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Official Journal of Pabna Medical College, Bangladesh

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- When registering an account we ask you to log in and provide certain personal information (such as your name and email address), and there is the option to register using an ORCiD which will pre-fill the registration form.
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- On submitting a review, the reviewer includes a competing interest statement, they may answer questions about the quality of the article, and they will submit their recommendation.

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4.1 what data we collect

- Co-author data is entered by the submitting author. The submitting author will already have a user account. According to standard publishing practice, the submitting author is responsible for obtaining the consent of their co-authors to be included (including having their personal data included) in the article/book being submitted to the journal/press.
- The requested personal data for co-authors are at the bare minimum; first name, last name, institution, country, email address. This can also include; ORCID ID, Title, Middle Name, Biographical Statement, Department, Twitter Handle, Linkedin Profile Name or ImpactStory ID.

4.2 why we collect the data

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Editorial

Reasons Why Articles can be Rejected

It is really disheartening when your paper gets rejected by a journal. Authors work very hard to conduct research if actually it done. They present their work in scientific seminar, symposia or conference and/or as a research article for publication. When their presentations get applauded by the audience, researchers feel encouraged to publish it. However, it may not be appreciated by editors and reviewers when the research is submitted to a journal for publication. One should not get disappointed by rejections. Most top journals have almost 75% rejection rates. This editorial will take a brief review of reasons for rejection and advise how to deal with rejections.

Sometimes authors keep sending email to Editor regarding reasons why their articles were rejected by their supervisors or peer reviewers. A number of them complained that they meet their supervisors many times but they were advised to rewrite it. Some of them had not checked their e-mail or messages at all. This article can inform you why most articles are rejected. Some articles are not sent for peer review even, because these were reserved to rewrite by author after primary vetting by Editor.

The following are the reasons of writing were rejected:

It fails the technical screening

The most reasons they're rejected are:

- After primary vetting by Editor, The articles are checked by Plagiarism checker. We check it by DrillBit. When originality of article is less than 80%, author is advised to rewrite the article
- The manuscript is not complete; it lacks key components of title, list of author and co-authors with superscripted affiliation number, list of affiliations, keywords, right references and every one table and figures).
- Discrepancy of authors and institutes.
- Poor English or it isn't enough for the review method
- The figures aren't complete or aren't clear enough to scan.
- The article doesn't adjust to the Guide for Authors for the journal it's submitted to.
- References are incomplete or terribly previous.
- The article contains observations that fail the criteria of full study.
- It discusses irrelevant findings.
- Added abbreviation without description
- The paper and the subject may be out of scope and not suitable for the journal and readership
- Weak hypothesis
- Poor methodology, small sample size, poor statistical analysis
- Conflict of interest not declared in appropriate cases; ethical committee permission not taken
- Informed consent of subjects not taken
- Single case reports not making a useful point (usually banking on rarity)
- The target journal may have similar research papers published or already in the process of getting published

All of these happen because of poor homework before submission of manuscript

Defective procedure and analysis

- The study lacks clear management teams or alternative comparison metrics.
- The study failed to adjust to recognized procedures or methodology that may be continual.
- Weak hypothesis or wrong research questions

Poor conclusive matters

- The arguments are illogical, unstructured or invalid.
- The data doesn't support the conclusions.
- The conclusions ignore major findings of manuscript.

Manuscript is only the extension or modification of previous published data

- The work is clearly a part of a bigger study, sliced up to form as several articles as doable.
- The language, structure, or figures are therefore poor that the advantage cannot be assessed. Have a native English speaker scan the paper.

The paper is BORING

- It is depository, progressive or of marginal interest to the sector
- The question behind the work isn't of interest within the field.
- The work is n't of interest to the readers of the precise journals

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Original Article

Prevalence and Antimicrobial susceptibility pattern of Bacterial Uropathogens in 250 Bedded General Hospital, Pabna, Bangladesh

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UTI, Uropathogens, MDR

Abstract

Background*: Urinary tract infections (UTIs) are one of the most common infectious diseases encountered in the medical practices and often caused by multi-drug resistant (MDR) organisms. This study was aimed to determine the prevalence of bacterial uropathogens and their antimicrobial susceptibility pattern. Midstream clean catch urine samples were collected from 875 patients of both sexes and different age groups attending Medicine outpatient department of 250 Bedded General Hospital, Pabna, Bangladesh from July 2021 to December 2022. Uropathogens were identified by standard and specific microbiological techniques and antimicrobial susceptibility pattern was determined by Kirby Bauer Disc diffusion method following Clinical and Laboratory Standards Institute (CLSI) guidelines.*

Results*: Culture yielded a total of 316 (36.11%) significant growth of uropathogens. Females were found to be much more prone to UTIs than males (2.89:1).* E. coli *was the most predominant (77.53%), followed by* Klebsiella spp. *(10.13%) and* S. saprophyticus *(7.91%). E coli was highly sensitive to amikacin (97.96%) and meropenem (97.55%), followed by gentamycin (76.73%) and nitrofurantoin (76.33%). Maximum resistance was shown to cloxacillin and penicillin-G while ampicillin, linezolid and co-trimoxazole were found to be largely ineffective.* Klebsiella spp. *demonstrated maximum sensitivity towards amikacin and meropenem, and good sensitivity to gentamicin but showed total resistance to penicillin-G, linezolid and cloxacillin and high resistance to third- and fourth-generation cephalosporins.* S. saprophyticus *showed high sensitivity to amikacin and meropenem, but absolute resistance to cefixime and ceftazidime, and high resistance to ceftriaxone and co-trimoxazole.*

Conclusion*: Uropathogens in the present study showed maximum susceptibility to amikacin and meropenem but increasing resistance to oral antibiotics is very alarming. Commonly prescribed antimicrobials need to be continuously evaluated and empirical therapy must be considered accordingly.*

Pabna Medical Journal 2022;1(1): 3-9.

Introduction:

Urinary tract infection (UTI) refers to the presence of micro-organism in the urinary tract including urinary bladder, prostate, collecting system or kidney. The syndrome ranges from asymptomatic bacteriuria to perinephric abscess with sepsis[1]. UTI is the second most common infection in community practice[2]. About 35% of healthy women suffer from symptoms of UTI at some point in their life. The incidence of UTI is greater in women as compared to men, which may be

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due to either anatomical predisposition or other host factors[3]. About 150 million people suffer from UTIs each year globally which results in greater than 6 billion dollars in direct health care[4]. The prevalence increases among patients from lower socio-economical group[5].

Indiscriminate use of antimicrobial agents is a common practice in underdeveloped and many developing countries that often leads to emergence of resistant microorganisms[6]. As a common practice, empirical antimicrobial treatment is initiated before the laboratory results of urine culture are available which may lead to emergence and spread of antimicrobial resistant strains[7]. The prevalence and pattern of antimicrobial susceptibility of uropathogens are constantly changing with the ever-increasing use of antimicrobials[8]. For the selection of appropriate drugs as well as for rational choice of empirical therapy proper knowledge and continuous monitoring of the susceptibility pattern is of paramount importance. The present study was carried out to determine the prevalence of bacterial pathogens responsible for UTIs and their antimicrobial susceptibility pattern with the aim to disseminate information about choice of empirical antibiotics.

Materials and Methods:

This study was done at the Department of Medicine, 250 Bedded General Hospital, Pabna for a period of eighteen months from July 2021 to December 2022. A total of 875 urine samples were collected from patients who visited Medicine Out Patient Department of 250 Bedded General Hospital, Pabna, Bangladesh during the study period. Patients of both sexes and all age groups from 15 years and above were included. Midstream clean catch urine samples were collected in two sterile containers by standard procedures. Semiquantitative culture was done on blood agar and MacConkey's agar media. The plates were incubated aerobically at 37°C overnight. Isolated organisms were identified by colony morphology, Gram staining and relevant biochemical tests. Samples showing significant colony count were taken into consideration. Sensitivity patterns of the organisms were determined by modified Kirby-Bauer Disc diffusion method using Mueller-Hinton agar according to Clinical and Laboratory Standards Institute (CLSI) guidelines[9,10]. The following antibiotic discs were used in antibiogram: amikacin, amoxycillin, ampicillin, azithromycin, cefepime, cefixime, cefotaxime, cefradine, ceftazidime, ceftriaxone,cefuroxime, ciprofloxacin, cloxacillin, colistin, co-amoxiclav, co-trimoxazole, doxycycline, gentamicin, levofloxacin, linezolid, meropenem, nalidixic acid, nitrofurantoin, penicillin-G and tetracycline.

The protocol was approved by the Ethical Review Committee of 250 Bedded General Hospital, Pabna, Bangladesh and informed written consent was taken from patients before collection of their samples.

Statistical analysis was done with Statistical Package for Social Sciences (SPSS) version 23.0.

Results:

225 (25.71%) of the population under study were males and 650 (74.29%) females with a male to female ratio of 1:2.89. Out of the total 875 samples, 316 (36.11%) showed significant growth of bacteria, of which 50 (15.82%) isolates were from male and 266 (84.18%) were from female patients. Bacterial growth was found in 22.22% of the urine samples (50 out of 225) in men compared to40.92% of the samples (266 out of 650) in women.

Table 1. Distribution of specimens with significant growth

	Number of samples	Percentage	Number of positive cultures	Percentage of positive cultures
Female	650	84.18	266	40.92
Male	225	15.82	50	22.22
Total	875	100	316	36.11

Three age groups were considered to determine the distribution of uropathogens according to age; highest significant bacterial growth (38.35%) was observed in the 15-29 age group, followed by 45+ age group (35.71%) in females and in the 45+ age group (48%) in males.

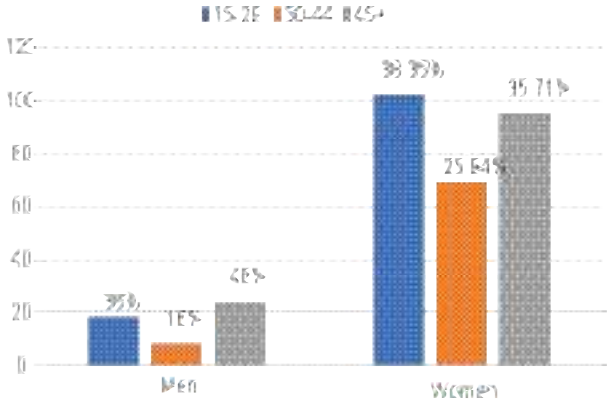

Fig.-1: *Distribution of positive growth of uropathogens in age groups*

Table II. *Frequency of isolated uropathogens*

Isolated uropathogens	Number	Percentage
Escherichia coli	245	77.53
Klebsiella spp.	32	10.13
Staphylococcussaprophyticus	25	7.91
Staphylococcus aureus	6	1.89
Pseudomonas spp.	4	1.27
Enterococci	2	0.63
Proteus spp.	1	0.32
Staphylococcus epidermidis	1	0.32
Total	316	100

Gram negative bacteria overwhelmingly outnumbered (89.24% versus 10.76%) Gram positive ones in frequency of uropathogens. *Escherichia coli* was the most predominant (77.53%), followed by *Klebsiella* spp. (10.13%), *Pseudomonas* spp. (1.27%) and *Proteus* spp. (0.32%).

Table III. *Antimicrobial sensitivity and resistance pattern of E. coli(n=245)*

Antibiotic	Sensitive	Antibiotic	Resistance
Amikacin	240 (97.96%)	Cloxacillin	228 (93.04%)
Meropenem	239 (97.55%)	Penicillin-G	226 (92.24%)
Tobramycin	211 (86.12%)	Ampicillin	217 (88.57%)
Gentamicin	188 (76.73%)	Linezolid	200 (81.63%)
Nitrofurantoin	187 (76.33%)	Cefradine	184 (75.10%)
Levofloxacin	166 (67.76%)	Amoxycillin	180 (73.47%)
Ciprofloxacin	152 (62.04%)	Co-trimoxazole	180 (73.47%)
Doxycycline	133 (52.29%)	Cefixime	167 (68.16%)
Ceftriaxone	99 (40.41%)	Co-amoxiclav	166 (66.12%)
Cefepime	91 (37.14%)	Cefuroxime	160 (65.31%)

*Klebsiella spp.*showed maximum sensitivity to amikacin and meropenem (96.88% each) followed by gentamicin (75%).

Table IV. *Antimicrobial sensitivity and resistance pattern of Klebsiella spp.(n=32)*

Antibiotic	Sensitive	Antibiotic	Resistance
Amikacin	31 (96.88%)	Cloxacillin	32 (100.00%)
Meropenem	31 (96.88%)	Penicillin-G	32 (100.00%)
Gentamicin	24 (75.00%)	Linezolid	32 (100.00%)
Tobramycin	20 (62.50%)	Ampicillin	29 (90.63%)
Nitrofurantoin	18 (56.25%)	Amoxycillin	29 (90.63%)
Cefotaxime	16 (50.00%)	Co-trimoxazole	29 (90.63%)
Levofloxacin	13 (40.63%)	Co-amoxiclav	24 (75.00%)
Ciprofloxacin	13 (40.63%)	Cefradine	23 (68.16%)
Ceftazidime	13 (40.63%)	Tetracycline	21 (66.12%)
Azithromycin	12 (37.50%)	Cefuroxime	20 (62.50%)

Most predominant Gram-positive bacteria found in this study, *S. saprophyticus*, showed high sensitivity to amikacin (88%), meropenem (80%), nitrofurantoin (72%) and gentamicin (72%).

Table V. *Antimicrobial sensitivity and resistance pattern of staphylococcus saprophyticus (n=25)*

Antibiotic	Sensitive	Antibiotic	Resistance
Amikacin	22 (88.00%)	Cefixime	25 (100.00%)
Meropenem	20 (80.00%)	Ceftazidime	25 (100.00%)
Tobramycin	19 (76.00%)	Cefepime	24 (96.00%)
Gentamicin	18 (72.00%)	Colistin	23 (92.00%)
Nitrofurantoin	18 (72.00%)	Ampicillin	21 (84.00%)
Ciprofloxacin	16 (64.00%)	Nalidixic acid	21 (84.00%)
Cefradine	16 (64.00%)	Cefotaxime	20 (80.00%)
Tetracycline	15 (60.00%)	Ceftriaxone	20 (80.00%)
Doxycycline	13 (52.00%)	Co-trimoxazole	20 (80.00%)
Levofloxacin	13 (52.00%)	Cefuroxime	17 (68.00%)

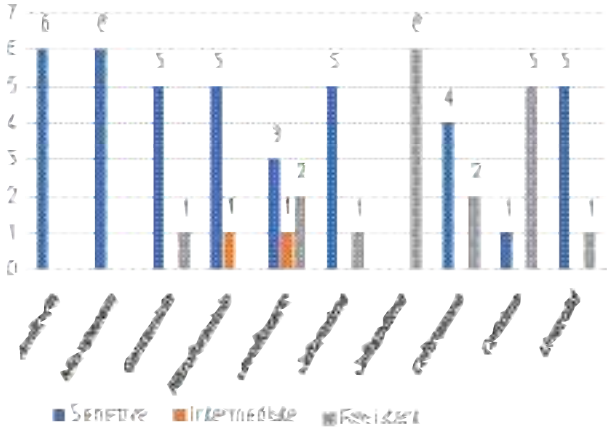

Fig.-2. Antibiogram profile of *S. aureus* (n=6)

Pseudomonas spp. were fully susceptible to amikacin and meropenem, and 75% susceptible to gentamicin; but showed total resistance to cefuroxime, cefixime, ceftriaxone, co-trimoxazole and linezolid, and 75% resistance to both nitrofurantoin and ciprofloxacin.

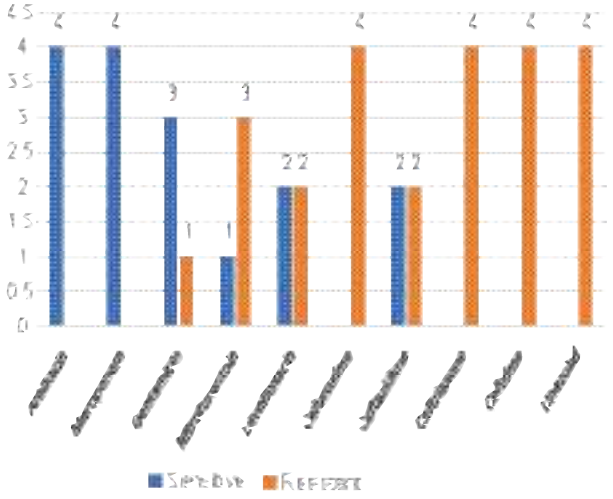

Figure 3. *Antibiogram profile of Pseudomonas spp. (n=4)*

Discussion:

Urinary tract infections are one of the most common infectious diseases encountered in the medical practices and only second to respiratory tract infections as a cause of hospital visit[11]. Antimicrobial resistance to various classes of antimicrobials to uropathogens continues to be a major health problem in different parts of the world[12,13]. Consequently, the empirical treatment of UTIs becomes difficult and unpredictable due to the lack of alternative effective antibiotics[14]. As urinary pathogens vary considerably in different geographic areas, antibiogram profile of the isolates is a must for the physicians to combat drug-resistant organisms. This study has been carried out to determine the prevalence of bacterial pathogens causing uncomplicated UTIs and their antibiotic susceptibility pattern.

It is well established that UTI is more common in females than in males and our findings have rightly coincided with those in other studies[5, 14-16]. Regarding prevalence of the uropathogens, our observation is in good agreement with several previous reports[15-18].

In the present study, 15-29 years age group had the greatest number of positive bacterial growth, followed by 45+ age group in females and in the 45+ age group in males, which corelates with the observations by some other researchers[14,19]. The variation of prevalence within different age groups may be attributed to the hormonal changes affecting the mucosal adherence of bacteria, frequent sexual activity, use of spermicidal agents, menopause for women and prostate gland enlargement of men[20].

E.coli was found to be the predominant organism with a prevalence rate of 77.53%, followed by Klebsiella spp. and S. saprophyticus. Again, Gram-negative bacteria greatly outnumbered Gram-positive ones. These findings are remarkably consistent with previous studies conducted home and abroad[14, 21-25]. The prevalence of *E. coli* as the most common organism causing UTIs is due to the fact that they are the normal fecal flora and possess several adhesion factors such as adhesin, pili, P-fimbriae and P1-blood group phenotype receptor responsible for their attachment to the uroepithelial cells[26,27].

The most common bacterial agent of UTI, *E. coli*, showed maximum sensitivity to amikacin and meropenem. Gentamycin and nitrofurantoin were found to be sensitive in 76.73% and 76.33% cases respectively. Maximum resistance was shown by *E. coli* to cloxacillin and penicillin-G while ampicillin,linezolidand co-trimoxazole were found to be largely ineffective. Similar findings were also observed by Jhora et al and Shahnaz et al[5,28].

Most isolates of *Klebsiella spp.*are susceptible to fluoroquinolones, aminoglycosides, and carbapenems[8], therefore *Klebsiella pneumoniae* demonstrating maximum sensitivity towards amikacin and meropenem, andgood sensitivityto gentamicin was expected. Nitrofurantoin showing fair sensitivityand quinolonesshowing less sensitivity contradicts with the findings of Haque et al and Bouza et al[8,15]. *Klebsiella spp.* are intrinsically resistant to penicillins and can acquire resistance to third- and fourth-generation cephalosporins owing to the production of plasmid-mediated extended-spectrum beta-lactamases (ESBLs), so penicillin-G being totally useless and ampicillin, amoxycillin, cefuroxime, cefixime and ceftriaxone being found to be highly resistant supports the findings of other researchers[8,15].

S. saprophyticus has shown high sensitivity to carbapenem and gentamicin, and moderate sensitivity to ciprofloxacin which was similar to the findings of Jhora et al[2].The organism being absolutely resistant to cefixime and ceftazidime, and highly resistant to ceftriaxone and co-trimoxazole was supportive of the findings of Haque et al[15]but contrary to the findings of Jhora et al[2].

Amikacin found to be completely ineffective against *S. aureus*in a previous study[14]has shown 100% susceptibility in the present one and in another study from Bangladesh[29] while high sensitivity towards gentamicin and remarkable resistance to cefixime (83.33%) were consistent with the findings of other researchers[14,29].

Pseudomonas spp. being fully susceptible to amikacin and carbapenemhas been contradictory to but showing total resistance to ceftriaxone, co-trimoxazole and nalidixic acid, and 75% resistance to nitrofurantoin has been supportive of the findings of Sanjee et al [14]. Carbapenem (meropenem) having been considered as the most effective anti-pseudomonal drug in our study was also observed by Begum et al in a study in Bangladesh in 2013[30].

Almost all the uropathogens have shown remarkable amount of susceptibilityto gentamicin from aminoglycoside group and meropenem from carbapenem group. In addition, gentamicin and nitrofurantoin were also found to be strongly effective and quinolones were observed to be fairly sensitive. All the drugs from 2nd, 3rd and 4th generation cephalosporins (cefuroxime, cefixime,ceftriaxone, cefepime), co-trimoxazole and co-amoxiclav were found to be either ineffective or less effective against most of the uropathogens, which is a red alert for empirical treatment of uncomplicated UTIs.

This study has clearly demonstrated that the uropathogens are becoming resistant to the most commonly prescribed antibiotics for the treatment of uncomplicated UTIs. Extended spectrum â-lactamase (ESBL) of Gram negative uropathogens help them to gain resistance against 3rd and 4th generation cephalosporins[8,15] whereas resistance to carbapenem antibiotic group is often due to loss of outer membrane proteins and up-regulation of active efflux pumps or production of metallo-â-lactamase (MBL)[31]. Major factors known to influence the evolution and transfer of multi drug resistance among microorganisms are incomplete doses, ease of access, over prescription, prescription of higher generation antimicrobials, prescribing antibiotics without laboratory results and indiscriminate use of antimicrobials in agriculture and livestock sectors[32]. As drug resistance is mainly an acquired property which can also be lost in any time, the resistance profile of some drugs shows rises and downfalls with course of time towards a particular pathogen[33].

No fundamentally new classes of antibiotic drugs have been developed since the 1950s, and the means of diagnosing bacterial infections remains largely

unchanged since the 19th century which accounts for the death of 700,000 people each year from infection by drug-resistant pathogens and parasites. If left unchecked, by 2050, drug-resistant bacteria could kill 10 million people each year - more than currently death from cancer, knocking 2.0-3.5% off of the global GDP[34]. To prevent the emergence of MDR pathogens globally continuous surveillance and monitoring is a must.

The present study, conducted on a small number of samples in a small District Hospital, Bangladesh, hardly represents the total scenario. As the resistance pattern of the uropathogens is ever changing and continuous, we recommend for a broad-based longitudinal study that can reflect the broader perspective which may serve as a basis for the development of the national antibiotic guideline and timely revision of the existing guideline in response to the emerging MDR pathogens. We do emphasize molecular level researches on the mechanism of drug resistance coupled with computational biology for identification of potent drug target so that novel therapeutic agents are designed against MDR pathogens.

Conclusion:

The present study found *E. coli* to be the predominant uropathogen, followed by Klebsiella spp. and S. saprophyticus. High resistance was documented towards second-, third- and fourth-generation cephalosporins. Amikacin and meropenem were found to be the most effective drugs with over 95% overall sensitivity but resistance to oral antibacterials was increasing. The rapid emergence of antimicrobial resistance is a serious warning sign that we must be cautious with overprescribing and indiscriminate use of antibiotics. Appropriate antimicrobial drugs should be prescribed in accordance with culture and sensitivity reports, and empirical therapy must be considered on the recent antibiogram profile of a particular geographic area.

References:

1. Johnson CC: Definition, classification, & clinical presentation of Urinary tract infections. Med Clin North Am. March 1991; 75 (2): 241-52.
2. Jhora ST, Paul S. Urinary Tract Infections Caused by *Staphylococcus saprophyticus* and their antimicrobial sensitivity pattern in Young Adult Women. Bangladesh J Med Microbiol 2011; 05 (01): 21-5.
3. Schaeffer AJ, Rajan N, Cao Q, Anderson BE, Pruden DL, Sensibar J, Duncan JL. Host pathogenesis in urinary tract infection. Int J Antimicrob Agents. 2001; 7: 245–51.
4. Odoki M, Aliero AA, Tibyangye J, Maniga JN,Wampande E, Kato CD, Agwu E, Bazira J. Prevalence of Bacterial Urinary Tract Infections and Associated Factors among Patients Attending Hospitals in Bushenyi District, Uganda. Int J Microbiol. 2019; 2019:4246780. Published Feb 17.
5. Jhora ST, Paul S, Begum BA, Chowdhury AQ. Antibiogram of Urinary *Escherichia coli* isolated in Sir Salimullah Medical College Mitford Hospital, Dhaka. Bangladesh J Med Microbiol 2011; 05 (02): 23-6.
6. Gold HS, Moellering RC. Antimicrobial drug resistance. N Eng J Med. 1996; 335:1445-53.
7. Gupta K. Addressing antibiotic resistance. Am J Med. 2002; 113: 295-345.
8. Bauza E, Cercenado E. *Klebsiella* and *Enterobacter* antibiotic resistance and treatment implications. Semin Respis Infect. 2002; 17: 215–30.
9. Akter ML, Haque R, Salam MA. Comparative evaluation of chromogenic agar medium and conventional culture system for isolation and presumptive identification of uropathogens. Pak J Med Sci. 2014;30(5):1033–8.
10. Bauer AW, Kirby WMM, Sherris JC, Turek M. Antibiotic susceptibility testing by a standardized single disc method. Am J Clin Pathol. 1966;36:493–6.
11. L iperky BA. Urinary tract infection in men: epidemiology, pathophysiology, diagnosis & treatment. Ann Intern Med 1989; 111: 138-50.
12. Oliveira FA, Paludo KS, Arend LNVS, Farah SMSS, Pedrosa FO, Souza EM, Surek M, Picheth G, Fadel-Picheth CMT. Virulence characteristics and antimicrobial susceptibility of uropathogenic *Escherichia coli* strains. Genet Mol Res. 2011; 10: 4114–25.
13. Farshad S, Ranjbar R, Japoni A, Hosseini M, Anvarinejad M, Mohammadzadegan R. Microbial susceptibility, virulence factors and plasmid profiles of uropathogenic *Escherichia coli* strains isolated from children in Jahron. Iran. Arch Iran Med. 2012; 15: 312–6.
14. Sanjee SA, Karim ME, Akter T, Parvez MAK, Hossain M, Jannat B, Pervin S. Prevalence and antibiogram of bacterial uropathogens of urinary tract infections from a tertiary care hospital of Bangladesh. J Sci Res. 2017; 9(3): 317-28.

15. Haque R, Akter ML, Salam MA. Prevalence and susceptibility of uropathogens: a recent report from a teaching hospital in Bangladesh. BMC Res Notes. 2015; 8: 416.

16. Deshpande KD, Pichare AP, Suryawanshi NM, Davane MS. Antibiogram of gram negative uropathogens in hospitalized patients. Int J Recent Trends Sci Technol. 2011;1(2):56–60.

17. Qaiser S, Zeeshan M, Jabeen K, Ahsan T, Zafar A. Comparison of chromogenic urinary tract infection medium with cysteine lactose electrolyte deficient media in a resource limited setting. J Pak Med Assoc. 2011;61:63255.

18. Keah S, Wee E, Chng K, et al. Antimicro-bialsusceptibility of community-acquired uropathogens in general practice. Malays Fam Phys. 2007;2:64-9.

19. Khan SA, Feroz F, Noor R. Study of extended-spectrum â-lactamase-producing bacteria from urinary tract infections in Bangladesh. Tzu Chi Med. J. 2013; 25(1), 39-42.

20. Mahajan R, Gupta S, Mahajan B, J. Rat. Pharmacothera. Res. **2(02**), 44 (2014).

21. Gonzalez CM, Schaeffer AJ.Treatment of urinary tract infection: what's old, what's new, and what works. World J. Urol. **17**, 372 (1999).

22. Gul N, Mujahid TY, Ahmad S. Isolation, Identification and Antibiotic Resistance Profile of Indigenous Bacterial Isolates from Urinary Tract Infection Patients. Pakistan J. Bio. Sci. **7**, 2051 (2004).

23. J.H. Lee, W.K. Sun, I.Y. Byung, H. U-Syn, W.S. Dong, C. Yong-Hyun. Factors that affect nosocomial catheter-associated urinary tract infection in intensive care units: 2-year experience at a single center. Korean J Urol, 54 (2013), pp. 59-65

24. M.M. Mahbub, N. Azmuda, B. Maumood, S.I. Khan, N.K. Birkeland, H. Akhter. Drug resistance and curli fimbrination of *Escherichia coli* isolated from Bangladeshi patients with urinary tract infections. Dhaka Univ Biol Sco, 20 (2011), pp. 123-30.

25. T.T. Lina, S.R. Rahman, D.J. Gomes. Multiple-antibiotic resistance mediated by plasmids and integrons in uropathogenic *Escherichia coli* and *Klebsiella pneumoniae.* Bangladesh J Microbial. 2007;24:19-23

26. Das R, Chandrasekhar TS, Joshi HS, Gurung M, Shreshtha N, Shivananda PG. Frequency and susceptibility profile of pathogens causing urinary tract infections at a tertiary care hospital in western Nepal. *Singapore Med J.* 2006;474:281–5.

27. Johnson JR. V irulence factors in Escherichia coli urinary tract infection. Clin Microbiol Rev. 1991;4(1):80-128.

28. Shahnaz S. Murshed M. Rahman T. Urinary pathogens & its culture sensitivity pattern in Holy Family Red Crecent Medical College Hospital, Dhaka, Bangladesh. Bangladesh Private Practitioners' Journal. 2005; 11(1):19-22.

29. Saha S, Rahman MS, Nazmul Hassan FM, Sarkar S, Islam MK, Saha P, Alam MB, Sultana N, Rahman KMT, Sumi SS, Islam MF, Hasan S. Antimicrobial resistance in uropathogen isolates from patients with urinary tract infections. Biomed. Res. Ther. 2015;2(5):263.

30. Begum S, Salam MA, Alam KhF, Begum N, Hassan P, Haq JA. Detection of extended spectrum ß-lactamase in *Pseudomonas* spp. isolated from two tertiary care hospitals in Bangladesh. *BMC Res Notes.* 2013;6:7.

31. Buscher KH, Cullman W, Dick W, Wendt S, Opferkuch W (2000).Imipenem resistance in P. aeruginosa is due to *diminished expression* of the outer membrane proteins. J. Infect. Dis. 156:681-5.

32. Islam MB, Hasan M. Antibiotic Sensitivity Pattern of the Isolated of Urinary Pathogens at Dhaka National Medical College & Hospital. J. Dhaka Nat. Med. Colleg. Hospit. 2012;18(01):4.

33. Munshi MH, Sack DA, Haider K, Ahmed ZU, Rahaman MM, Morshed MG. Plasmid-mediated resistance to nalidixic acid in Shigella dysenteriae type 1. Lancet.1987 Aug 22;2(8556):419-21.

34. O'Neill J. The Review on Antimicrobial Resistance: Tackling Drug-resistant Infections Globally: Final report and recommendations. 2016 May.

Original Article

Cerebrospinal fluid examination findings in infections of the brain and its meningeal coverings

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Abstract

Background*: Examination of the CSF is the most important diagnostic test in the management of patients with features of infection of the brain and its meningeal coverings.*

Objective*: To study the effectiveness of investigating the CSF in diagnosing infections of the brain and its meningeal coverings and treating such patients who are admitted in our tertiary care hospital.*

Methodology*: All patients admitted in Holy Family Red Crescent Medical College Hospital from July to December 2021 whose CSF was examined were included in the study. The course of the patients were followed till discharge, and the patients were followed up for 6 months after discharge. All the investigation reports were studied and their usefulness in reaching a specific diagnosis of these patients and their management were assessed.*

Result*: 12 patients met the criteria for inclusion in the study. Specific bacteriologic diagnosis was made by examination of CSF in one patient only in whom gram-ve intracellular diplocci were found suggestive of Meningococcal Meningitis. All the other CSF investigation reports helped as ancillary data in the management of these patients. All the 12 patients improved after treatment and left the hospital in stable condition.*

Conclusion*: Admission in a tertiary care hospital carries a good prognosis for patients suffering from the grave condition of infection in the brain and its meningeal coverings. In our patients CSF examination may help in reaching a specific diagnosis occasionally but mostly it provides ancillary data in reaching a diagnosis and in management of these patients.*

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Introduction

Bacterial meningitis causes approximately 318,000 deaths annually worldwide, resulting in an estimated 20,383 years of life lost. The incidence ranges from approximately 0.9 per 100 000 individuals per year in high-income countries to approximately 10 to 80 per 100 000 individuals per year in low income and middle-income countries. Mortality rates in adults and neonates with bacterial meningitis range from 6% to 54%.Mortality also varies from 10% in high-income countries to up to 58% in low-income countries. The risks of neurological sequelae, such as focal neurological deficits (eg, hemiparesis, cranial neuropathies), hearing loss, and memory impairment, also vary, from 9.4% in Europe to 25% in Africa.[1,2,3,4]

Bacterial meningitis is an acute medical emergency whose successful treatment requires highly bactericidal antibiotics. Many challenges have to be overcome to achieve optimal patient outcome. Firstly, the antibiotics must be able to penetrate the blood brain barrier and achieve significant bactericidal levels in the CSF. Finally bactericidal therapy produces lysis of the bacteria and these lytic products are highly inflammatory. To prevent damage from these lytic products adjunctive therapy have to be given to prevent neuronal death. These challenges are an extreme example of the different requirements for treating infections in different body sites.[5]

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Infections of the brain and its meningeal coverings require urgent specific diagnosis and choice of appropriate antibiotic treatment. For the diagnosis of the infection the most important investigation is the examination of the Cerebrospinal fluid and should be undertaken promptly before CSF is rendered sterile by broad-spectrum antibiotics.CSF culture is considered the gold standard for diagnosis of bacterial meningitis, yet it is only positive in 70–85% of persons with bacterial meningitis who have not received antimicrobial therapy prior to lumbar puncture.[6,7,8] Microbiological diagnostic tests such as culture, Gram stain, polymerase chain reaction, latex agglutination and immunochromatographic antigen testing can confirm the diagnosis of bacterial meningitis but, when negative, cannot rule out bacterial meningitis.[9] Gram stain is more rapid and has good specificity but sensitivity is poor (10–93% depending on the organism and whether or not antibiotics were given prior to CSF collection).[14,16]

This study was done to find out the CSF findings in patients presenting with features of infection of the brain and its meningeal coverings to assess the usefulness of this investigation in the specific diagnosis of such patients.

Materials and Method

This study was carried out in the Holy Family Red Crescent Medical College Hospital. Patients admitted in the different wards from July to December, 2021 and in whom Cerebro-Spinal Fluid examination was done were included in the study. CSF was collected by conventional lumbar puncture and examination of the CSF was done in the pathological laboratory of the hospital.

The CSF was first examined physically and the physical properties noted.

Then Gram stain and ZN staining was done to detect the presence of organisms including Mycobacteria.

Cytological examination was done to detect the type and number of different types of cells in the CSF.

Biochemical examination detected the presence of glucose and protein in the CSF and at the same time peripheral blood was collected and the Random blood sugar estimated.

CSF culture was done in all the patients. Culture for Mycobacteria was not done in any patient.

Amongst special investigations Gene Expert for detection of Mycobacteria and also PCR for Mycobacteria were done in some patients.

The patients were discharged after they improved. They were followed up once after one month and asked to report back again if they had any problem. 6 months after discharge the patients were contacted at the mobile number they provided and their condition noted.

Results

12 patients were included in the study.

Table I. Demographic Data of thePatients and their Chief Complaints.

Patient	Age (yrs)	Sex	Bed No	Address with Mobile number	Chief complaints
1.	18	F	SFG 2	Munshiganj	Low back pain for 10 days. Weakness both lower limbs - 3 days
2.	70	F	ICU 5	Brahmanbaria	Fever, cough, respiratory distress – 7 days. Disorientation – 2 days
3.	18	F	SC - C6	Cox's Bazaar	Fever, Headache – 17 days. Lower abdominal pain – 10 days
4.	19	F	ICU - 8	Brahmanbaria	Fever, headache for 4 days. Unconsciousness for 2 days.
5.	70	F	MF 9	Narsingdhi	Fever 3 days, Severe headache 1 day, Vomiting 3 times, Disoriented 7 hours
6.	50	F	MF 9	Noakhali	Fever for 15 days, Semiconscious for few hours.
7.	70	F	SC – 2/D	Narsingdhi	Fever for 4 days, Altered level of consciousness for 3 days

Table I. Cont'd

Patient	Age (yrs)	Sex	Bed No	Address with Mobile number	Chief complaints
8.	13	M	MM – 1/10	Cumilla 01843885261	Headache and Vertigo for 10 days, Vomiting for several episodes.
9.	40	F	314 C	Noakhali 01741048185	Fever for 3 days, Vomiting several episodes 1 day, Headache and generalized bodyache for 1 day.
10.	70	F	MF 10	East Rampura, Dhaka 01674862125	Fever for 20 days. Unconsciousness from 4 days back
11.	35	M	C - 227	BecharamDeuri, Dhaka01717067660	Unconsciousness for 8 hours, Convulsions for 3 episodes.
12.	55	M	MM - 3/8. ICU - 2A	Hobiganj, Sylhet 01722687898	Disorientation for 3 days. Headache and Fever for 1 day.

Table II. *Examination Findings of the Cerebro - Spinal Fluid (CSF)*

Patient	Physical Appearance			Cytological Report				Microbio-logical Report		Biochemical Report		Blood Sugar
	C	A	CS	Total WBC /cmm	N %	L %	RBCs /cmm	Gram Stain	Z N Stain	Glucose mmol/L	Pro tein Gm/L	mmol /L
1.	W	Cl	Nil	20	10	90	Nil	Nd	Nd	3.4	0.40	6.8
2.	W	Cl	Nil	50	10	90	Nil	Nd	Nd	9.0	0.48	17.8
3.	W	Cl	Nil	50	10	90	Nil	Nd	Nd	3.9	0.18	6.6
4.	W	Hazy	Nil	110	25	75	160	Nd	Nd	4.5	2.63	7.3
5.	W	Cl	Nil	60	15	85	40	Nd	Nd	6.8	1.88	12.7
6.	Red-dish	Hazy	Nil	30	30	70	950	Nd	Nd	3.8	1.03	6.1
7.	Red-dish	Hazy	Nil	100	10	90	Plenty	Nd	Nd	8.0	4.25	10.4
8.	W	Cl	Nil	620	75	25	100	Nd	Nd	4.3	1.72	7.8
9.	W	Cl	Nil	140	10	90	Nil	Nd	Nd	2.2	186.0	5.8
10.	W	Cl	Nil	100	20	80	20	Nd	Nd	2.4	2.1	6.1
11.	Straw	Hazy	++	300	90	10	100	Nd	Nd	3.4	3.0	10.1
12.	Red-dish	Hazy	Nil	200	20	80	600	Gram staining of smear shows some gram -ve diplococci within neutrophils, suggestive of meningococci	Nd	6.5	1.70	

C=Colour; A=Appearance; CS=Clot or Sediment; W=Watery; Cl=Clear N=Neutrophil; L= Lymphocytes; Nd=Not detected; Ng=No growth; PCR-M=Polymerase Chain Reaction for Mycobacteria; CSF Culture=CSF Cu; aom – after one month; ADL – Activities of Daily Living; Treatment=Trt.

Table III. Final Diagnosisand Result of Treatment

Patient	Special Reports	Clinical Diagnosis	Final Diagnosis	Follow up	Result of Treatment
1.	PCR -M: Nd	GBS	AMAN variety GBS	29.10.21 aom	Can walk with help. Some residual disability present
2.		Ischaemic Stroke with Lhp, DM, Encephalitis	Ischaemic Stroke with Lhp, DM	15.8.21 aom	Was improved with trt. Expired after 6 months - COVID
3.		Meningo-Encephalitis	TB brain.	15.8.21 aom	Continued anti TB trt for 2 yrs. Was improved but developed blindness
4.	CSF Cu -Ng. PCR -M: Nd	Viral Encephalitis	Viral Encephalitis	17.9.21 aom	Improved with trt. No residual disability
5.		Meningo Encephalitis DM, Hypt	Viral Encephalitis	17.9.21 aom.	Improved with residual disability. Can perform ADL with help.
6.	CSF Cu -Ng	Meningo Encephalitis	Meningo - Encephalitis	29.10.21 aom.	Improved.
7.	CSF Cu -Ng. Malignant cells- Absent	Encephalitis	Encephalitis	17.10.21 aom.	Improved with residual disability. Expired after 4 months at home, cause unknown
8.	MRI & MRV of Brain - NAD	Encephalitis Stroke.	Encephalitis	17.10.21 aom	Improved with normal activities
9.	CSF Cu-Ng.	Meningo-Encephalitis	Tubercular Meningitis	15.11.21 aom	Completely improved after full Anti-TB trt.
10.		Meningo-Encephalitis	Meningo - Encephalitis		Improved. Went off to Canada
11.	CSF Cu-Ng PCR -M: Nd	Meningo-Encephalitis	Meningitis	29.08.21 aom	Improved. No residual disability
12.	CSF Cu -Ng. PCR-M= Nd	Meningo-Encephalitis DM,CKD	Meningococ-cal Meningitis DM, CKD	20.10.21 aom	Improved & discharged. Expired suddenly after 25 days, cause unknown

C=Colour; A=Appearance; CS=Clot or Sediment; W=Watery; Cl=Clear N=Neutrophil; L= Lymphocytes; Nd=Not detected; Ng=No growth; PCR-M=Polymerase Chain Reaction for Mycobacteria; CSF Culture=CSF Cu; aom – after one month; ADL – Activities of Daily Living; Treatment=Trt; Lhp – Left Hemiparesis

Discussion

The Holy Family Red Crescent Medical College Hospital is a multi-disciplinary 720 bedded hospital situated in the heart of Dhaka City. It is one of the oldest high profile private hospital of Dhaka, established in the year 1954. Initially it was the choice institution for obtaining healthcare for the upper echelon of the society, but with the advent of the more posh private medical institutions, it has been relegated to the second division and now mostly caters to the need of the middle class people of the society. Apart from the major Medicine, Surgery, Gynae & Obstetrics, Pediatrics units, sub-specialty units are also available mostly for medicine.

In this study, all patients admitted in the Holy Family Red Crescent Medical College Hospitalfrom July to December 2021 and in whom cerebrospinal fluid examination was done were included. The patients

were followed up during their stay in the hospital and after discharge when they came for follow up mostly one month after discharge. 6 months after discharge the patient was contacted by the mobile number provided by them during hospitalization to know about the general condition of the patient.

Table I shows that 9 of the 12 patients (75%) were female. It is difficult to explain the preponderance of females in this study. 4 patients were below the age of 20 years and the other 8above 35 years, with 4 patients being 70 years old.

Physical Appearance of the CSF

Normal CSF is crystal clear. However, as few as 200 white blood cells (WBCs) per mm^3 or 400 red blood cells (RBCs) per mm^3 will cause CSF to appear turbid.[10] Xanthochromia is a yellow, orange, or pink discoloration of the CSF, most often caused by the lysis of RBCs resulting in hemoglobin breakdown to oxyhemoglobin, methemoglobin, and bilirubin. Discoloration begins after RBCs have been in spinal fluid for about two hours, and remains for two to four weeks.[11] In this study in 8 of the 12 patients the colour of the CSF was clear watery CSF. Out of these 8 patients 5 had WBCs ≤60, 1 had 620 and the other 2 had 100 and 110. Out of these 8 patients one had RBCs 160, another 100 and the other 2, 40 and 20, and the rest 4 had no RBCs. In 3 patients the colour was Reddish and in these patients the number of RBCs were 600, 950 and plenty. The appearance of CSF in 7 patients was crystal clear. Out of these 7 patients, 4 had no RBCs, while 2 patients had 20 and 40 RBCs and one had 100. The appearance of the CSF was Hazy in 5 patients. In all these 5 patients the number of RBCs were ≥100.

Cytological Examination of the CSF

Eighty-seven percent of patients with bacterial meningitis will have a WBC count higher than 1,000 per mm^3, while 99 percent will have more than 100 per mm^3. Having less than 100 WBCs per mm^3 is more common in patients with viral meningitis.[12]

In this study 5 patients had total WBCs < 100/cmmbut ≥20/cmmin the CSF, none of the patient had a WBC count > 1000/cmm^3 and 7 patients had a CSF count between 100 and 1000/cmm.

Peripheral blood in the CSF after a "traumatic tap" will result in an artificial increase in WBCs by one WBC for every 500 to 1,000 RBCs in the CSF. This correction factor is accurate as long as the peripheral WBC count is not extremely high or low. A traumatic tap occurs in approximately 20 percent of lumbar punctures.

The WBC count seen in normal adult CSF is comprised of approximately 70 percent lymphocytes and 30 percent monocytes. Occasionally, a solitary eosinophil or polymorphonucleocyte (PMN) will be seen in normal CSF.

Lymphocytosis is seen in viral, fungal, and tuberculous infections of the CNS, although a predominance of PMNs may be present in the early stages of these infections. CSF in bacterial meningitis is typically dominated by the presence of PMNs. However, more than 10 percent of bacterial meningitis cases will show a lymphocytic predominance, especially early in the clinical course and when there are fewer than 1,000 WBCs per mm^3.

In this study the lymphocyte count was 90% in 5 of the patients, and between 70 and 90 % in 5 patients. The other 2 had 10% and 20% lymphocytes. In one patient who was diagnosed as suffering from Meningococcal meningitis, there were 600 RBCs/cmm and 200 WBCs/cmm in the CSF out of which 80% were lymphocytes and 20% were neutrophils.

Microbiological Examination of the CSF

Gram stain is positive in 60 to 80 percent of untreated cases of bacterial meningitis and in 40 to 60 percent of partially treated cases. The sensitivity according to the causative organism ranges from 90 percent in pneumococcal or staphylococcal meningitis to less than 50 percent in Listeria meningitis. Hyphae can occasionally be seen in Candida or other fungal meningitis case.

Several factors influence the sensitivity of Gram stain. Laboratory techniques used to concentrate and stain CSF can greatly influence reliability. Cytocentrifugation increases the ability to detect bacteria.[13] Greater numbers of colony-forming units (CFU) per mm^3 of CSF increase the likelihood of a positive result. Staining will be positive in 25 percent of cases if fewer than 1,000 CFU per mm^3 are present, and in 75 percent of cases if more than 100,000 CFU per mm^3 are present. Lastly, the experience of laboratory personnel is very important. Up to 10 percent of initial Gram stains are misread.[14]

In this study no organisms were detected by gram staining in 11/12 patients. 10 patients had already started taking antibiotics 2 to 4 days before coming to

the hospital, which could have decreased the chances of detecting organisms by gram staining. In only one patient gram staining of the CSF showed some gram -ve diplococci within neutrophils, which was suggestive of meningococci. This patient was treated as a case of Meningococcal meningitis and the patient improved with treatment.

Acid-fast staining should be done if tuberculosis is clinically suspected. Only 37 percent of initial smears will be positive for acidfast bacilli. This result can be increased to 87 percent if four smears are done.[15] Sensitivity can also be increased by examining the CSF sediment.[16]

Acid-fast staining was also done in all the 12 patients in this study but no AFB was detected in any slide. 2 patients were diagnosed as Tubercular Meningitis and was cured with full course of anti-tuberculous treatment.

Biochemical Examination of the CSF

CSF Protein

The adult range of 18 to 58 mg per dL (0.18 to 0.58 g per L) is reached between six and 12 months of age.[17] Elevated CSF protein is seen in infections, intracranial hemorrhages, multiple sclerosis, Guillain Barré syndrome, malignancies, some endocrine abnormalities, certain medication use, and a variety of inflammatory conditions. Protein concentration is falsely elevated by the presence of RBCs in a traumatic tap situation. This can be corrected by subtracting 1 mg per dL (0.01 g per L) of protein for every 1,000 RBCs per cmm.[18] This correction is only accurate if the same tube is used for protein and cell counts.CSF protein levels do not fall in hypoproteinemia.

In this study, only 3 patients had CSF protein less than 0.58 gm/L. In these 3 patients the CSF was watery in colour and clear in appearance. RBCs were nil and WBCs were d" 50/cmm. The highest amount of protein detected in the CSF in this study was 4.25 gm/L and in this patient the colour of CSF was Reddish, appearance was Hazy, RBCs were plenty and WBCs were 100/cmm. In another patient the protein was 3 gm/L and in this patient the colour was straw, appearance was hazy, RBCs were 100 and WBCs were 300 and sediment was present ++. In the patient who had RBCs 950, and WBCs 30, the protein was 1.03 gm/L, and in the patient who had RBCs 600 and WBCs 200 the protein was 1.0 gm/L.

CSF Glucose

A true normal range cannot be given for CSF glucose. As a general rule, CSF glucose is about two thirds of the serum glucose measured during the preceding two to four hours in a normal adult. This ratio decreases with increasing serum glucose levels. CSF glucose levels generally do not go above 300 mg per dL (16.7 mmol per L) regardless of serum levels.[9]

CNS infections can cause lowered CSF glucose levels, although glucose levels are usually normal in viral infections. Normal glucose levels do not rule out infection, because up to 50 percent of patients who have bacterial meningitis will have normal CSF glucose levels.

Elevated level of glucose in the blood is the only cause of having an elevated CSF glucose level. There is no other pathologic process that causes CSF glucose levels to be elevated.

In the 12 patients of this study the CSF glucose was not markedly reduced in any patient. 2 patients had CSF glucose less than 2.5 mmol/L and the corresponding blood sugar was 5.8 and 6.1 in these two patients. One of them was diagnosed as Tubercular meningitis and the other as viral meningo-encephalitis. The highest CSF Glucose was 9 mmol/L in one patient and his corresponding blood sugar was 17.8 mmol/L. In another patient the CSF Glucose was 8 mmol/L and the corresponding blood sugar was 10.4 mmol/L. In most of the other patients the CSF Glucose was proportionately less than the corresponding blood sugar.

CSF Culture

Cultures done on 5 percent sheep blood agar and enriched chocolate agar remain the gold standards for diagnosing bacterial meningitis. Antibiotic treatment prior to lumbar puncture can decrease the sensitivity of culture, especially when given intravenously or intramuscularly.[19]

Mycobacterium tuberculosis is best grown using multiple large volume samples of CSF. At least 15 mL and preferably 40 to 50 mL of CSF are recommended. Culture is positive 56 percent of the time on the first sample, and improved to 83 percent of the time if four separate samples are cultured. These cultures often take up to six weeks to bepositive.[20]

In this study CSF culture was done in six patients, all of them were negative. All these patients had already started different broad-spectrum antibiotics before

coming to the hospital which could have decreased the CSF culture positivity.

CSF culture for Mycobacterium tuberculosis was not done for any patient in this study.

PCR Examination of the CSF

Polymerase chain reaction (PCR) has been a great advance in the diagnosis of meningitis. PCR has high sensitivity and specificity for many infections of the CNS, is fast, and can be done with small volumes of CSF. Although testing is expensive, there is a potential for cost savings by decreasing overall diagnostic testing and intervention. PCR has been especially useful in the diagnosis of viral meningitis,in which patients the sensitivity is 95 to 100 percent, and a sensitivity of 100 percent for herpes simplex virus type 1, Epstein-Barr virus, and enterovirus.

PCR has a sensitivity of 54 to 100 percent and a specificity of 94 to 100 percent for tuberculous meningitis, and could replace acid-fast bacillus smear and culture as the test of choice.[21] PCR is sensitive for acute neurosyphilis but not for more chronic forms. PCR also is being studied as a diagnostic tool for bacterial meningitis and other infections of the CNS.

In this study PCR for Mycobacteria was done in 4 patients out of the 12, and all of them were negative. In this study only one patient was diagnosed as Tubercular Meningitis but in that patient PCR was not done. In our country PCR is only done to diagnose Tuberculosis. PCR for diagnosis of Viral and other bacterial infections is generally not available in our country.

Conclusion:

In this study 12 patients whose CSF was studied were included. Final diagnosis of the patients was made on the basis of the clinical manifestations and the results of the tests done of the CSF. All the patients improved with treatment in the hospital and were discharged in a stable condition. At the follow-up after 6 months, 3 patients had died and 9 patients were alright. All the 3 patients had died at home and no exact cause of death could be ascertained. 1 patient died 25 days after discharge, one after 3 months and 1 after 6 months. Of the 9 patients who survived, four had residual disability though all of them could perform the activities of daily living independently.

This study shows that patients admitted with features suggestive of infection of the Central Nervous system or its covering membranes, had a good prognosis as all of them improved with treatment in the hospital and could be discharged in a stable condition. The examination and investigation of the CSF played a major part in the diagnosis of these patients. Thus examination of the CSF should be done at the earliest possible time after admission in a hospital so that a specific diagnosis can be made and the appropriate treatment started as soon as possible.

References

1. Hasbun R. Progress and Challenges in Bacterial Meningitis A Review. JAMA 2022;328(21):2147-2154. doi:10.1001/jama.2022.20521
2. van de Beek D, Brouwer MC, Koedel U, Wall EC. Community-acquired bacterial meningitis. Lancet. 2021;398(10306):1171-1183. doi:10.1016/S0140-6736(21)00883-7
3. GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1151-1210. doi:10.1016/S0140-6736(17)32152-9
4. Hasbun R. Update and advances in community acquired bacterial meningitis. Curr Opin Infect Dis. 2019;32(3):233-238. doi:10.1097/QCO. 0000000000000543
5. Kietzman C, Tuomanen E. Acute Bacterial Meningitis: Challenges to Better Antibiotic Therapy. ACS Infect Dis 2019 Dec 13;5(12):1987-1995. DOI: 10.1021/acsinfecdis.9b00122 Epub 2019 Jul 3.
6. Leber AL, Everhart K, Balada-Llasat JM, et al. Multicenter evaluation of BioFire FilmArray meningitis/encephalitis panel for detection of bacteria, viruses, and yeast in cerebrospinal fluid specimens. J Clin Microbiol 2016;54(9):2251–261.
7. Shokrollahi MR, Shabanzadeh K, Noorbakhsh S, et al. Diagnostic value of CRP, procalcitonin, and ferritin levels in cerebrospinal fluid of children with meningitis. Cent Nerv Syst Agents Med Chem 2018;18(1):58–62.
8. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis 2004;39(9):1267–84.
9. CN van Ettekoven, D van de Beek, MC Brouwer. Update on community-acquired bacterial meningitis: guidance and Challenges. Clinical Microbiology and Infection 2017;23:599 - e600.

10. Seehusen DA, Reeves MM, Fomin DA. Cerebrospinal Fluid Analysis. Am Fam Physician 2003;68:1103-08.

11. Dougherty JM, Roth RM. Cerebral spinal fluid. Emerg Med Clin North Am 1986;4:281-97.

12. Fishman RA. Cerebrospinal fluid in diseases of the nervous system. 2d ed. Philadelphia: Saunders, 1992.

13. Kaplan SL. Clinical presentations, diagnosis, and prognostic factors of bacterial meningitis. Infect Dis Clin North Am 1999;13:579-94.

14. Pruitt AA. Infections of the nervous system. Neurol Clin 1998;16:419-47.

15. Niu MT, Duma RJ. Meningitis due to protozoa and helminths. Infect Dis Clin North Am 1990;4:809-41.

16. Leonard JM, Des Prez RM. Tuberculous meningitis. Infect Dis Clin North Am 1990;4:769-87.

17. Conly JM, Ronald AR. Cerebrospinal fluid as a diagnostic body fluid. Am J Med 1983;75(1B):102-08.

18. Dougherty JM, Roth RM. Cerebral spinal fluid. Emerg Med Clin North Am 1986;4:281-97.

19. Wubbel L, McCracken GH Jr. Management of bacterial meningitis:1998. Pediatr Rev 1998;19(3):78-84.

20. Zunt JR, Marra CM. Cerebrospinal fluid testing for the diagnosis of central nervous system infection. Neurol Clin 1999;17:675-89.

21. Garcia-Monco JC. Central nervous system tuberculosis. Neurol Clin 1999;17:737-59.

Detection of Carbapenemase Producing Enterobacteriaceae by Modified Hodge Test in Rajshahi Medical College Hospital

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Keywords:
Carbapenemase, Enterobacteriaceae, Modified Hodge Test, Carbapenem resistant.

Abstract

Background: *Carbapenem drugs are used as last resort antibiotic for the treatment of extended spectrum beta-lactamase (ESBL) and AmpC beta lactamase enzyme producing gram negative bacteria. But some bacteria produce carbapenemase enzymes and hydrolyze these drugs. Carbapenamase genes are present on plasmid and these plasmid can contain other drug resistant gene also as well as these plasmid can transfer to other bacteria of the same or different species. So extended drug resistant bacteria originate and disseminate. Misuse of antibiotics have a role for these purposes which cause gene mutation and appearance of new mechanism of drug resistant. Members of enterobacteriaceae are gram negative bacteria and many of them are normal flora of human colon and can easily be spread among human. So, carbapenemase producing enterobacteriaceae can disseminate in the hospital and make infection control difficult. There are a few antibiotics remaining for the control of infection with such type of bacteria. So, early detection of these enterobacteriaceae and rational use of antibiotics are essential for infection control in hospital.*

Aims and objectives: *The aim of this study is to identify carbapenemase producing enterobacteriaceae which would help proper infection control.*

Materials and methods: *A descriptive type of study was carried out for the detection of carbapenemase producing enterobacteriaceae members in the department of Microbiology, department of Surgery and its allied branches of Rajshahi Medical College and Hospital. A total 233 enterobacteriaceae were isolated from wound swab and antibiogram were done using standard procedure between January 2014 to Decmber 2014. The enterobacteriaceae isolates which showed resistant to both meropenem (Zone of inhibition d" 22mm) and ceftriaxone were studied for the detection of carbapenemase production by Modified Hodge test(MHT).*

Results: *Within 152 meropenem and ceftriaxone resistant isolates 47 (30.92%) showed carbapenemase production by MHT. The species distribution amongcarbapenemase producer were*Escherichia coli*68.08%,* Proteus *spp. 12.77%,* Enterobacter *app. 17.02%,* Klebsiella *app. 02.12% and* Providentia *spp. 0.00%*

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Introduction:

Carbapenemase enzymes producing gram negative bacterial infection is an everyday's challenge for the clinicians to combat with. In the last two decades, gram negative bacteria gain more importance than gram positive bacteria regarding this problem.[1,2] The prevalence of carbapenemase producing bacteria in France is 3%- 5% and in India more than 80%.[3]

Clinicians often use beta-lactum drugs like penicillin, cephalosporin, monobactum etc for infection control. But extended spectrum beta-lactamase (ESBL) and AmpC beta-lactamase producing gram negative bacteria are resistant to those antibiotics in most cases now. Thus, carbapenem group of beta-lactum drugs i.e imipenem, meropenem, doripenem, itrapenem etc are now used as last resort antibiotics for controlling gram negative becterial infection.[4] But many members of gram negative bacteria again becomes resistant to carbapenem antibiotics by producing carbapenem hydrolyzing carbapenemase enzymes besides

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modification of membrane permeability, excessive drug efflux or by producing certain ESBL or AmpC beta-lactamase with increase carbapenem hydrolyzing capacity. These occur most often due to gene mutation by misuse of antibiotics.[5]

There are three classes of carbapenemase enzymes belonging to Ambler classification of beta-lactamase enzymes such as class A, class B and class D.[6] Class A carbapenamase include *Klebsiella pneumoniae* carbapenemase (KPC), *Serratia marcescens* enzyme (SME), in Imipenem hydrolyzing enzyme (IMI) etc. KPC are the most common and found mostly from *Klebsiella pneumoniae*and to a lesser extent from Escherichia coli and other enterobacteriaceae species. Class B carbapenemase include Active on imipenem (IMP) carbapenemase, Verona-Integron encoded beta-lactamase (VIM), New Delhi metallobeta-lactamase (NDM) etc. These enzymes mainly produced by *Klebdiella pneumoniae*, *Escherichia coli (E. coli)*, *Serratia* spp. and other enterobecteriaceae species. Oxa-48, Oxa-181 etc are class D carbapenemase and produced mainly by *Klebsiella pneumoniae* & *Escherichiacoli*.[7] Death rate among KPC producing bacterial infection attributed to 50% and that of the MBL producers infection is 18%-64% whereas that in case of OXA-48 is unknown.[7–9]

Enterobacteriaceae is a group of gram negative becteria among others. Many members of enterobacteriaceae are normal flora of colon and cause various infection as wound infection, urinary tract infection, peritonitis, meningitis, pneumonia, septicaemia etc. They can spread easily among human by hand contact and by contaminated food and water. They carries the gene for carbapenemase enzymes mainly on their plasmid. So, they have the capacity to transmit it to other bacteria of same or different species by conjugation and contribute drug resistant transfer. These phenomenon occurs mainly in hospitals and its surrounding environment. The bacteria carries genes for carbapenemase enzymes may also carry other drug resistant gene in their plasmid resulting in extended drug resistant (XDR) highly virulent bacteria. There are a few antibiotics against such type of bacteria.[6,10,11]

Bacteira producing carbapenemase enzyme can be detected by molecular methods and enzyme detection methods. Molecular methods are polymerase chain reaction (PCR), DNA sequencing, iso-electric focusing, spectrophotometry etc.[12] Enzyme detection methods include Modified Hodge test(MHT), double disc synergy test, combined disc test, EDTA-imipenem microdilution MIC test, E-test, MBL strip test etc. Molecular methods detect carbapenemase enzyme encoding gene but enzymatic methods detect carbapenemase enzyme activity. MHT is a CLSI recommended low cost enzyme detection method and it can easily be performed in every microbiology laboratory fascilities.[13]

Objectives:

The aim of the study was to identify carbapenemase producing enterobacteriaceae in Rajshahi Meidcal College Hospital. This would help in early detection of these resistant pathogen, early start of proper treatment and their effective control.

Materials and methods

Total 233 enterobacteriaceae were isolated from wound swab in microbiology laboratory in Rajshahi Medical College during the period of January, 2014 to December, 2014. Standard methods were employed for the collection of sample and isolation and identification of the organism. The identified enterobacteriaceae were studied for drug sensitivity by modified CarbyBauer disc diffusion method on Muller-Hinton agar media. Antibiotic disc were Meropenem (10 µg), Ciprofloxacin (5 µg), Levofloxacin (5 µg), Ceftriaxone (30 µg), Aztreonam (3 µg), Gentamycin (10 µg), Amicacin (30 µg), Azythromycin (15 µg), Collistin (10 µg) and Cloramphenicol (30 µg). Zone of inhibition was detected by CLSI, 2012 recommendation and technical data of Hi-media, 2012. The isolated enterobacteriaceae which showed zone of inhibition to meropenem d" 22 mm and resistant to cephtriaxone were considered as carbapenemase producing enterobacteriaceae. The carbapenemase producer were confirmed by MHT.[13,14]MHT can detect carbapenemase producers with sensitivity and specificity of 94% and 100% respectively.[15]

Procedure of Modified Hodge test: 5 ml inoculum of *E.coli* (ATCC 25922) was prepared and standardized by 0.5 McFarland standard. The inoculum was diluted 1:10 by adding 4.5 ml of sterile normal saline. The diluted inoculum was spread on Muller-Hinton agar plate with cotton swab and allowed to dry in air for 3-10 minutes then an Imipenem (10 µg) disc was placed at the centre of the plate. A straight line was drawn with the help of inoculating wire loop containing identified test bacteria from margin of the

disc to the end of the Muller-Hinton agar plate. 4 identified test bacteria were tested in a single Muller-Hinton plate and incubate overnight at 37p C. Reading was taken after 24 hrs to see clover-leaf type of indentation at the intersection of the test bacteria and the *E. coli* (ATCC 25922) within the zone of inhibition. Positive result was indicated by presence of clover-leaf like indentation of the *E.coli* (ATCC 25922) along the streak line of test bacteria within the zone of inhibition. Negative result showed no growth of *E. coli* (ATCC 25922) along the test bacterial streak within the zone of inhibition. Indeterminate result showed by inhibition of the growth of *E. coli* (ATCC 25922) around the streak line of test bacteria.[4,16]

Result:

A total 233 enterobecteriaceae was isolated among them *E. coli* 122 (52.35%), *Proteus* spp. 54 (23.17%), *Enterobecter* spp. 37 (15.88%), *Klebsiella* spp. 14 (6.00%) and *Providentia* spp. 6 (2.58%). Within those enterobacteriaceae both Meropenem and Ceftriaxone resistant were 152 (65.24%) where *E. coli* 70.49% (86/122), *Proteus* spp. 51.85% (28/54), *Enterobecter* spp. 72.97% (27/37), *Klebsiella* spp. 57.14% (8/14) and *Providentia* spp. 50.00% (3/6). Carbapenemase producer among these resistant isolates were 30.92% (47/152) and the species distribution among them were *E. coli* 37.21% (32/86), *Proteus* spp. 21.43% (6/28), *Enterobecter* spp. 29.63% (8/27), *Klebsiella* spp. 12.50 % (1/8) and *Providentia* spp. 0.00% (0/3). Distribution of carbapenemase producing enterobacteriaceae species within total carbapenemase producing enterobacteriaceae were *E. coli* 68.08% (32/47), *Proteus* spp. 12.77% (6/47), *Enterobacter* spp. 17.02% (8/47), *Klebsiella* spp. 2.12% (1/47) and *Providentia* spp. 0.00 % (0/47).

Table I: *Enterobacteriaceae species isolated from wound swab*

Organism isolated	Numbers	Percentage
E.coli	122	52.35%
Proteus spp.	54	23.17%
Enterobacter spp.	37	15.88%
Klebsiella spp.	14	6.00%
Provindentia spp.	6	2.58%
Total	233	100%

Table II : *Organism resistant to Meropenem and both Meropenem and Ceftriaxone:*

Organism	Meropenem resistant	Meropenem+Ceftriaxone resistant
E.coli (N=122)	88 (72.13%)	86 (70.49%)
Proteus spp.(N=54)	30 (55.55%)	28 (51.85%)
Enterobacter spp.(N=37)	27(72.97%)	27 (72.97%)
Klebsiella spp. (N=14)	8(57.14%)	8 (57.14%)
Provindentia spp.(N=06)	3(50%)	3 (50%)
Total (N=233)	156 (66.95%)	152 (65.24%)

N=Number

Table III : *Carbapenemase producing enterobacteriaceae isolates among Meropenem+ Ceftriaxone resistant isolates*

Number of resistant organisms	Number of Carbapenemase producing organisms	Percentage
E.coli (N=86)	32	37.21%
Proteus spp.(N=28)	06	21.48%
Enterobacter spp.(N=27)	08	29.63%
Klebsiella spp. (N=08)	01	12.50%
Provindentia spp.(N=03)	00	00.00%
Total (N=152)	47	30.92%

N=Number

Table IV: *Distribution of Carbapenemase producing enterobacteriaceae isolates among total carbapenemase producing enterobacteriaceae.*

Name of the organisms	Total number of Carbapenemase producers	Percentage
E.coli (N32)	47	68.08%
Proteus spp.(N=06)		12.77%
Enterobacter spp.(N=08)		17.02%
Klebsiella spp. (N=01)		02.12%
Provindentia spp.(N=00)		00.00%

N=Number

Figure 1: *Positive result shows by bacteria of 4R striking line in Modified Hodge test.*

Discussion:

Enterobacteriaceae are resistant to carbapenem drugs due to production of carbapenemase enzymes, increase membrane permeability, excessive drug efflux and by production of ESBL or AmpC beta-lactamase enzymes with increase carbapenem hydrolysing capacity. In our study isolated enteriobacteriaceae showed resistant to carbapenem drugs was 66.95%.In a similar study at Franch by Birgy A et al, 2012 [17]showed Meropenem resistant 53.33% which is nearly similar to our study. A study in Dhaka by Noorjahan Begum and S.M. Shamsuzzaman[18] and a study in Mumbi, India by Nair P.K. and Vaz M.S.[19]showed the prevalence of carbapenem resistant was 14.49% and 12.26% respectively which are much lower than our study. In another study by Priyadarshini Shanmugam et al, 2013in Chennai, India[20] showed 93.4% enterobacterioceae were resistant to Meropenem which is much higher than our study. The dissimilarities between different studies may be due to the random use of 3rd generation cephalosporins and carbapenem without culture and sensitivity which leads to the emergence of resistance to them and their dissemination throughout the hospital. This dissimilarities may also be due to inadequate measure taken to prevent the spread of resistant pathogen, no antibiotic policy in our hospital and inadequate antibiogram of imperical antibiotic therapy.

In our study, 30.92% of isolated enterobacteriaceae was detected carbapenemase producer by Modified Hodge test which is nearly similar to a study in Hyderabad, India where Ramana KV. et al, 2013[21] showed carbapenemase production in enterobacteriaceae was 35.9%. Our study is also similar to a study of Cury AP et al, 2012 in Brazil[22] and that showed carbapenemase production within carbapenem resistant isolates were 35.46% by Modified Hodge test. But our study is dissimilar with the study of Priyadarshini Shanmugam et al, 2013[20] and Arend et al, 2015[23] who reported 82.6% and 83.23% isolates were positive by MHT which are much higher in comparison to our study.

In our study carbapenemase production within carbapenem resistant isolates of same enterobacteriaceae species were *E.coli* 37.21%, *Proteus* spp. 21.43%, *Enterobacter* spp. 29.63%, *Klebsiella* spp. 12.50% and *Provindentia* spp. 00.00% which is dissimilar with the study of Priyadarshini Shanmugam et al, 2013 in Chennai, India[20] who found *E. coli* 80.95%, *Proteus* spp. 100%, *Klebsiella* spp. 86.36% and *Citrobacter* spp. 50% And with a study of Anita E. et al, 2016 in Rajasthan, India[24] who showed E.coli 66.7% *Klebsiella* spp.78.6 % and *Enterobacter*spp

100% where*Proteus* spp and *Citrobacter* app.were not resistant to carbapenem which are also dissimilar with our study. In our study the species distribution among the enterobacteriaceae isolates which produces carbapenemase by MHT were *E.coli* 68.08%, *Proteus* spp. 12.77%, *Enterobacter* spp.17.02% *Klebsiella* spp. 2.12% and *providentia* spp. 0.00%. In a similar study by Ramana KV. et al, 2013 from Hyderabad, India[21] showed *E.coli* 19.28%, *klebsiella* spp. 40.61%, *Proteus* spp. 4.57%, *Enterobacter* spp. 22.84% and *Citrbacter* spp. 12.69% and Priyadarshini Shanmugam et al, 2013 from Chennai India[20] showed *E.coli* 44.74% *Klebsiella* spp. 50%, *Proteus* spp. 2.63% and *Citribacter* spp. 2.63%. Those study are dissimilar to our study. In another study of Dr. Ph. Henkhoneng Mate et al, 2014 in Monipur, India[28] found *E.coli* was 88.89%, *Klebsiella* spp. 5.55%, *Proteus* spp. 5.55% which is dissimilar to our study. In a study, Bora et al, 2014 at Bharatpur, Nepal[16] found *E.coli* was 51.25% and *klebsiella* spp. 48.75% which is also dissimilar to our study. In the study of Datta et al, 2012 in Chandigarh[25] and Smita sood, 2014 in Joypur, India[26] showed carbapenemase producing *klebsiella-pneumoniae* was 0% and 100% respectively, which are also dissimilar with our study. In the study by Hayder et al, 2012 of Dhaka, Bangladesh[27] and a combind study in India, Pakistan and UK by Kumarassamy K K et al, 2010[1] showed carbapenemase producing *Klebsiellapneumoniae* were 4.8% and 1.7& respectively which are also dissimilar to our study. The dissimilarities may be due to the prevalence of carbapenamese producing gram-negative bacilli varies greatly from country to country and among different institution within the same country.[29] The dissimilarities may also be due to defective culture and sensitivity report and inadequate dose and duration of used antibiotics. Other factors may be organism varies in different geographical location and in different environment as well as sanitation habit of the patients and variation of antibiotic use in different hospital.

Though PCR is the gold standard for carbapenemase producing bacteria detection but we were unable to use that procedure due to lack of facilities. It is the limitation of the study.

References:

1. Kumarasamy KK, Toleman MA, Walsh TR, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: A molecular, biological, and epidemiological study. *Lancet Infect Dis*. 2010;10(9):597-602. doi:10.1016/S1473-3099(10)70143-2
2. Thuan TT. "Future" threat of gram-negative resistance in Singapore. *Ann Acad Med Singapore*. 2008;37(10):884-890.
3. Jean SS, Hsueh PR. High burden of antimicrobial resistance in Asia. *Int J Antimicrob Agents*. 2011;37(4):291-295. doi:10.1016/j.ijantimicag.2011.01.009
4. Haider M, Fatima N, Malik A, Rizvi M, Shukla I. Necessity of detection of extended spectrum beta-lactamase, AmpC and metallo-beta-lactamases in Gram-negative bacteria isolated from clinical specimens. *Muller J Med Sci Res*. 2014;5(1):23. doi:10.4103/0975-9727.128939
5. Noyal MJC, Menezes GA, Harish BN, Sujatha S, Parija SC. Simple screening tests for detection of carbapenemases in clinical isolates of nonfermentative Gram-negative bacteria. *Indian J Med Res*. 2009;129(6):707-712.
6. Queenan AM, Bush K. Carbapenemases: The versatile â-lactamases. *Clin Microbiol Rev*. 2007;20(3):440-458. doi:10.1128/CMR.00001-07
7. Nordmann P, Naas T, Poirel L. Global spread of carbapenemase producing Enterobacteriaceae. *Emerg Infect Dis*. 2011;17(10):1791-1798. doi:10.3201/eid1710.110655
8. Borer A, Saidel-Odes L, Riesenberg K, et al. Attributable Mortality Rate for Carbapenem-Resistant Klebsiella pneumoniae Bacteremia . *Infect Control Hosp Epidemiol*. 2009;30(10):972-976. doi:10.1086/605922
9. Daikos GL, Petrikkos P, Psichogiou M, et al. Prospective observational study of the impact of VIM-1 metallo-â- lactamase on the outcome of patients with Kebsiella pneumoniae bloodstream infections. *Antimicrob Agents Chemother*. 2009;53(5):1868-1873. doi:10.1128/AAC.00782-08
10. Baiden F, Owusu-Agyei S, Webster J, Chandramohan D. The need for new antibiotics. *Lancet*. 2010;375(9715):637-638. doi:10.1016/S0140-6736(10)60265-6
11. Schwaber MJ, Carmeli Y. National Center for Infection Control, Ministry of Health, 6 Weizmann St. *Isr (mitchells @tasmc.health.gov.il) JAMA*. 2008;64239(24):2911.
12. Doyle D, Peirano G, Lascols C, Lloyd T, Church DL, Pitouta JDD. Laboratory detection of Enterobacteriaceae that produce carbapenemases. *J Clin Microbiol*. 2012;50(12):3877-3880. doi:10.1128/JCM.02117-12

13. Miriagou V, Cornaglia G, Edelstein M, et al. Acquired carbapenemases in Gram-negative bacterial pathogens: Detection and surveillance issues. *Clin Microbiol Infect*. 2010;16(2):112-122. doi:10.1111/j.1469-0691.2009.03116.x

14. Amjad A, Ia M, Sa A, Farwa U, Malik N, Zia F. Modified Hodge test/ : A simple and effective test for detection of carbapenemase production The isolates which showed intermediate or susceptible zones for imipenem were tested for carbapenemase Modified Hodge test , as CL recommends the MHT to be perform. 2011;3(4):189-193.

15. Bartolini A, Frasson I, Cavallaro A, Richter SN, Palù G. Comparison of phenotypic methods for the detection of carbapenem non-susceptible Enterobacteriaceae. *Gut Pathog*. 2014;6(1):1-7. doi:10.1186/1757-4749-6-13

16. Bora A, Sanjana R, Jha BK, Narayan Mahaseth S, Pokharel K. Incidence of metallo-beta-lactamase producing clinical isolates of Escherichia coli and Klebsiella pneumoniae in central Nepal. *BMC Res Notes*. 2014;7(1):1-7. doi:10.1186/1756-0500-7-557

17. Birgy A, Bidet P, Genel N, et al. Phenotypic screening of carbapenemases and associated â-lactamases in carbapenem-resistant Entero-bacteriaceae. *J Clin Microbiol*. 2012;50(4):1295-1302. doi:10.1128/JCM.06131-11

18. Begum N, Shamsuzzaman SM. Emergence of carbapenemase-producing urinary isolates at a tertiary care hospital in Dhaka, Bangladesh. *Tzu Chi Med J*. 2016;28(3):94-98. doi:10.1016/j.tcmj. 2016.04.005

19. Nair PK. Prevalence of carbapenem resistant Enterobacteriaceae from a tertiary care hospital in Mumbai, India. *J Microbiol Infect Dis*. 2013;03(04):207-210. doi:10.5799/ahinjs.02.2013.04.0110

20. Shanmugam P, Meenakshisundaram J, Jayaraman P. BlaKPC gene detection in clinical isolates of carbapenem resistant Enterobacteriaceae in a tertiary care hospital. *J Clin Diagnostic Res*. 2013;7(12):2736-2738. doi:10.7860/JCDR/2013/ 7759.3747

21. Ramana K V., Rao R, Sharada C V., Kareem MA, Rajashekar Reddy L, Ratna Mani MS. Modified Hodge test: A useful and the low-cost phenotypic method for detection of carbapenemase producers in Enterobacteriaceae members. *J Nat Sci Biol Med*. 2013;4(2):346-348. doi:10.4103/0976-9668.117009

22. Cury AP, Andreazzi D, Maffucci M, Caiaffa-Junior HH, Rossi F. The modified Hodge test is a useful tool for ruling out klebsiella pneumoniae carbapenemase. *Clinics*. 2012;67(12):1427-1431. doi:10.6061/clinics/2012(12)13

23. Arend LN, Pilonetto M, de Alencar Siebra C, Tuon FF. Phenotypic and molecular characterization of 942 carbapenem-resistant Enterobacteriaceae (CRE) in southern Brazil. *J Infect Chemother*. 2015;21(4):316-318. doi:10.1016/j.jiac.2014.11.011

24. Maheshwari D, Verma D, College GM. Research article detection of carbapenemase producing enterobacteriaceae by modified hodge test anita e . Chand ,. 2016.

25. Datta P. henotypic method for differentiation of carbapenemases in Enterobacteriaceae: Study from north India.pdf.

26. Sood S. Identification and differentiation of carbapenemases in Klebsiella Pneumoniae: A phenotypic test evaluation study from Jaipur, India. *J Clin Diagnostic Res*. 2014;8(7):6-8. doi:10.7860/ JCDR/2014/7027.4614

27. Hayder N, Hasan Z, Afrin S, Noor R. Determination of the frequency of carbapenemase producing Klebsiella pneumoniae isolates in Dhaka city, Bangladesh. *Stamford J Microbiol*. 2013;2(1):28-30. doi:10.3329/sjm.v2i1.15210.

28. Mate, Ph Henkhoneng, et al. "Prevalence of carbapenem resistance among Gram-negative bacteria in a tertiary care hospital in north-east India." *IOSR J Dent Med Sci* 13.12 (2014): 56-60.

29. Balan, K., P. Sireesha, and C. R. Setty. "Study to detect incidence of carbapenemase among Gram negative clinical isolates from tertiary care hospital." *Journal of Dental and Medical Sciences* 1.6 (2012): 08-12.

Role of Polyethylene Plastic Bags for Prevention of Hypothermia in Preterm and Low Birth Weight Infants in a Tertiary Level Hospital in Bangladesh

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Abstract

Background: *Preterm and low birth weight infants have difficulty in maintaining body temperature specially after birth and contributes to a major cause of neonatal mortality and morbidity. Polyethylene plastic bags covering the trunk and extremities reduces hypothermia without causing hyperthermia.The objective was to determine if placing preterm and low birth weight infants inside plastic bags at birth maintains normothermia.*

Methods: *A total 108 infants with gestational age 28 weeks to before 37 weeks and/or with birth weight of 1000 to 2499 grams, born at Labour and Gynae Ward (LGW) of Rajshahi Medical College Hospital during the study period were randomly selected. 54 newborns received standard thermal care and the other 54 were placed under polyethylene plastic wraps.Axillary temperature was measured in the World Health Organization defined normal range (97.7°-99.5°F), or mild, moderate or severe hypothermiaat 1 day after admission and final outcome as discharged healthy or death was documented.*

Result: *Among infants randomized to polyethylene plastic bags,35(64.81%) maintained normothermia, 7(12.96%) developed mild hypothermia, 10(18.52%) moderate and 2 (3.70%) severe hypothermia. In control group, 42(77.78%) infants maintained normothermia, 4(7.40%) developed mild, 5(9.26%) moderate and 3(5.56%) severe hypothermia.Regarding clinical outcome, 47 (87.04%) infants in intervention group were discharged healthy and 7(12.96%) died(p>0.05).In control group, 45 (83.33%) infants were discharged healthy, 1(1.85%) was referred to Paediatric Surgery Department and 8(14.81%) died (p>0.05). None developed hyperthermia.*

Conclusion: *Placing preterm LBW infants inside polyethylene plastic bags soon after birth reduces hypothermia and hypothermia related complications without causing hyperthermia.It is a low-cost and promising intervention in limited resource setting with limited availability of radiant warmers and incubators. Polyethylene plastic bags are not superior tostandard care but can be an alternative in our resource-poor setting.*

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Introduction

Temperature control immediately after birth, especially during resuscitation is particularly important in reducing neonatal mortality & morbidity[1]. In preterm & low birth weight infants, there will be a drop in body temperature unless measures are taken to prevent this heat loss. Current resuscitation guidelines recommend placing the infants under a radiant warmer, drying the skin, removing wet linen & placing on a dry prewarmed blanket to reduce heat loss[2]. Despite these measures preterm very low birth infants are at high risk for cold stress. The EPICURE study showed that with decreasing gestational age, there was a very high incidence of cold stress.[3]Extended period of cold stress can lead to harmful side effects, which include

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hypoglycemia, respiratory distress, hypoxia, metabolic acidosis, coagulation defects, delayed readjustment from fetal to neonatal circulation, acute renal failure, necrotizing enterocolitis, failure to increase weight or weight loss and in extreme cases death[1,4] Rapid postnatal fall on body temperature is attributable to a combination of the physical characteristics of the infant (e.g. large body surface & thin layer of insulating fat) & environmental factors in the delivery suite. Extent of heat loss & the four modes of heat exchange (conduction, convection, radiation & evaporation) are influenced by the ambient air, temperature, pressure and relative humidity and temperature of surrounding surface.[5] Increased rate of heat loss is mainly caused by evaporation of amniotic fluid from the skin surface when the wet newborn moves from the warm environment of uterus into a cool, dry delivery suite.[6]In attempt to maintain core body temperature within normal range, the term infants respond mainly by production of heat from breakdown of brown fat & peripheral vasoconstriction.[7] When skin temperature falls to 35-36°C, non-shivering thermogenesis is initiated. The preterm infant has the combined disadvantages of decreased fat for heat production and insulation, decreased glycogen stores, immature skin which increases water loss & poor vascular control. They experience even higher evaporative heat losses than term infants in the first day especially at low ambient relative humidity.[8]

It is thought that the plastic bags reduce evaporative & convective heat loss, insensible water loss & the need for metabolic heat production.[9,10] The International Liaison Committee on Resuscitation consensus statement recommends the use of a plastic bag in the delivery room for very low birth weight infants[11] So in our poor country it is possible that the addition of the plastic bag to standard WHO thermoregulation care may be an effective intervention to decrease the rate of hypothermia in preterm LBW infants where others facilities like incubator, radiant warmers are not so available. There are not so many studies done in Bangladesh in this perspective. So this study was done to determine if placing preterm low birth weight infants in polyethylene plastic bags after birth reduces hypothermia and thus reduces hypothermia related mortality and morbidities.

Materials and Methods

This study was conducted at Special Care Neonatal Unit (SCaNU) of Department of Paediatrics, Rajshahi Medical College Hospital (RMCH),Rajshahi, Bangladesh from 01 February 2014 through 31 July 2014. A total of 108 babies born before 37 completed weeks of gestation, in LGW with birth weight between 1000 to 2499 grams, age less than 24 hours and whose parents gave informed written consent for the study, were selected for the study. After admission, the infants were randomized into control (n=54) and intervention group (n=54) by simple random sampling.

All infants were weighed first and axillary temperature was recorded by clinical thermometer and thorough clinical examination was done. Then the infants of control groupreceived standard hospital care that is providing warm room, immediate drying and resuscitation under radiant warmers or placing inside incubators. Infants of the intervention group, after immediate drying and resuscitation, were placed inside a plastic bag (nonmedical polyethylene plastic bags measuring about 400×250×1mm costing about taka 20 (US$ 0.20) per piece) covering trunk and extremities up to neck. A woolen linen was provided beneath the plastic bags to prevent skin excoriation; head and hands and feet were covered with woolen cap and socks respectively. Auscultation was done over the bag and had umbilical access been required, a hole was made in the bag to provide access.

For recording axillary temperature, the clinical thermometer was placed high in the axilla and the arm then held against the side of the baby for 2 minutes.Then the recorded temperaturewas categorized as normothermia (97.7°-99.5° F), mild (96.8°-97.52° F), moderate (89.6°-96.6° F) and severe hypothermia (<89.6° F)[12].

Axillary temperature and other vital parameters were recorded every day 4 hourly at 6 am, 10 am, 2 pm, 6 pm, 10 pm and any time when sign of hypothermia and other features of complications like brady- or tachycardia, apnoea or tachypnea, prolong CRT (capillary refill time), convulsion, vomiting or abdominal distension developed and were managed accordingly. Infants in the intervention group received with hypothermia were first tried with using table lamp with 200-watt bulb to maintain normothermia and then wrapped in plastic bags. This technique was also applied anytime whenever they developed hypothermia after wrapping in.

Blood samples (Hb%, TC, DC, CRP) were sent on 2nd day of admission and CBG (capillary blood glucose) was done immediately after admission. Other investigations like serum bilirubin, blood grouping and blood C/S and plain X-ray abdomen were done according to patient's clinical condition. All serological investigations were done from the Department of Pathology, RMC and X-ray from the Department of Radiology, RMCH. Babies' weight was

recorded daily and OFC weekly. Gestational age was assessed by the last menstrual period or from early ultrasound scans in the 1st trimester and clinically by new Ballard score. Maternal information like age, antenatal care, and complications during pregnancy was ascertained by history and pathology records.

The numerical data obtained from the study were analyzed by computer using Statistical Programs for Social Science (SPSS, Version 15.0) and the results were presented in tables, graphs & charts.

The protocol was approved by the Ethical Committee of Rajshahi Medical College, Rajshahi, Bangladesh and informed written consent was taken from the guardians of the patients before collection of their samples.

Results

A total of 108 infants were enrolled in this study. The baseline characteristics of neonates randomized to the intervention and control groups were almost similar. 8(14.81%) neonates in intervention group had gestational age within 28-30 weeks, 18 (33.33%) within 31-33 weeks and 28 (51.85%) within 34-37 weeks.

Table I. Baseline characteristics of study population

Characteristics	Intervention group (n=54)	Control group (n=54)	Probability
Gestational age (weeks)	33.2±2.1	33.1±1.7	p>0.05
Birth weight (grams)	1800±415	1740±402	p>0.05
Sex (M/F)	(24:30)	(24:30)	
Mode of delivery	36 (66.67%)	32 (59.26%)	p>0.05
Multiple birth (twin)	9 (16.67%)	8 (14.81%)	p>0.05
Maternal age	23±4.8	23.9±5.2	p>0.05
Antenatal care	39 (72.22%)	33 (61.11%)	p>0.05
Admission age in hour	6.3±5.8	4.7±3.4	p>0.05
Axillary temperature on admission	95.3±1.5	95±1.3	p>0.05

After 1 day of admission, among 8 neonates in 28-30 weeks of gestational age group, 1 (12.5%) developed mild, 4 (50%) developed moderate and 2 (25%) developed severe hypothermia. In 31-33 weeks of gestational age group, among 18 neonates, 3 (16.6%) developed mild and 6 (33.33%) developed moderate hypothermia; in 34-<37 weeks of gestational age group, among 28 neonates, 3 (10.71%) developed mild hypothermia.

Table II. Distribution of temperature Maintenance according to gestational age after 1 day of admission in intervention group

Gestational age	Frequency	Normothermia	Mild hypothermia	Moderate hypothermia	Severe hypothermia
28-30 weeks	8	1 (12.5%)	1 (12.5%)	4 (50%)	2 (25%)
31-33 weeks	18	9 (50%)	3 (16.6%)	6 (33.33%)	0
34- <37 weeks	28	25 (89.29%)	3 (10.71%)	0	0
Total	54	35 (64.81%)	7 (12.96%)	10(18.52%)	2 (3.70%)

Table III. *Distribution of temperature maintenance according to gestational age after 1 day of admission in control group*

Gestational age	Frequency	Normothermia	Mild hypothermia	Moderate hypothermia	Severe hypothermia
28-30 weeks	4	1 (25%)	1 (25%)	1 (25%)	1 (25%)
31-33 weeks	25	17 (68%)	2 (8%)	4 (16%)	2 (8%)
34-<37 weeks	25	24 (96%)	1 (4%)	0	0
Total	54	42 (77.78%)	4 (7.40%)	5 (9.26%)	3 (5.56%)

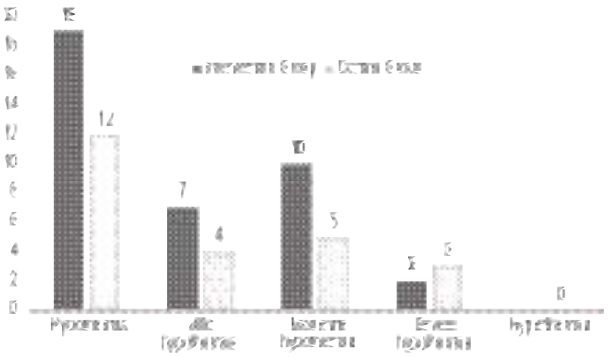

Figure 1. *Temperature maintenance after 1 day of admission in both study groups*

The development of complications after hospital admission is higher in control than intervention group (Table IV). 15 (27.78%) infants in intervention & 20 (37.04%) in control group developed septicemia. 2 (3.70%) babies in polyethylene bag group and 7 (12.96%) in control group developed NEC. Development of NEC is higher in control than intervention group & 1 infant in control group developed perforation following NEC. 2 infants of intervention group developed neonatal convulsion.

Apnoea of prematurity was one of the common causes of death of the sample population. 7 (12.96%) infants in intervention and 13 (24.07%) in control group developed apnoea which is also higher (almost double) in control population. The rate of development of apnoea was decreasing with increasing gestational age. 15 (27.78%) infants in intervention and 11 (20.37%) in control group developed hypoglycemia after admission.

The most common complication of the infants of both group is neonatal jaundice, the incidence is also higher in control 33 (61.11%) than in intervention 24 (44.44%) group. Development of neonatal jaundice is a limitation of the study as after development due to phototherapy infants were kept exposed & polyethylene bags could not be introduced. In that condition, infants were warmed with table lamp with 200-watt bulb. 1 infant in both group & 1 infant in control group developed umbilical sepsis & IVH respectively.

Table-IV. *Comparison of clinical outcome between intervention & control group*

Variables	Intervention group (n=54)	Control group (n=54)	Probability
Mean birth weight	1800 ± 415	1740 ± 402	p > 0.05
Gestational age	33.2 ± 2.1	33.1 ± 1.71	p > 0.05
Admission age in hour	6.3 ± 5.8	4.7 ± 3.4	p > 0.05
Maternal age	23 ± 4.8	23.9 ± 5.2	p > 0.05
Temperature on admission	95.3 ± 1.5	95 ± 1.3	p > 0.05
Hypothermia after 1 day	19 (35.19%)	12 (22.22%)	p > 0.05
Temperature on discharge	98.9 ± 0.4	99 ± 0.6	p > 0.05
Hypoglycaemia	15 (27.78%)	11 (20.37%)	p > 0.05
Septicemia	15 (27.78%)	20 (37.04%)	p > 0.05
NEC	2 (3.70%)	7 (12.96%)	p < 0.05
Neonatal convulsion	2 (3.70%)	0	p > 0.05
Apnoea	7 (12.96%)	13 (24.07%)	p > 0.05
Neonatal jaundice	24 (44.44%)	33 (61.11%)	p > 0.05
Umbilical sepsis	1 (1.85%)	1 (1.85%)	p > 0.05
Intraventricularhaemorrhage	0	1 (1.85%)	p > 0.05
Perforation	0	1 (1.85%)	p > 0.05
Skin problem	0	0	
No. of discharge	47 (87.04%)	45 (83.33%)	p > 0.05
No. of death	7 (12.96%)	8 (14.81%)	p > 0.05
No. of referral	0	1 (1.85%)	p > 0.05

Table V. *Clinical outcome of study groups*

Study group	No. of discharge	No. of death	No. of referral	Total	Probability
Intervention	47 (87.04%)	7 (12.96%)	0	54	p >0.05 (NS)
Control	45 (83.33%)	8 (14.81%)	1 (1.85%)	54	
Total	92	15	1	108	

NS : Non-significant in chi-square (χ^2) test of significance

Discussion

Keeping preterm LBW infants sufficiently warm immediately after birth, specially during resuscitation is problematic even when routine thermal care guidelines are followed. The newborn cannot shiver[13]& relies on interventions to protect it against exposure to cold. The ability to maintain an equilibrium between heat loss & heat gain[14] despite variation in environmental temperature is restricted during the first 12 hours of life.[15] So early intervention in the delivery room or immediately after admission to NICU is vital. The current trial shows that placement of the trunk and extremities of preterm LBW infants in polyethylene plastic bags reduces hypothermia without causing hyperthermia.

In this study total 108 preterm LBW infants were randomized enrolled, among them 54 were wrapped with polyethylene plastic bags immediately after admission and 54 were given standard thermoregulation. Most of the infants of the study were hypothermic (axillary temperature on admission in intervention group was 95.3±1.5°F & in control group was 95±1.3°F, p>0.05), documenting the high prevalence of this problem. Axillary temperature recorded after 1 day of admission was 97.6±1.4°F in intervention and 98.1±1.2°F in control group, p>0.05 and 35 infants (64.81%) in intervention & 42 (77.78%) in control group maintained normothermia. In x^2 test, at 5% level of significance against df=1, the table x^2 value is 3.841 but test statistic=2.3, so p>0.05 & there is no statistical significance of the study result.

There was also no significant difference of axillary temperature on discharge between intervention & control groups (98.9±0.4°F vs 99±0.6°F), in z distribution table, the z value at 5% level of significance 1.96 but the calculated z value =-1 , so p>0.05. These findings concurred with those of previous randomized controlled trials on the effectiveness of polyethylene wrap in lowering the rate of hypothermia in premature infants in delivery room or after admission in NICU[16,17,18].

Sunita et al[16] compared the effects of wrapping (with polyethylene) neonates of <31 weeks of gestation (n=62) by measuring rectal temperature at nursery admission. They reported that the use of occlusive wrapping resulted in significantly higher admission rectal temperature in infants <28 weeks compared to non wrapped group (36.94±0.56°C vs 35.04±1.08°C respectively p<0.001). No significant difference in temperature was seen in neonates 28 to 31 weeks of gestation. In the present study, the mean gestation was 33.2 weeks in the polyethylene group & 33.1 weeks in control group and like the observations of Sunita et al[16] the present study also recorded no significant difference of axillary temperature after 1 day of admission & also at discharge of the 2 groups.

Another study conducted between 60 neonates of d" 32 weeks of gestation & d" 1.5 kg birth weight in the Neonatal Service Division of the Department of Pediatrics, Pt. B.D.Sharma PGIMS, Rohtak[19] from 1.8.07 to 31.10.08 showed that polyethylene wrap decreased hypothermia after birth & mean axillary & rectal temperature recorded in both intervention and control group were comparable. Similar observation was made by Mathew et al[20] among 27 premature neonates less than 28 weeks of gestation & reported that vinyl bags prevented hypothermia at birth. The average axillary temperature recorded at admission to NICU in vinyl bag group was significantly higher (35.9±0.13°C vs 34.9±0.24°C) than control group. In my study I only observed axillary temperature not the rectal temperature (study limitation) which also shows no significant difference.

Kent et al.[21] observed improved admission temperature in infants<31 weeks gestation by increasing the ambient temperature in operation theatre & wrapping premature infants in polyethylene wrap. Ibrahim et al.[22]& Mc Call et al.[23] made similar observations.

The rate of maintenance of normothermia is slightly lower in intervention than control group (64.81% vs 77.78%), one possible cause may be that the room & environmental temperature were not well controlled. We used only 4 room heater to warm the room but the room temperature can t be monitored. Again most of the infants, were received at about 4-12 hours after birth, not immediately (mean admission age in hour 6.3±5.8 vs 4.7±34), which worst the outcome. Another problem we faced during the study period was the development of neonatal jaundice, which was the most common complications and the infants had to keep naked for phototherapy. As a result, most infants became hypothermic during phototherapy. However we overcomed the problem by using 2 table lamp of 200 watt bulb from both sides of phototherapy machine.

The final outcomes (the rate discharge 87.04% vs 83.33%) was better in intervention than control & also the rate of development of complications and the number of death was lower in polyethylene group which showed statistically no significant differences, similar to the study done by Alicia et al[24]. The rate of development of hypothermia and other complications were decreasing with increasing gestational age and birth weight in both groups.

Evaporation of amniotic fluid from the infant's skin surface is the mechanism of heat loss during immediate postnatal period. Plastic bag reduces evaporative heat loss[6] & allow radiative heat to pass through the plastic barrier to increase an infant´s body temperature. So considering importance of temperature maintenance in preterm LBW infants, it could be concluded that it would make sense to recommended the use of polyethylene plastic bags during their resuscitation.

Conclusion

Neonatal hypothermia after birth is a worldwide issue across all climates and placement of preterm LBW infants inside polyethylene plastic bags soon after birth reduces hypothermia and hypothermia related mortalities and morbidities without causing hyperthermia. It is a low-cost and promising intervention for infants born in limited resource settings where there is limited availability of radiant warmers and incubators. As hypothermia in preterm LBW infants and its consequences impose a significant burden in our country and scarcity of incubators and radiant warmers and affordability of these to general people has made our infants even more vulnerable, so polyethylene plastic bags can be applied as an alternative of incubators or radiant warmers for reducing hypothermia in preterm LBW infants of our country where these facilities are not so available.

References

1. Sedin G. To avoid heat loss in very preterm infants. *J. Pediatr* 2004 Dec; 145(6) ;720-2.
2. Niermeyer S, Kattwinkel J, Van Reempts P, Nadkarni V, Phillips B, Zideman D *et al*. International Guidelines for Neonatal Resuscitation: An excerpt from the Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care: International Consensus on Science. Contributors and Reviewers for the Neonatal Resuscitation Guidelines. *Pediatrics* 2000 Sep;106(3):E29.
3. Costeloe K, Hennessy E, Gibson AT, Marlow N, Wilkinson AR. The EPICure study: outcomes to discharge from hospital for infants born at the threshold of viability. *Pediatrics* 2000 Oct;106(4):659-71.
4. McCall EM, Alderdice F, Halliday HL, Jenkins JG, Vohra S. Interventions to prevent hypothermia at birth in preterm and/or low birthweight infants. *Cochrane Database Syst Rev*. 2010;(3):CD004210
5. Thomas K. Thermoregulation in neonates. Neonatal Network 1994;13:15-25.
6. Hammarlund K, Nilsson GE, Oberg PA, Sedin G. Transepidermal water loss in newborn infants. V. Evaporation from the skin and heat exchange during the first hours of life. *Acta PaediatrScand* 1980 May;69(3):385-92.
7. Davis V. The structure and function of brown adipose tissue in the neonate. Journal of Obstetric, Gynaecologic& Neonatal Nursing. 1980;9:368-72.
8. Hammarlund K, Sedin G. Transepidermal water loss in newborn infants. III. Relation to gestational age. *Acta PaediatrScand*1979 Nov; 68(6):795-801.
9. World Health Organization, Department of Reproductive Health and Research. Thermal Protection of the Newborn: A Practical Guide. Geneva, Switzerland. 1997.
10. Baumgart S. Reduction of oxygen consumption, insensible water loss, and radiant heat demand with use of a plastic blanket for low-birth-weight infants under radiant warmers. *Pediatrics*. 1984;74(6): 1022-8.

11. Periman JM, Kattwinkel J, Richmond S, et al; International Liaison Committee on Resuscitation. The International Liaison Committee on Resuscitation (ILCOR) consensus on science with treatment recommendations for pediatric and neonatal patients: pediatric basic and advanced life support. *Pediatrics*. 2006;117(5). Available at: www.pediatrics.org/cgi/content/full/117/5/e955.

12. World Health Organization. Protection of the newborn: A practical Guide, Geneva, Switzerland: World Health Organization;1997.

13. Scopes JW, Tizard JP. The effect of intravenous noradrenaline on the oxygen consumption of newborn mammals. Journal of Physiology. 1963:165;305-26.

14. Buczkowski-Bickmann MK. Thermoregulation in the neonate and the consequences of hypothermia.CRNA;The Clinical Forum for Nurse Anaesthetists 1992;3:77-82.

15. Smales ORC, Kimi R. Thermoregulation in babies immediately after birth. Archives of Disease in childhood. 1978;53:58-61.

16. V0hra S, Frent G, Campbell V, Abbott M, Whyte R. Effect of polyethylene occlusive skin wrapping on heat loss in very low birth weight infants at delivery; a randomized trial. *J Pediatr*. 1999;134(5):549-51.

17. Vohra S, Robert Rs, Zhang B, Janes M, Schmidt B. Heat Loss Prevention (HeLP) in the delivery room: a randomized controlled trial of polyethylene occlusive skin wrapping in very preterm infants. *J Pediatr*. 2004;145(6):750-3.

18. Knobel Rb, Wimmer JE Jr, Holbert D. Heat loss prevention for preterm infants in the delivery room. *J Perinatol*. 2005;25(5):304-8.

19. Gathwala G, Singh G, Kunal, Agrawal N. Safety and Efficacy of Vinyl Bags in prevention of hypothermia of preterm neonates at birth. Indian J pub health. 2010;54(1):24-6.

20. Mathew b, Lakshminrusimha S, Cominsky K, Schroder E, Carrion V. Vinyl Bags prevent hypothermia at birth in preterm infants. Indian J Pediatr 2007; 74(3):249-53.

21. Alison K, Joniz W. Increasing ambient operation theatre temperature and wrapping in polyethylene improves admission temperature in premature infants. J. Paediatr Child Health. 2008;44:325-31.

22. Ibrahim C, Yoxall C. Use of plastic bags to prevent hypothermia at birth in preterm infants-do they work at lower gestation. Acta Paediatr2009;98:256-60.

23. McCall EM, Alderdice FA, Halliday HL, Jenkins JS, Vohra S. Interventions to prevent hypothermia at birth in preterm and/or low birthweight infants. Cochrane Database Syst. Rev. 2008;23:CD004.

24. Leadford AE, Warren JB, Manasyan A, Chomba E, Salas AA, Schelonka R et al. Plastic Bags for prevention of hypothermia in preterm and low birth weight infants. Pediatrics. 2013;132(1):1-7.

Case Report

Laryngeal Tuberculosis: A Case Report

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Introduction

Tuberculosis (TB) accounts for the highest number of mortalities among infectious diseases world wide. Laryngeal TB is an extremely rare presentation of TB. It has many similarities to laryngeal carcinoma.[1] Laryngeal TB used to be a common complication in advanced pulmonary TB. However, it has become a rare occurrence in developed countries since the introduction of anti-tuberculous agents. In 2007, approximately 13.7 million people contracted TB and 1.8 million died as a result of the disease. A total of 68% of newly infected people were of Asian or African origin, whereas ethnic Europeans only made up 5% of global TB case.[2]

After the introduction of anti-tuberculous agents, preventive programs and better socio-economic conditions, TB incidence decreased dramatically up until the 1980s.[3,4,5]

In subsequent years, however, the epidemic spread of HIV, illicit drug use and the emergence of multi-drug-resistant mycobacteria have resulted in a resurgence of TB. In 1993, it became the leading cause of death from a single infectious agent. Increased numbers of migration and traveling to and from less-developed countries also contributed to the worldwide spread.[3,4,5,6,7,8]

Laryngeal TB used to be a common complication of pulmonary TB. At the start of the 20th century it affected 25-30% of all infected patients. Today, laryngeal TB occurs in only 1% case.[5,9,10,11] the pattern and clinical symptoms of laryngeal TB have also changed. Currently, it has may similarities to laryngeal carcinoma.[5,6,8,12]

Highlighting the aforementioned dilemma we present this case to emphasize the point that although primary laryngeal tuberculosis is a rarity, it must be considered among the differentials when evaluating dysphonia and/or considering laryngeal carcinoma in our population.

Case Report

Mr. Wahidur Rahman, 72 years old male presented in our department with a four-month history of persistent hoarseness. He did not have any history of tobacco or irritant use. He had experienced recurrent aspiration of liquid and had lost 4kg in weight. His previous medical history was unremarkable.

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However, he gave no history of fever, night sweats and/or dysphagia. There was no history of tuberculosis (TB) contact. He had significant hoarseness of voice.

Fiberoptic laryngoscopy revealed swelling, polypoid and odematous of the whole length of it vocal cord. Movement of the vocal cords were normal with adequate airway. There was no lymphadenopathy as confirmed by an ultrasonograpy of neck.

The initial anterposterior chest X-ray, being as a part of the routine diagnostic work up showed inhomogenous opacity of the right upper zone with multiple carily lesions in the right intra hilar region increasing pulmonary TB. His complete blood count and electrolytes were within normal limits. A sputum sample was not analyzed initially as the patient did not have any symptoms of cough or spulum production. His cardiac, liver and renal function were all right. Direct laryngoscopy performed under general anaesthesia revealed a oedematous swelling in the whole length of the Lt. vocal cord and tissue taken from Lt. cord and sent to histopathology.

Histopathological examination of the excised tissue revealed the subepithelial region showed a few epithelial cell tubercles without Casious necrosis. Sputum sample was then collected which also revealed acid fast bacilli or Ziehl-Neclsen staining and grew mycobacteriua tuberculosis or culture. The patient was referred to the Dot's centre in our university for further treatment an started on a four drug anti-tuburculous therapy.

Repeated chest radiograph two month after the start of anti-tuberculous therapy showed partial resolution of the opacity and multiple carity lesions. On four month follow up the patient reported feeling better and clinical improvement had been noted in his symptoms.

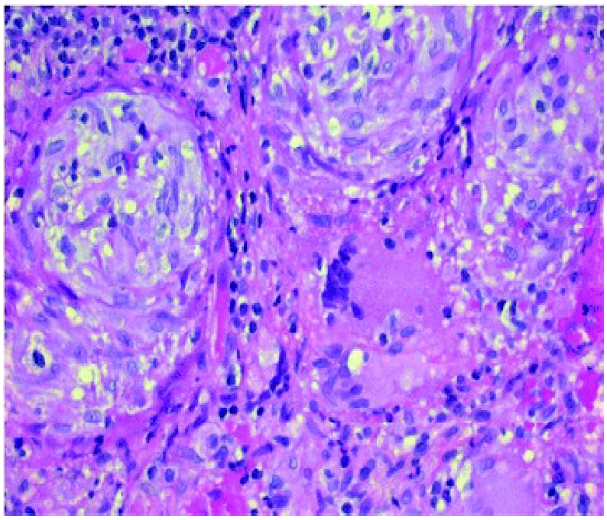

Figure 1: *Histological Finding*

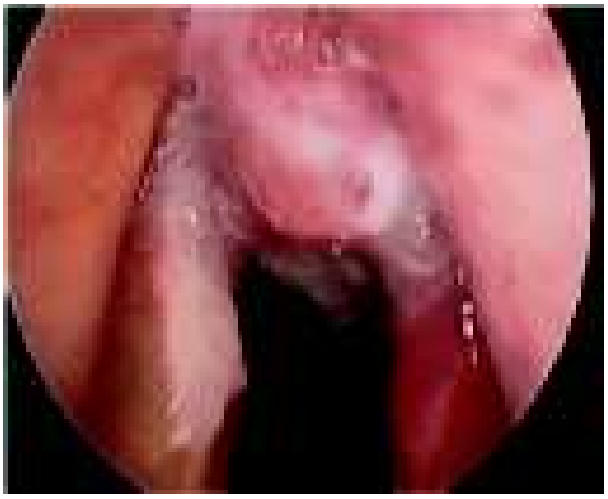

Figure 2: *FOL Finding*

Discussion

Extra pulmonary TB in the head and neck region most frequently occurs in the cervical lymph nodes (>90%), followed by the larynx (2% to 6%).[9,10] Involvement of the temporal bone, sinonasal cavity, eye, pharynx, thyroid and skull base are even less frequently observed.[5,9,10] The characteristics of laryngeal TB have changed over the years and it has become a challenge for otolaryngologists to distinguish this disease from others. In the past, laryngeal TB typically affected young people in the second or third decade of life with advanced pulmonary TB. Symptoms were cough, haemoptysis, fever, weight loss and night sweats. An ulcerative, granulomatous lesion was generally positioned on the posterior part of the larynx due to accumulation of sputum in the arytenoid region in bed-bound patients. Today, laryngeal TB mainly involves people in their 50 s or 60 s presenting first and foremost with hoarseness (80% to 100%). Other symptoms are odynophagia (50% to 67%) and to a lesser extent, dysphagia, dyspnoea, stridor, cough and haemoptysis.

Systemic symptoms have become rare.[3,5-8,9,11] Laryngeal TB can involve all parts of the larynx and there is no longer an unmistakable association with pulmonary TB. The larynx becomes infected either by a direct spread from the lungs, or by a haematogenous spread from sites other than the lungs.[5,11,12]. The former mechanism is most common and probably relevant for the patient in our case. In the case of a haematogenous spread, there is no evidence of

pulmonary disease.[3,7,9] The distinction between laryngeal TB and chronic laryngitis or laryngeal carcinoma in particular has become difficult. Odynophagia is described as an important discriminating symptom, since it is considered rare in laryngeal cancer.[2,5-7,11] Yet, from experience we know that painful dysphagia is a well-known symptom reported among patients suffering from a supraglottic laryngeal carcinoma. In a physical examination, the true vocal cords are most frequently affected by laryngeal TB, followed by the epiglottis, false vocal cords and ventricles, arytenoids, posterior commissure and the subglottic area.[4,7,12]. Laryngeal TB can manifest as oedema, hyperaemia or ulcerative lesions, but can also present as a nodule, an exophytic mass or obliteration of an anatomical structure.[12]. Aside from chronic laryngitis and laryngeal carcinoma, these various presentations give rise to a comprehensive differential diagnosis including cat-scratch disease, syphilis, sarcoidosis, Wegener's granulomatosis and fungal infections.[8]

Laryngoscopy revealed an oedematous tumour with decreased mobility of the vocal cord. The clinical signs, supported by the findings on the initial CT scan of the larynx, led us to the diagnosis of a laryngeal carcinoma. Laryngeal TB, however, can have the exact same symptoms. In the majority of cases, there is an association with pulmonary TB.[2,4] Therefore, an anomalous chest X-ray, if not compatible with pulmonary metastasis, should alert the radiologist and otolaryngologist to the possibility of TB, especially when former chest X-rays were normal.

Laboratory techniques for detecting TB infections include histopathological tissue examinations with Ziehl-Neelsen histochemical staining for acid-fast bacilli and identification of M. tuberculosis by polymerase chain reaction or bacterial culture. The latter method, although time-consuming, is considered the reference standard.[12] A CT of the neck cannot definitively identify laryngeal TB since, as in a chest X-ray, it can imitate many other diseases. Antituberculous agents are the primary treatment for laryngeal TB. If not treated early, laryngeal TB can result in (sub) glottic stenosis, muscular involvement and vocal cord paralysis when the cricoarytenoid joint or recurrent laryngeal nerve are invaded.[5,12]

Conclusion

Laryngeal TB is uncommon, particularly in developed countries, but it still occurs. There are no pathognomonic features indicative of this disease and it can mimic many others. If misdiagnosed, laryngeal TB can have severe consequences for the patient and anyone he comes into contact with. Therefore, it is important for otolaryngologists to recognise the altered pattern of laryngeal TB and to be familiar with its resemblance to malignancy. This is not only in view of clinical symptoms, but also from a radiological point of view. Laryngeal TB should be considered as a differential diagnosis in any laryngeal disease and in particular in the case of a laryngeal carcinoma.

References

1. Yvette E Smulders1, Bert-Jan De Bondt, Martin Lacko1, Janice AL Hodge and Kenneth W Kross: Laryngeal tuberculosis presenting as a supraglottic carcinoma: a case report and review of the literature. *Journal of Medical Case Reports* 2009, 3:9288.
2. World Health Organization (WHO): Global Tuberclosis Database 2009 [http://www.who.int/tb/country/ global_tb_database/en/index.html]
3. Harney M, Hone S, Timon C, Donnelly M: Laryngeal tuberculosis: an important diagnosis. J Laryngol Otol 2000, 114:878-880.
4. Rizzo PB, Da Mosto MC, Clari M, Scotton PG, Vaglia A, Marchiori C: Laryngeal tuberculosis: an often forgotten diagnosis. Int J Infect Dis 2003, 7:129-131.
5. Williams RG, Douglas-Jones T: Mycobacterium marches back. J Laryngol Otol 1995, 109:5-13.
6. Lim JY, Kim KM, Choi EC, Kim YH, Kim HS, Choi HS: Current clinical propensity of laryngeal tuberculosis: review of 60 cases. Eur Arch Otorhinolaryngol 2006, 263:838-842.
7. Lin CJ, Kang BH, Wang HW: Laryngeal tuberculosis masquerading as carcinoma. Eur Arch Otorhinolaryngol 2002, 259:521-523.
8. Shin JE, Nam SY, Yoo SJ, Kim SY: Changing trends in clinical manifestations of laryngeal tuberculosis. Laryngoscope 2000,110:1950-1953.
9. Moon WK, Han MH, Chang KH, Im JG, Kim HJ, Sung KJ, Lee HK: CT and MR imaging of head and neck tuberculosis. Radiographics 1997, 17:391-402.
10. Nalini B, Vinayak S: Tuberculosis in ear, nose, and throat practice: its presentation and diagnosis. Am J Otolaryngol 2006,27:39-45.
11. Topak M, Oysu C, Yelken K, Sahin-Yilmaz A, Kulekci M: Laryngeal involvement in patients with active pulmonary tuberculosis. Eur Arch Otorhinolaryngol 2008, 265:327-330.
12. Hunter AM, Millar JW, Wightman AJ, Horne NW: The changing pattern of laryngeal tuberculosis. J Laryngol Otol 1981, 95:393-398.

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