 37(74%) cases were in the left colon and 13(26%) cases in the right colon. In Among 37 cases of left colon cancer cases, 33 cases were in rectum. This shows higher percentage of rectal cancer in this study. Recent trend of shifting of CRC towards right colon observed by Gomez *et al* is not supported by this present study.[14] However, studies done by other researchers found left sided colon cancer more to the right sided colon cancer. This is shown in table V.

Table V: Distribution of RCC and LCC in other studies.

Investigator	Left colon cancer	Right colon cancer
Riddell et al(2003)[15]	75	25
Leon et al (2004)[16]	70	30
Ayyub et al (2002)[17]	70	30
Hossain (2007)[4]	63	37
Present study	74	26

On histological examination, 44(88%) of cases were adenocarcinoma NOS and 6(12%) cases were mucin secreting adenocarcinoma. 39(78%) cases were moderately differentiated and 11(22%) cases were poorly differentiated cancer. Of the thirty nine moderately differentiated cases, 10(26%) originated in right colon and 29 (74%) in the left colon. Of the 11 poorly differentiated carcinomas, 4 were in the right colon and 7 were in the left colon. In this study left colon cancer were less well differentiated than right side. Poorly differentiated cancers were more among the left sided cancer indicating bad prognosis of those patients. Keating et al found right sided tumour were less well differentiated than left sided tumour which is different from this study.[18]

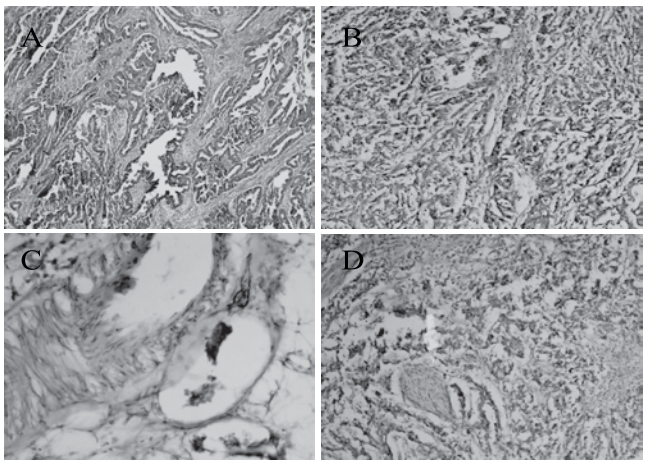

Figure: A, B, C, D

Figure: A: Moderately differentiated adenocarcinoma; B: Poorly differentiated adenocarcinoma; C: Lymphovascular invasion; D: Perinureal invasion. [A and B 40x, C and D 100x, H & E stain]

TNM Staging was done in all the cases. The maximum number of cases 22 (44%) were in stage III, 14 (28%) were in stage II and 13 (26%) in stage I and one (2%) in stage IV. This study show 44% cases diagnosed at stage III indicating advanced stage of the disease at diagnosis. Derwinger *et al* found 41% cases in stage III, which is consistent with our study.[19] Twenty three (46%) of the stage III and IV cases, 14 cases were in left colon and 9 cases were in right colon indicating more advanced disease in the left colon at the time of diagnosis. This fact probably can be explained by a delay in the diagnosis of cancer in the right side of the colon. Disease in the right colon can give more subtle symptoms than cancer located on the left side colon as per rectal bleeding is the commonest symptoms in left sided colon cancer. Another fact is diagnosis by doing procto-colonoscopy followed by biopsy is easier in the left colorectal region. Lymphovascular invasion was present in 16 (32%) cases and absent in 34 (68%) cases. Out of 16 positive cases 12(75%%) cases had stage III disease and 3(19%) cases had stage II and one (6%) case in stage IV disease, which indicates higher stage disease in lymphovascular invasion positive tumour.

Conclusion

Clinicopathological difference exists between right and left sided CRC cases. In our study most patients with left sided colon cancer were in higher grade and stage compared to right sided colon cancer. National programme for the early detection of CRC should be implemented to reduce mortality in our country.

Conflict of interest

The authors declare no conflict of interest.

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Original Article

Cardiovascular Autonomic Response during Cold Pressor Test in Post-Menopausal Women

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Abstract

Background: Variation in autonomic nervous system functions is seen in postmenopausal women. Autonomic nervous system control is a major determinant in various cardiovascular diseases. In premenopausal and postmenopausal women the risk of cardiovascular diseases gradually increases and alteration in autonomic nervous functions. **Objectives:** To assess the cardiovascular response to cold pressor test in postmenopausal women. **Materials and Methods:** This cross sectional analytical study was conducted from July 2019 to June 2020 in the Department of Physiology, Rangpur Medical College, Rangpur. After obtaining permission, a total 120 subjects who meet the inclusion and exclusion criteria were enrolled in the study after briefing them objectives of the study. Among them 40 were reproductive women (Group-A), 40 were premenopausal women (Group-B) and 40 were postmenopausal women (Group-C). The blood pressure responses could be used as a tool for cold pressor test which is indicator of sympathetic activation and thus of cardiac status. The subjects were selected from different areas of Rangpur district. For statistical analysis one-way ANOVA (post-Hoc) test was performed by computer based software SPSS-23.0 version for windows. **Results:** Resting systolic blood pressure and resting diastolic pressure were significantly higher in group C ($p<0.001$). Systolic blood pressure in response to cold pressor test was significantly higher in group C ($p< 0.001$). Diastolic blood pressure in response to cold pressor test was significantly higher in group C ($p< 0.001$). **Conclusion:** The study concluded that the changes in systolic and diastolic blood pressure after cold pressor test increased in Postmenopausal women and thus indicating increased sympathetic activity.

Key words: Postmenopausal women, Cold pressor test, Sympathetic Nervous System.

Introduction

The normal reproductive years of the female are characterized by monthly rhythmical changes in the rates of secretion of the female hormones and corresponding physical changes in the ovaries and other sexual organs. The age of reproductive period is about 13 to 46 years[1]. Menopause is defined as the permanent cessation of menses for 1 year and physiologically correlated with the decline in estrogen secretion resulting from the loss of follicular function.[2] It is a normal aging phenomenon, involves gradual transition of woman from reproductive to non-reproductive phase of life.[3] The menopause usually occurs between the ages of 45 and 52 years.[2] Joshi PK et al studied upon 60 premenopausal women of age 25 to 45 years and 60 postmenopausal women of age 46 to 60 years. They demonstrated systolic and diastolic pressure change in cold pressor test in postmenopausal women was significantly higher compared to premenopausal women.[4] Postmenopausal women have higher risk of cardiovascular disease, anxiety and depression. Hence health management is important for postmenopausal women.[5] Hormonal changes are associated with menopause.[6] Changes in the hormone levels is responsible for autonomic system variations seen in pre- and post-menopausal women.[7] According to the survey conducted by the Korean Society of Menopause, of 707 women who underwent natural menopause, 89% answered that experienced

menopausal symptoms or have symptoms currently.[8] The effect of menopause on cardiovascular disease (CVD) in women has been studied by kannel et al. It has been found that autonomic dysfunction is an important factor for the evaluation of risk of cardiovascular events in CVD patients.[9] Data from the Framingham study shows a two-fold age-adjusted increase in risk for coronary heart diseases in post-menopausal compared with pre-menopausal women.[10] The high incidence of ischemic heart disease after menopause suggested a close association between ovarian hormone levels and cardiovascular system.[11] In women, both pre and postmenopausal hormonal changes contribute to modifications of the autonomic control of the heart.[12] Vongpatanasin W. has studied the increase of sympathetic tone and blood pressure in menopause. Lee et al. have found a relationship between postmenopausal symptoms and changes in cardiovascular autonomic functions in women. For example, hot flashes and sleep disorders are strongly associated with increased sympathetic tone.[9]

Materials and Methods

A Cross-sectional analytical study was conducted in the Department of Physiology, Rangpur Medical College Hospital, Rangpur, Bangladesh from june 2019 to July 2020. A total number of 120 apperently healthy women ware available within the study period. Among them 40 reproductive women, 40 premenopausal and 40 postmenopausal women. All the study individuals were apparently healthy women and their age ranged from 20 to 55 years. Samples of Reproductive, premenopausal and postmenopausal women were collected from housewives at different areas in Rangpur city matched with age and socioeconomic condition.

Inclusion criteria

a) Age group of 20 to 55 years.
b) Healthy women individual of- Reproductive women (20-35 years), Premenopausal women (40-45 years) and Postmenopausal women (45-55 years).

Exclusion criteria

a) History of diabetes mellitus, hypertension, chronic renal failure, cardiac complication, obstructive lung diseases, liver diseases.
b) Tobacco users.
c) Psychiatric disorders (depression)
d) Any Neurological disorder
e) Previous history of head injury.
f) History of taking neurotoxic drug, Tranquilizers (barbiturates), Antidepressants (tricyclic antidepresant).
g) After exercise, meal and trained athletes.
e) Overweight and obese women.
h) Pregnancy and lactating mother.

Reproductive women, premenopausal and postmenopausal women in different areas of Rangpur city, who fulfill the inclusion criteria, were included by numbering. After selection of all subjects, the objectives and the procedure of the study were explained clearly to them and their informed written consent were taken. Detailed medical and family history were taken and thorough clinical examinations were done. All information were recorded in a preformed questionnaire. Each of those workers were briefly explained about the procedure in detailed encouraged to obtain maximum efficient performance. From the previous night up to the examination, they should not undergo any physical or mental stress and not to take any sedatives or any drugs affecting central nervous system. Then the autonomic nerve function assessed by Cold Pressor Test using sphygmomanometer. Blood glucose, serum creatinine level and serum alanine amino transferase were measured to exclude diabetes mellitus, chronic renal failure and liver diseases respectively. Autonomic nerve function test was conducted in a comfortable environment in the department of physiology laboratory from 9.00 am to 2.30pm.

Statistical Analysis Method: All data were recorded systematically in a preformed history sheet and all statistical analysis was done by computer using the software SPSS-23.0 version for windows. Comparison of reproductive, premenopausal and postmenopausal women were done by one-way ANOVA (post–Hoc) tests. In the interpretation of results, < 0.05 level of probability (p) were accepted as significance.

Results

Table-I: Mean ± SD of age, height, and weight and body mass index of the study subjects of different groups.

Parameters	Mean ± SD			P-value
	Group A (n= 40)	Group B (n= 40)	Group C (n= 40)	
Age- Year	27.600±3.934	42.175±1.662	51.425±2.600	0.001***
Height-m²	1.564±0.021	1.546±0.024	1.524±0.069	0.146^{NS}
Weight-kg	56.550±3.993	58.450±2.960	57.450±4.320	0.453^{NS}
BMI-kg/m2	23.657±1.805	24.460±1.406	24.330±1.567	0.920^{NS}

Table-I showing Mean ± SD of age were 27.600±3.934, 42.175±1.662, 51.425±2.600 years in group A, B and C respectively. Mean ± SD of height were 1.564±0.021, 1.546±0.024, 1.524±0.069 m in group A, B and C respectively. Mean ± SD of weight were 56.550±3.993, 58.450±2.960, 57.450±4.320 kg in group A, B and C respectively. Mean ± SD of body mass index were 23.657±1.805, 24.460±1.406, 24.330±1.567 kg/m 2 in group A, B and C respectively. Mean age had significant differences ($p<0.001$) but height, weight, and BMI almost similar and statistically no significant differences ($p>0.05$) in different groups

Table-II: Mean ± SD resting systolic blood pressure and diastolic blood pressure of study subjects in group A, B and C.

Variable	Mean ± SD			P-value
	Group A (n=40)	Group B (n= 40)	Group C (n= 40)	
Resting systolic blood pressure (mm of Hg)	120.875±7.602	122.7500±3.387	130.000±3.922	0.000***
Resting diastolic blood pressure (mm of Hg)	76.500±9.837	80.000±2.773	^{8}4.275±7.404	0.004**

Table-II Showing mean ± SD of resting systolic blood pressure were 120.875±7.602, 122.7500±3.387, 130.000±3.922 mm of Hg in group A, B and C respectively. The mean ± SD of resting diastolic blood pressure were 76.500±9.837, 80.000±2.773, 84.275±7. 404 mm of Hg in group A, B and C respectively. In this study mean resting blood pressure were compared between group A and B, group A and C, group B and C. The mean systolic blood pressures were significantly ($p < 0.001$) higher in group C than A and also significantly ($p < 0.001$) higher in group C than B. Again the mean value non significantly ($p>0.05$) higher in group B than A. The mean diastolic blood pressures were significantly ($p<0.001$) higher in group C than A and also significantly ($p<0.01$) higher in group C than B. Again the mean value non significantly ($p>0.05$) higher in group B than A (Table-II).

Table-III: Mean ± SD systolic blood pressure and diastolic blood pressure of study subjects in group A, B and C after cold pressor test.

Variable	Mean ± SD			P-value
	Group A (n= 40)	Group B (n= 40)	Group C (n= 40)	
Systolic blood pressure (mm of Hg)	14.175±1.692 (12-13)	14.575±0.747 (14-18)	15.975±2.081 (18-19)	0.000***
Diastolic blood pressure (mm of Hg)	12.225±1.073 (11-12)	12.325±0.474 (12-13)	13.175±1.217 (11-16)	0.000***

Table-III Showing mean ± SD of systolic blood pressure of cold pressor test were 14.175±1.692, 14.575±0.747, 15.975±2.081 in group A, B and C. In this study mean values of cold pressor test were compared between group A and B, group A and C, group B and C. In systolic blood pressure changes, the mean values were significantly ($p< 0.001$) higher in group C than group A. also significantly ($p<0.01$) higher in group C than B. Again the mean value non significantly ($p > 0.05$) higher in group B than A. The mean ± SD of diastolic blood pressure of cold pressor test were 12.225±1.073, 12.325±0.474, 13.175±1.217 in group A, B and C respectively. In this study mean values of cold pressor test compared between group A and B, group A and C, group B and C. In diastolic blood pressure changes, the mean values were significantly ($p< 0.001$) higher in group C than group A. also significantly ($p<0.01$) higher in group C than B. Again the mean value non significantly ($p > 0.05$) higher in group B than A (Table-III).

Discussion

The present study was carried out to observe the changes in cardiovascular autonomic functions in apparently healthy premenopausal and postmenopausal women. Height, weight and BMI were calculated to exclude the overweight and obesity and cardiovascular reflexes test was performed to evaluate the changes in autonomic functions. cold pressor test was studied in reproductive, premenopausal and postmenopausal women for comparison. Moreover, scoring of autonomic nerve dysfunction was assessed in order to detect its degree of involvement. In the present study, the findings of the parameter in apparently healthy control group were within normal ranges and also similar to those reported by the various investigators from different countries. Random blood sugar, serum creatinine, SGPT & PEFR levels were estimated in subjects of all groups of the present study for exclusion of diabetes mellitus, kidney diseases, liver diseases & pulmonary diseases as these diseases are well known to affect cardiac autonomic nerve function parameters. In this study, both the values were within the normal range in all the study subjects. Therefore, all the subjects were non diabetic, they did not suffer from chronic renal failure, chronic liver diseases or pulmonary diseases. In this study, resting blood pressure was measured in all healthy reproductive, premenopausal and postmenopausal women to find out their basal status. In premenopausal women mean values of systolic and diastolic blood pressures were non-significantly ($p>0.05$), higher. These findings are in agreement with those reported by Shivwani et al[13]. In postmenopausal women mean values of systolic blood pressures and diastolic blood pressures were significantly ($p<0.001$) higher. These findings are in agreement with those reported by Nahar L A D et al[14] and Shivwani et al[13]. In this study, cold pressor test was measured in all healthy reproductive, premenopausal and postmenopausal women to find out their sympathetic nerve function status. In premenopausal women non-significantly ($p>0.05$) higher systolic and diastolic blood pressure was found in cold pressor tests when compared to reproductive women. These findings are in agreement with those reported by Joshi PK et al[4] and Srivastava RD et al[15] In postmenopausal women significantly ($p<0.001$) higher systolic and diastolic blood pressure was found in cold pressor tests, when compared to reproductive and premenopausal women. These findings are in

agreement with those reported by Joshi PK et al[4] and Srivastava RD et al[15]

Conclusion

In this study, impairment in autonomic nerve function was observed in postmenopausal women. Increased sympathetic nerve function was observed by increased resting blood pressure, increased diastolic pressure response to increase blood pressure response to cold stimulus.

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Original Article

Comparison of Therapeutic Response of Keloid to Intralesional Injection of Triamcinolone Acetonide and Bleomycin

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Abstract

Background: Keloids are an aberration of normal healing process. Majority of the cases are symptomatic and indolent to treat. Though there is no ideal monotherapy, intralesional injection of triamcinolone acetonide is one of the first line treatment. Triamcinolone has a variable sensitivity, chance of complication and recurrence. As an emerging novel treatment, intralesional application of bleomycin shown promise in several studies. **Materials and Methods:** Single blind comparative study done at Sheikh Hasina National Institute of Burn and Plastic Surgery, Dhaka, Bangladesh from February, 2019 to August, 2020. Purposive sampling of 50 adult patients with keloid were enrolled, later by lottery with sealed envelope were done, to allocate into two groups A and B. They were given intralesional injection of triamcinolone acetonide and bleomycin every four weeks respectively. Both groups were assessed before and followed up every two months for a total of six months after completion of three dose of intralesional infiltration. Outcomes were compared against each other as per Vancouver scar scale score, numeric rating scale score for pain and itching. **Results**: Majority of the subjects (23) belonged to 18-24 years age group. In group A (triamcinolone acetonide), mean Vancouver scar scale score remission rate was 34.46% and In group B (bleomycin), it was 49.6% over 6 months follow up. Remission rate of pain in group B was 92%, while in group A it was 42%. Remission rate of itching in group B was 77.7% and in group A it was 34.2%. **Conclusion:** Intralesional injection of bleomycin is better for the treatment of keloid than triamcinolone acetonide.

Keywords: Keloid, Intralesional, Bleomycin, Triamcinolone acetonide.

Introduction

Keloid is a benign fibro-proliferative disorder which results from an up-regulation of collagen synthesis, deposition and accumulation. It is a cicatricle lesion that extends beyond the limits of the trauma, with invasion of adjacent healthy tissue. There is significant impairment of quality of life for patients, with physical, motor, aesthetic and psychosocial sequel. There are multiple treatment methods for keloids. Despite several reported strategies, no standard treatment protocol exists.Intralesional injection of corticosteroid triamcinolone acetonide (TAC) is one of the first line treatment modalities for keloid treatment.[1] It could promote vasoconstriction in the keloid scar and control local inflammation by reducing expression of TGF ß receptors.[2] Though triamcinolone acetonide (TAC) has been the first line agent for treatment, its response rates vary with higher recurrence rates.[3,4] Despite good tolerance, a significant fraction of keloids are steroid resistant. Recent studies shown hope in treatment of steroid resistant as well as steroid sensitive cases with intralesional injection of bleomycin.

Materials and Methods

A single blind comparative study carried out at Sheikh Hasina National Institute of Burn and Plastic Surgery, Dhaka, Bangladesh from February, 2019 to August, 2020. Due to time constraints and unavailability of the patients

due to COVID19 pandemic total 50 samples with keloid were selected aged between 18-50 years were enrolled by purposive sampling, later by lottery with sealed envelope were done to allocate into two groups A and B. They were given total 3 doses of intra-lesional injection of triamcinolone acetonide and bleomycin every four weeks apart respectively. Both groups were assessed before and followed up every two months for a total of six months after completion of three dose of intralesional infiltration. Outcomes were compared against each other as per Vancouver scar scale score (VCSSS),[5] (Annexure-01) Numeric rating scale score (NRSS) for pain[6] and itching[7]. Post infiltration complications were also compared. Both group A and B included 25 subjects. Prior to the infiltration, detailed history regarding natural history of the keloid, co-morbidities and possible contraindications were recorded, photograph taken and VCSSS for keloid scar evaluation, NRSS for pain and itching were recorded in semi structured questionnaire form. All infiltration procedures were done by the investigator with standard asepsis under protection of personal protection gear at operative complex. Insulin syringe 100 IU was used for infiltration. Both groups were infiltrated with local anesthetic (2% lidocane) at lesion site before injecting with study drugs.

In group A, Triamcinolone acetonide was diluted with 0.9% saline solution and given at 20mg/ml concentration into the papillary dermis until skin blanching is produced. Maximum dosage in a single setting was not more than 120mg to avoid systemic side effects.

Patients of Group B were given intradermal injection of bleomycin by the investigator in a dose of 0.5-1 ml/cm^2 with maximum dose of 6mg (6IU) per session at 1.5mg/ml concentration. Each 15mg (15IU) lyophilized powder of bleomycin sulfate vial dilution was carried out by mixing the powder with 10 cc 0.9% saline solution. Infiltration of both group stopped after total 3 doses or when Vancouver scar scale become 0 or in case of any major complication.

Clinical assessment was carried out using Vancouver scar scale score that includes vascularity, pigmentation, pliability and height. Height was measured by using a slide calipers. The results were recorded from 0 to 14 where 0 reflected normal skin. Pain and itching were assessed as per NRSS. Complications following infiltration were also recorded.

Findings of observation and interview with the patient and attendants were recorded in preformed data collection sheet using a pre-designed structured questionnaire and were filled up by the investigator. Data from both groups were collected before first session of infiltration. Following intervention follow up was done by the investigator and data were recorded accordingly. Besides the local examination findings, the records also included pre-infiltration and post-infiltration photograph of the involved part.

In group A, TAC was given at a concentration of 20mg/ml. Maximum dosage of TAC in a single setting was not more than 30mg (1.5 ml). Dilution of bleomycin was carried out by mixing the 15 mg of powder with 10 cc 0.9% saline solution. It was given at a concentration of 1.5 IU/ml without exceeding the maximum dose of 6 IU. In this study, both groups were infiltrated with local anesthetics prior to infiltration. A total of 3 doses were given at 4weekly interval but infiltration of both groups were stopped when Vancouver scar scale become 0 or in case of any major complication.

Annexure-01: Outcome measurement by The Vancouver Scar Scale.

Sl. No	Criteria	Clinical findings	Score
1	Vascularity	Normal	0
		Pink	1
		Red	2
		Purple	3
2	Pigmentation	Normal	0
		Hypo-pigmentation	1
		Hyper-pigmentation	2
3	Pliability	Normal	0
		Supple	1
		Yielding	2
		Firm	3
		Ropes	4
		Contracture	5
4	Height	Flat	0
		<2mm	1
		2-5mm	2
		>5mm	3
	Total score		13

Results

Majority of the subjects 23(46%) belonged to 18-24 years age group. (Table –I)

Table I: Distribution of the respondents by age group (n=50)

Age Group (years)	Frequency (n)	Percentage (%)
18–24	23	46.0
25-34	17	34.0
35-44	7	14.0
45-50	3	6.0
Mean age	28±8	
Range	18-50	

Table II: Distribution of the respondents by family history (n=50)

Family History	Frequency (n)	Percentage (%)
Negative	44	88
Positive	6	12
Total	50	100.0

6(12%) cases had a positive family history. (Table-II)

Table -III: Distribution of the respondents by site of keloid (n=50)

Site	Frequency		Percentage (%)
	Group A	Group B	
Neck	2	1	6
Ear lobule	3	0	6
Shoulder	2	4	12
Pre-sternal area	2	4	12
Anterior trunk	2	3	10
Back	1	4	10
Upper limb	8	4	24
Lower limb	5	5	20
Total	25	25	100.0

Maximum 12(24%) of the respondents had keloid over upper limb followed by 10(20%) over lower limb and 6(12%) over shoulders. (Table-III)

Table IV: Distribution of the respondents by previous treatment modality (n=50)

Previous history of treatment	Frequency		Total Percentage (%)
	Group A n (%)	Group B n (%)	
Steroid	10(40)	8(32)	36
Surgery	2(8)	5(20)	14
Other	1(4)	3(12)	8
None	12(48)	9(36)	42
Total	25(100)	25(100%)	100

Majority of the respondents 42% had no treatment for keloid and 36% patient took intralesional triamcinone (Table-IV)

Table V: Distribution of the respondents by duration of keloid (n=50)

Duration of keloid (months)	Frequency		Percentage (%)
	Group A	Group B	
6	6	5	22
7	4	5	18
8	2	1	6
9	3	1	8
11	0	1	2
12	4	4	16
13	0	1	2
14	3	0	6
16	0	1	2
18	0	2	4
20	0	1	2
24	1	2	6
36	0	1	2
180	1	0	2
480	1	0	2
Total	25	25	100

Majority of the respondents had keloid for 6 months . (Table-V)

Table VI: Comparison of pre-intervention numeric rating scale score (NRSS) for pain mean and follow up scores between group A & group B (n=50)

Visits	Group A NRSS for pain mean ± SD	Group B NRSS for pain mean ± SD	Total NRSS for pain mean ± SD
Pre-intervention	4.16±2.76	3.92±2.8	4.04±2.75
1st Follow up	3.6±2.3	2.76±2.12	3.2±2.22
2nd Follow up	3±2.18	1.32±1.28	2.16±1.9
3rd Follow up	2.4±2.08	0.6±0.91	1.5±1.8

Table VII: Mean remission of NRSS for pain from pre-intervention state to 3rd follow up between group A & group B

Groups	Mean pre-intervention NRSS for pain	Mean 3rd F/U NR SS for pain	Mean remission	Remission rates (%)	P value
Group A	4.16	2.4	1.76	42.3	.000
Group B	3.92	0.6	3.32	92.3	

Remission rate of itching in group B from pre-intervention state to 3rd follow up was 92.3%, while in group A it was 42.3% (p=.000). Table-VII

Table VIII: Mean remission rate of NRSS for itching from pre-intervention state to 3rd follow up between group A & group B

Visits	Group A NRSS for itching mean ± SD	Group B NRSS for itching mean ± SD	Total NRSS for itching mean ± SD
Pre-intervention	4.68±2.2	5.04±2.4	4.86±2.3
1st Follow up	4.28±2.2	3.72±1.8	3.1±2.1
2nd Follow up	3.64±2.2	2.56±1.3	3.1±1.4
3rd Follow up	3.08±2.1	1.12±1.1	2.1±1.9

Table IX: Mean remission rate of NRSS for itching from pre-intervention state to 3rd followup between group A & group B

Groups	Mean pre-intervention NRSS for itching	Mean 3rd F/U NRSS for itching	Mean remission	Remission rates (%)	P value
Group A	4.68	3.08	1.6	34.18	.000
Group B	5.04	1.12	3.92	77.77	

Table-VIII and IX In group A (triamcinolone acetonide), mean Vancouver scar scale score was found initially 9.4±2.29, after final follow up it became 6.16±2.6 with remission rate of 34.46%. In group B (bleomycin), initial mean score was 10.3±1.91, after final follow up it became 5.2±2 with a remission rate of 49.6% (p=.002).

Table X: Comparison of mean pre-intervention VCSSS and 3rd follow up VCSSS between group A & group B

Groups	Pre-intervention VCSSS mean ± SD	3rd Follow up VCSSS mean ± SD	Mean reduction rate of mean VCSSS at 3rd follow up	Remission rate(%) as per mean VCSSS at 3rd follow up	P value
A (n=25)	9.4±3.39	6.16±2.26	3.24	34.4%	.002
B (n=25)	10.32±1.91	5.2±1.94	5.12	49.6%	
Total (n=50)	9.86±2.1	5.76±2.2	4.12	41.78%	

Remission rate of itching in group B from pre-intervention state to 3rd follow up was 49.6%, while in group A it was 34.4% (p=.000). (Table-X)

Figures

A. Pre-Intervention picture Group-B B. 1st follow up picture Group-B C. 3rd follow up picture Group-B

Fig 1: (A- C) Pre-intervention and follow up pictures of a group B respondent.

A. Pre-Intervention picture Group-A B. 1st Follow up picture Group-A C. 3rd Follow up showing remission Group-A

Fig 2 :(A-C) Pre-intervention and follow up pictures of a group A respondent.

Table XI: Distribution of Complications after infiltration (n=50)

Complication	Frequency (n=50)	
	Group A	Group B
Skin ulceration	0	3
Hypo-pigmentation	6	0
Hyper-pigmentation	0	5
Skin atrophy	2	1
Telangiectasia	2	0
Total(Percentage)	40%	36%

High rate of complications were observed in this study (Group A 40% & Group B 36%).(Table-XI)

A. Before infiltration of bleomycin B. One week after first infiltration of bleomycin

Fig 3 :(A-B) Pre-intervention and follow up pictures of a group B respondent showing skin ulceration

Discussion

In this study, the mean age of the study cases was 28±8 years. Minimum age of the patients was 18 and maximum age of the patients was 50 years. Among the study cases maximum 23 (46%) patients were in 15-24 years age group. In a similar study found (Dash et al. 2010)[8] The highest percentage of the patients was in the age group 20-24 years (27.6%). Group A had 10 (40%) male and 15(60%) female subjects. Group B had 10 (40%) female and 15(60%) male subjects. This is a reflection of scar awareness among male patient also.The most common etiology of keloid in this study was burn 22 (44%) followed by trauma 19 (38%) and infection 9(18%). In a similar study by Hietanen [9] three most common etiologies were surgery (46%), acne scars (25%), and traumatic wounds 9.8% . Majority of the subjects had keloid over upper limb 12(24%). Lower limbs 10(20%), Back 6(12%) & shoulder 5(10) are other common site for keloid.

According to Kabel et al[10], The most common affected sites were mainly chest, shoulder, back, forearm and neck.The mean duration of keloid in this study was 23.82±70.29. Group A had a mean of 35.24±98.18. Group B had a mean of 12.4±7.48. Maximum duration of keloid was 480 months and minimum duration was 6 months. In Reddy et al[11] the duration of keloid ranged from 3 to 14 (mean 6.6) years.There is no

previous keloid treatment history among 42% (21) subjects. Other 58% (29) had treatment. From group A, 10 (20%) took steroid injection, 2(4%) had surgery. From group B, 8 (16%) took steroid injection, 5(10%) had surgery. In a study by Dash et al[8] found 31% subjects took steroid, 36% surgery, 7% both and 26% took no previous treatment. The mean of pre intervention numeric rating scale for pain score was(n=50) 4.04±2.72, Maximum pain score was 8 and minimum were 0, Mean for group A was 4.16±2.76 , Mean for group B was 3.92±2.8.After final follow up, mean pain score was (n=50) 1.5±1.8. Maximum pain score was 7 and minimum were 0, Mean for group A (n=25) was 2.4±2.08, Mean for group B (n=25) was 0.6± 0.9. A study with bleomycin by Saray and Güleç[12] showed Complete resolution of pain in (67 %) cases.

On the other hand, The mean of pre intervention itching score was (n=50) 4.86±2.3, Maximum NRSS for itching was 8 and minimum were 0, Mean for group A was 4.68±2.2, Mean for group B was 5.04±2.4. After final follow up, Maximum itching score was 7 and minimum were 0, Mean for group A (n=25) was 3.08±2.1, Mean for group B (n=25) was 1.12±1.1.In a similar study found the complete resolution of itching in (80 %) cases.[12] In group A, VCSS score mean was found in pre-intervention 9.86±2.1, after final follow up it became 5.76±2.2 with remission rate of 41.78% . In group B mean score was 10.3±1.91, after final follow up it became 5.2±1.94 with a remission rate of 51.45%. Espana et al[13] found 54% complete flattening with a similar study with bleomycin. In group A, 6 cases (24%) of Hypopigmentation were found, and 2 cases (8%) of simultaneous Skin atrophy & telangiectasia (n=25). which is similar to a study.[14] In Group B, there were 5 cases (20%) of Hyperpigmentation, 3 cases (12%) of skin ulceration.

In similar studies, most common complication noted was minor ulceration which healed within 10 days and hyperpigmentation that resolved after 1 year of follow up.[12]

Conclusion

Following post-infiltration observation of the patients, it can be concluded that overall outcome, aesthetic outcome and rate of complications were different on both group. Bleomycin showed statistically better response in terms of Vancouver scar scale score, numeric rating scale score for pain & itching which proved to be effective intralesional agent than TAC but it has some reversible complication like skin ulceration and hyper-pigmentation where TAC had more hypopigmentation, irreversible skin atrophy and telangiectasia. So it is reasonable to say that bleomycin is a better alternative than TAC in treatment of keloid.

Limitation of the study

- The sample size was not large to infer the findings in general population.
- All data were collected from a single tertiary care center.
- Long term follow up was beyond scope of this study.

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Case Report

Bombay Phenotype- A Rare Blood Group Detected First Time in TMSS Medical College Hospital, Bogura: A Case Report

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Abstract

Bombay phenotype (Symbol Oh), popularly well-known as Bombay blood group was first discovered by Y M Bhende et al in 1952 at Bombay (now known as Mumbai). It is a rare phenotype which shows absence of A, B, H antigens on red cell membrane and presence of anti-A, anti-B and anti-H antibodies in serum. H antigen on RBCs is the precursor structure on which *ABO* genes act to produce A and B antigens. As H antigen is absent, no A and B antigens are produced. Bombay phenotype (Oh) lacks normal expression of the A, B and H antigens because of the inheritance of the hh genotype. Their blood is incompatible with any other blood groups, except blood of another Bombay if they need blood transfusion. Prevalence of Oh is 1 per 10,000 in India and 1 per 1,000,000 in Europe. In Bangladesh, it is 1 per 0.006%. We found a first case of Bombay phenotype at TMSS Medical College, Bogura, which was confirmed by testing of blood and saliva using anti-H lectin.

Key words: A Rare Blood Group, Antigen, Bombay phenotype.

Introduction

Bombay phenotype (Symbol Oh), popularly well-known as Bombay blood group was first discovered by Y M Bhende et al in 1952 at Bombay (now known as Mumbai), India. This is the reason why this type of blood got the name Bombay phenotype. It is a rare phenotype which shows absence of A, B, H antigens on red cell membrane and presence of anti-A, anti-B and anti-H antibodies in serum.[1] The molecular basis of this blood group has been proven to be mutations of the FUT1 gene (H gene) which results in the formation of complete H-deficient phenotype (genotype hh).[1, 2]

After the cloning and characterization of the FUT1 gene in 1990 and proving that the gene was the molecular basis of the Bombay phenotype in 1994, the H blood group system was established. The H blood group system, ISBT symbol H (018), consists of a single antigen (H) defined by a terminal fucose residue found on red blood cells and in secretions.[3]

The H gene must be inherited to form ABO antigens on the RBCs. Inheritance of the H gene (genotype HH or Hh) results in the formation of the H antigen. The H antigen on RBCs is the precursor structure on which ABO genes act to produce A and B antigens. If H antigen is absent, no A and B antigens are produced. The term Bombay has been used to refer to the phenotype that lacks normal expression of the A, B and H antigens because of the inheritance of the hh genotype.[4]

Bombay phenotypes are commonly mistaken as O group. As like O group, it has no A and B antigen but differs from O group by lacking H antigen on RBC. In RBC testing using anti-A and anti-B, the Bombay would phenotype as O blood group but do not react with the anti-H lectin (Ulex europaeus), whereas normal O group individual react strongly with anti-H lectin. The Bombay anti-H can often be potent and reacts strongly at 37°C. It is an IgM antibody that can bind complement and cause RBC lysis. Transfusing normal group O blood (with the highest concentration of H antigen) to a Bombay recipient (anti-H in the serum) would cause immediate severe hemolytic transfusion reaction, which can be fatal and even lead

to death. Therefore, only blood from another Bombay individual will be compatible and can be transfused to a Bombay recipient.[4, 5]

This People who lack the H antigen do not suffer from deleterious effects and H-deficient is only an issue if they need a blood transfusion, because they would need blood without the H antigen present on red blood cells i.e. from another Bombay phenotype.[5] Bombay individuals can donate red cell concentrate (RCC) to any ABO group if Rh is compatible. They can receive fresh frozen plasma (FFP) and cryoprecipitate from any group but can receive red cells only from other Bombay individuals.[6]

About 99.9% of all individuals have an HH or Hh genotype in the world.[2, 4, 6] So the incidence of Bombay phenotype is 0.1%. This very rare phenotype is generally present in about 0.0004% (about 4 per million) of the human population, though in some places such as Mumbai locals can have occurrences in as much as 0.01% (1 in 10,000) of inhabitants.[5, 6] In Bangladesh, the first documented Bombay phenotype was found in the Miah family in 1990 at Narayanganj.[7] Now sporadic cases are identified in different laboratories where the facilities are available to confirm Bombay phenotype.

Case Report

A healthy male of 30 years came to our Transfusion Medicine Department for blood grouping as a routine health checkup including other laboratory tests as a prerequisite of joining a job. Although he told that his blood group is O positive and he justified his saying showing a blood report done from another tertiary care hospital.

Firstly, we noticed the anomaly in routine testing using forward grouping (cell grouping) and reverse grouping (serum grouping) and suspect the case as Bombay (Oh) phenotype. We confirmed this sample as Bombay phenotype by testing with anti-H lectin. Finally, we tested patient's saliva (hemagglutination inhibition test) and found that he is a non-secretor i.e., his body secretion does not contain ABO antigens which also confirmed the diagnosis of Bombay phenotype. Other pathological reports were all within normal limit.

Discussion

In our country, most of the private blood centers perform blood grouping using one slide method (Only cell grouping), but where transfusion specialists are present, whether in private or govt. blood transfusion centers, mostly double slide methods i.e., both cell grouping and serum grouping are used, although tube method is the best. If one slide method is used, incorrect grouping may occur, thus missing Bombay blood group. For confirmation of ABO grouping, we should do both cell grouping using anti-A, anti-B and anti AB against patient's cells and also serum grouping using A cell, B cell and O cells against patient's serum. During blood grouping, positive reaction with O cell in reverse grouping gives a clue to Bombay phenotype. Normally O cell has no A or B antigens but has potent H antigens which will react with anti-H of Bombay blood group.

Literature review revealed Bombay phenotype is more prevalent in closed communities with a higher rate of consanguineous marriage. It is very likely that other family members could carry the same phenotype. A study found the frequencies of Bombay phenotype 1 per 8,000 in Taiwan, 1 per 10,000 in India, and 1 per million in Europe.[2] A study in India revealed that out of 179 cases, incidence of Bombay phenotype in Maharashtra is the highest i.e., 62.6% followed by 7.8% in Karnataka, 4.5% in Andhraprodesh, 4.5% in Goa and then followed in other states.[6] Another report in India showed that in the states of Andhra Pradesh, Tamil Nadu, and Karnataka, prevalence of the Bombay phenotype is 0.048%, 0.004%, and 0.005%, respectively.[8]

No specific statistics of people with Bombay blood group in Bangladesh is available. A recent study in Bangladesh revealed that prevalence of Bombay Phenotype is 0.006%.[9]

In our case, father of the man belongs to blood group B group and mother belongs to O group. His blood group and also his only sister's blood group are supposed to be B or O but he is a Bombay and his sister is group O. We assumed that both of his father and mother are heterozygous for H gene i.e., their

genotypes Hh and they inherit hh to their son as he is Bombay and Hh or HH to their daughter as she is of group O. There was no consanguine history of marriage of his family. No other near relative was found to be of Bombay phenotype.

General Characteristics of Bombay Blood Group: a) Absence of H, A, and B antigens; no agglutination with anti-A, anti-B, or anti-H lectin, b) Presence of anti-A, anti-B, anti-A,B, and a potent wide thermal range of anti-H in the serum, c) A, B, H non-secretor (no A, B, or H substances present in saliva), d) Absence of α-2-L-fucosyltransferase (H enzyme) in serum and H antigen on red blood cells, e) Presence of A or B enzymes in serum (depending on ABO genotype). f) A recessive mode of inheritance (identical phenotypes in children but not in parents). f) RBCs of the Bombay phenotype (Oh) will not react with the anti-H lectin (Ulex europaeus), g) RBCs of the Bombay phenotype (Oh) are compatible only with the serum from another Bombay individual.[2, 4]

Conclusion

Compulsory use of cell grouping and serum grouping and in suspected cases of Bombay phenotype, use of anti-H lectin and detection of secretor status; all are important tools for detection of Bombay phenotype. As this condition is very rare, any person of this phenotype who needs an urgent blood transfusion will probably be unable to get Bombay blood, as no blood bank would have it in stock. So every blood bank should have registry of individuals of Bombay group which may help to find these individuals to get blood in this situation.

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Case Report

A Case of Endometrial Tuberculosis Causing Primary Infertility

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Abstract

Tuberculosis is a major public health problem worldwide. Urogenital tuberculosis is the 3rd most common manifestation of extrapulmonary tuberculosis. Endometrial tuberculosis is a rare form of genital tuberculosis infection. The diagnosis is not straightforward due to the nature of its presentation. We report a case of endometrial TB in a young, healthy and immunocompetent patient, who presented to us with primary infertility.

Key words: Infertility, Tuberculosis, Amenorrhea.

Introduction

Tuberculosis (TB) is a major public health problem worldwide. Despite a declining trend in mortality, with effective diagnosis and treatment, An estimated 10·6 million people became ill with tuberculosis in 2021, compared with 10·1 million in 2020.[1] Tuberculous infection of the female genital organs can result in infertility, dyspareunia, menstrual irregularities and chronic pelvic inflammatory disease.[2] However, the burden of genital TB in females is underestimated as most of the patients are asymptomatic and usually diagnosed during evaluation for infertility.[3] Genital TB in females is well recognized as an important etiological factor for infertility in countries with high prevalence of TB. Genital TB usually occurs secondary to TB in other sites primarily, the lungs from where spreads to the genital organs by hematogenous or lymphatic routs.[4] Drug therapy for female genital TB is similar to the standard treatment regimens used for pulmonary TB. Here we present a case of endometrial tuberculosis causing secondary amenorrhea with primary infertility.

Case report

A 28 years old nulliparous married for 7 years came to the Gynecology and Obstetrics department of Jahurul Islam Medical College Hospital outdoor with the complaints of amenorrhea for 1.5 years and expecting to get pregnant for 6 years. She also complains about occasional post coital bleeding. She had regular menstrual cycle 1.5 years back. He was treated with cabergoline and desogestrel, ethinylestradiol and norethisterone for last six months. But her menstruation did not start and was unable to become pregnant. Pelvic organ ultrasonography revealed normal cervix, adnexae with mild increase in the endometrial thickness. Her husband's semen analysis was done, the report was normal both in the count and in morphology. There was no history of chronic cough or loss of weight. No past, present or family history of tuberculosis. Her provisional diagnosis was chronic salphingo-oophoritis causing tubal abnormality with pelvic inflammatory disease (PID).

On general physical examination, she was well looking, all vital signs were within normal range. BMI was 19.5 kg/m^2 with no palpable lymph nodes. On abdominal examination, no significant findings were noted. On per vaginal examination, vulva was grossly normal looking. The bimanual and pre rectal examination were normal. On speculum examination, the cervix was normal looking. She was advised to get admitted in gynae and obs. ward for further evaluation. Laparoscopy was done to see adnexal region to see any visible adhesion, inflammation or tumourous lesion. Hysterosalphingogram was normal. The visual inspection by laparoscopy reveal normal. Diagnostic D & C with endometrial biopsy was done to see any endometrial lesion. The histopathology revealed

granulomatous inflammation, consistent with tuberculosis. Routine hematological test reveal high ESR and hemoglobin at its lower normal range. Chest radiograph were normal and sputum for AFB were negative.

Patient was given antitubercular treatment for six months. During and after anti TB, patients menstrual cycle become regular and occasional post coital bleeding subsided. Patient is now getting treatment in the infertility corner for conception management.

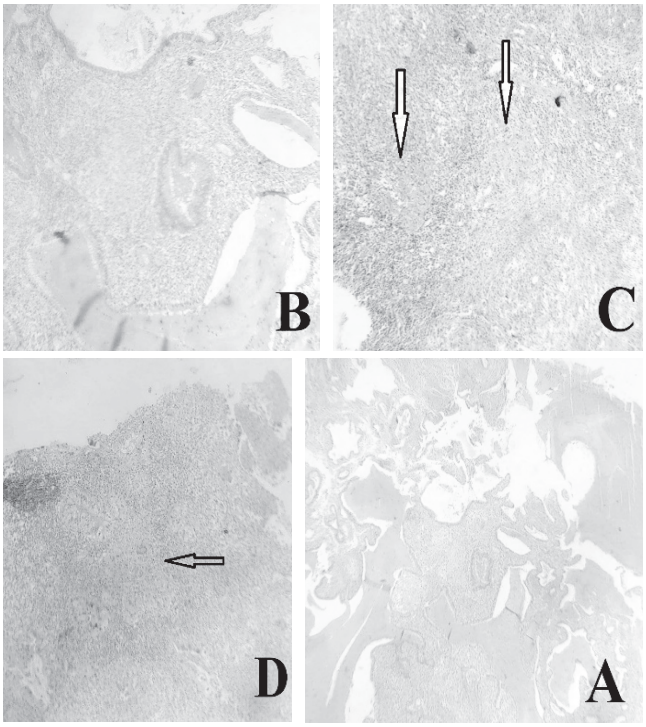

Figure 1: Photomicrographs show a case of endometrial tuberculosis. A, B shows low power view (4x) of endometrium. C, D shows high power view (40x) of granuloma (Arrow) composed of epithelioid cells. Haematoxilin & Eosin stain was done.

Discussion

Tuberculosis is a chronic bacterial infection caused by Mycobacterium Tuberculosis frequently seen in the developing and less developed countries. It is one of the important causes of chronic pelvic inflammation and infertility in women. The fallopian tubes are affected most commonly followed by endometrium and the ovaries.[5]

The actual incidence is under-reported due to asymptomatic presentation of genital tuberculosis and paucity of investigations. Other possible causes of under diagnosis of endometrial tuberculosis may be of the decreased vascularity of the endometrial tissue and the lack of endometrial shedding in those patients.[6] The possibility of female genital TB should be considered in patients with chronic PID not responding to standard antibiotic treatment, unexplained infertility or in women with irregular menstrual cycle or postmenopausal bleeding and persistent vaginal discharge.[7] Risk factors include contact with a smear-positive pulmonary TB patient, past history of TB infection, residence in or recent travel to endemic areas, low socio-economic background, and people living with HIV and drug abuse.[8] When the cervix is involved, it may appear inflamed and may resemble invasive carcinoma, both grossly and with the colposcope.[9] However, in our case the cervix was normal. In the early stages, no evidence of endometrial infection may be present. As the disease advances, confluence of the affected areas with caseation and ulcer may develop. In rare instances the uterine cavity may be entirely obliterated so that no dye can enter and hysterosalphingogram may show only a portion of the cervical canal.[10] Diagnosis is made by endometrial biopsy as one-third of the cases show a negative culture. Microscopically, chronic inflammation with caseating granulomas do the diagnosis.[10]

The efficacy and safety of treatment by antitubercular drugs should be monitored carefully. The surgical management of uterine adhesion, if present should be done to improve fertility. The post anti TB surveillance of tuberculosis of the endometrium requires regular follow up, menstrual history and biopsy, if nevessary.[11] Future fertility is poor (5%) even after treatment due to endometrial and tubal involvement. Fibrosis after treatment is another cause of poor fertility outcome.[12]

Conclusion

Endometrial tuberculosis is an uncommon genital lesion and prevalence is generally underestimated because of the asymptomatic nature of the infection and diagnostic challenges. There should be a suspicion of tuberculosis in women with an abnormal menstrual

history, chronic pelvic pain, infertility especially in areas where incidence of tuberculosis is high. And in also in patients getting long term antibiotic treatment for PID and other genital infections but not responding to treatment.

Conflict of interest: None declared

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