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

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Abstract

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

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

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

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

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

Acknowledgements

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

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

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

(iii) Internet

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

(iv) Thesis/Dissertations

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

(v) Scientific or technical report

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

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

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   Keywords: Yes

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   Key notes: Yes
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   Key notes: Yes
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   Headings: No
   Keywords: No

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Editorial

European-Paediatric Advanced Life Support (PALS) Training

Nabila Tabassum

Introduction

The constant advancements in medical science have enabled healthcare professionals to provide advanced life support in life-threatening Paediatric emergencies. One exemplary training course is the European-Paediatrics Advanced Life Support (E-PALS), which equips healthcare providers with such skills and knowledge. In this editorial, we will discuss the significance of APLS training, its applications in various settings, and the importance of making it accessible to healthcare professionals.

Resuscitation Council UK, established in 1983, is the leading authority on resuscitation in the United Kingdom. Their primary goal is to enhance survival rates for both in and out of hospital emergencies including cardiac arrest cases. E-PALS course, now considered the global standard, aims to enhance the initial management of acutely ill or injured children by providing healthcare professionals with training, education, and resources. The course consists of a full-color manual, online learning, and a two-day face-to-face course which is highly organized and comprehensive, covering a wide range of topics. It is specifically designed for post-graduate trainees and Specialist nurse practitioners working with Paediatrics emergencies. Although it is slightly expensive at 590 pounds, considering the quality of training provided, it is worth it.

Keywords: Course Review; Paediatrics Advanced Life Support; Professional Development;

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About the course

The main objective of the program is to enhance the competence and confidence of healthcare professionals when providing life-saving care to critically ill and injured children. This program is designed to apply the knowledge gained from the course manual and virtual learning environment (VLE) in the two-day face-to-face session that covers

- recognition of the seriously injured and ill child,
- performing basic life support,
- managing the airway,
- identifying cardiac rhythm abnormalities,
- administering defibrillation,
- accessing intraosseous sites,
- performing cardiopulmonary resuscitation (CPR),
- gaining intricate knowledge of emergency management for respiratory and circulatory failure in Paediatrics cases and
- the procedures involved in handling a child or infant experiencing cardiorespiratory arrest.

The program commences on the first day with registration and a welcome session, followed by a discussion on both basic and advanced life support. Participants engage in a variety of activities, such as attending lectures which serve as a concise summary of the extensive materials provided in the manual, workshops as well as taking part in breakout sessions and simulation practices. These activities are designed to demonstrate and reinforce the structured ABCDE approach, airway management, manual defibrillation, and other vital skills in dealing with time-critical Paediatrics scenarios. Furthermore, participants work collaboratively in small groups to enhance their understanding of managing and treating these urgent

cases, which can rapidly progress to cardiac arrest. The instructors are knowledgeable and friendly, making an effort to ensure that the training remains engaging and enjoyable for all participants.

The course concludes with a written or multiple-choice exam. The participants' practical skills are evaluated through objective simulated clinical examinations and scenarios.

The scenarios and skills stations in the course were impressive as they simulated real-life cardiac emergencies and the material presented was up-to-date. Overall, it was a good course for middle-grade trainees but could be frustrating for those with a lot of experience as the testing and scenarios lacked flexibility, which meant that more experienced clinicians couldn't exercise their judgment and had to blindly follow protocols. This may be due to the course covering a broad range of topics for a variety of healthcare professionals. It serves as a comprehensive resource for learning how to assess and manage sick children until help arrives or they are transferred to a different facility.

The training also includes BLS, making it unique and applicable in various situations such as air travel where medical resources are limited, maritime emergencies, and land-based incidents like near-drowning, road traffic accidents, or severe injuries. With such training, healthcare professionals can effectively stabilize patients until they reach a medical facility.

Prospects for Bangladesh

Bangladesh experiences high rates of death from conditions such as neonatal asphyxia, pneumonia, diarrhea, sepsis, and drowning, many of which can be reversed with proper resuscitation. E-PALS is a crucial training program for Pediatricians and specialist nurses working in critical Paediatric emergencies and postgraduate medical institutes in Bangladesh should prioritize funding and promoting it.

The Bangladesh College of Physicians and Surgeons (BCPS) has introduced the Advanced Trauma Life Support (ATLS) course for Surgeons and BLS course, however, there seems to be a lack of Paediatric advanced life support courses. Additionally, the Department of Anesthesia in Bangabandhu Sheikh Mujib Medical University (BSMMU) offers courses on Basic Life Support and Advanced Cardiac Life Support (ACLS) specifically tailored for adults.

- There are occasional Paediatric Advanced Life Support (PALS) courses, offered by the American Heart Association and American Academy of Paediatrics. These courses are organized by agencies like the Institute of Healthcare Development, but their frequency depends on the availability of foreign trainers and logistics. Additionally, Evercare Hospital offers Basic Life Support (BLS) and PALS courses exclusively for their employees. While BIRDEM Hospital provides BLS and Advanced Cardiac Life Support (ACLS) training open to employees from other hospitals. Unfortunately, for the time being there is no regularly run course specifically for Paediatrics in Bangladesh. It is momentous to have regular courses for maximum training of healthcare professionals in acute care Paediatrics and to ensure periodic recertification rather than a one-time course.
- Educators should consider incorporating simulation-based medical education (SBME) into resuscitation programs to optimize their effectiveness. In the UK, high-fidelity human patient simulators are commonly used for simulation-based medical education. However, these simulators are expensive and complex, making them less feasible for Bangladesh. Emphasizing low-cost and low-fidelity approaches can enhance the dissemination potential and sustainability of training programs in these settings. Many educational programs in Bangladesh have already incorporated simulation, with positive outcomes including the Helping Babies Breathe (HBB) initiative, created by the American Association of Paediatrics which aims to improve neonatal resuscitation and reduce mortality.
- It is important to address linguistic and cultural barriers in program development and implementation.
- The quality and relevance of protocols and teaching materials need input from local experts and stakeholders who understand the local context, including epidemiology, practice standards, available resources, and potential barriers to care. Modifications to existing international protocols are often necessary in settings with limited infrastructure and equipment.
- Securing finances for these programs can be achieved through partnerships with government bodies, healthcare institutions, and corporate entities with a focus on healthcare. By ensuring the availability of E-PALS training, we can cultivate a society that is well-equipped to address medical

emergencies effectively, consequently diminishing mortality rates resulting from insufficient initial care

Conclusion

Stress of handling emergencies can cause even the most seasoned individuals to experience fear and palpitations. However, employing a well-organized and structured approach in such situations offers a sense of direction and streamlines management. This program offers a structured approach to dealing with time critical Paediatric patients. The specific knowledge and skills gained from the course may vary depending on the trainees' background and experience in this area. However, overall, the course is top-notch and is highly recommended for Pediatricians as part of their continuing professional development requirements.

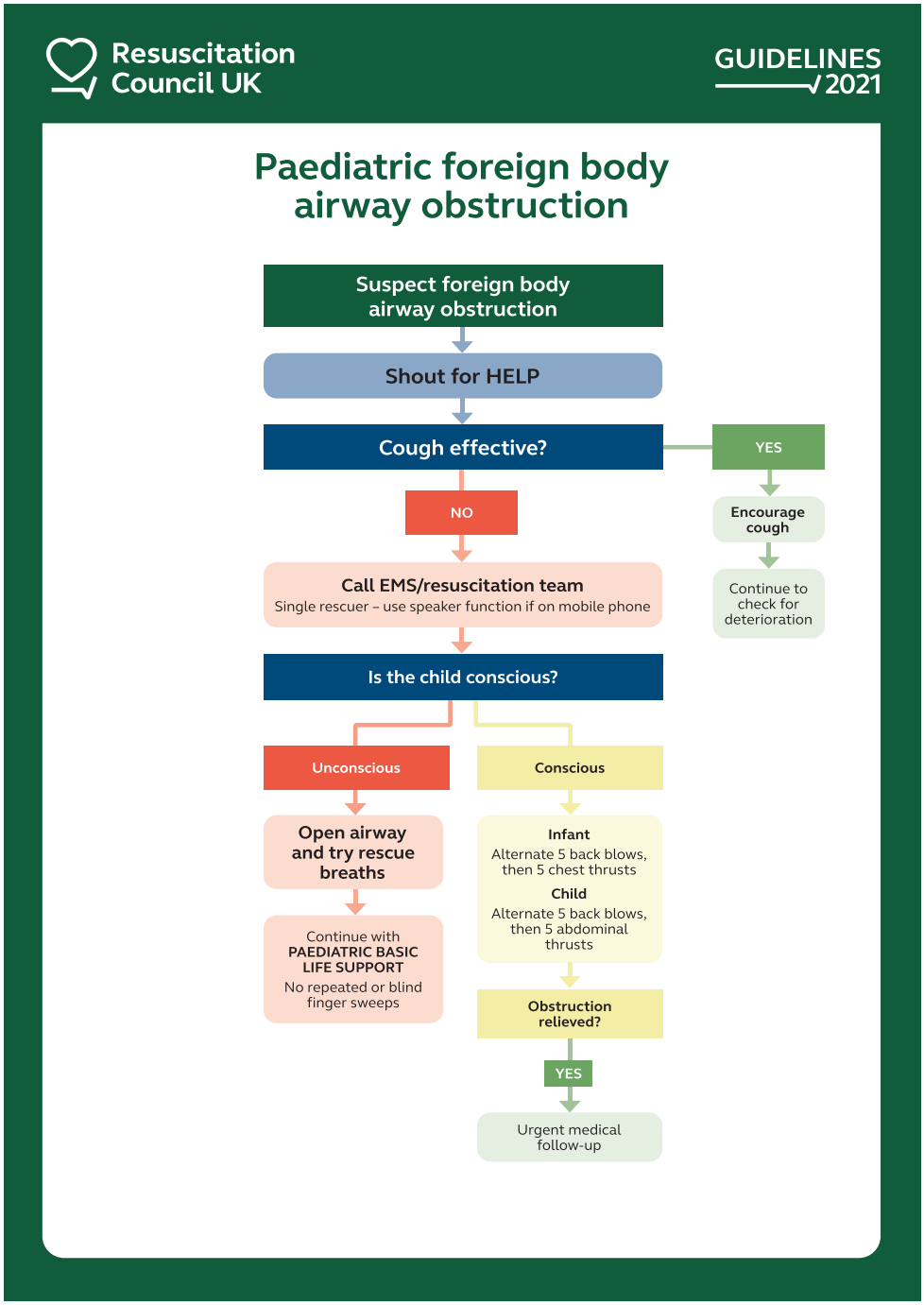

Figure-1. *APLS Paediatric life support algorithm*

Original Article

Primary Pterygium Excision with Amniotic Membrane Grafting among Rural Eye Patients in Bangladesh

*MD Abdul Matin[1], Mahbubur Rahman Shahin[2], Tasnia Nawreen[3], Mubashera Sara Khan[4]

Abstract:

Objective: Since treatment of pterygium by topical and systemic medications is not effective, surgical treatment remains the only way to resolve the problem. This study was therefore aimed to evaluate the outcome of primary pterygium excision with amniotic membrane graft among patient with eye diseases in rural Bangladesh.

Methodology: This study was conducted at the Pangsha Eye Hospital of District Rajbari among a total 280 pre-selected eye patients having primary pterygium over the period of 7 years (January 2012-June 2019). Surgical excision was performed with transplantation of preserved amniotic membrane on to the bare sclera. Every patient was followed up for at least next 6 months.

Results: The results were evaluated in terms of recurrent pterygium growth and related complications. Of total 280 patients, pterygium was excision both of 138 (49.29%) being male and 142(50.71%) being female with mean ages of 43.36±10.88. The pterygium extended on to the corneas for 4.76±1.4 mm (range 3 to 8) mm. Only 11(4%) eyes demonstrated recurrent pterygium. Seven of them were male and 4 were female which was managed by second grafting leading to complete resolution. Of various complications, mild hematoma was observed in 3 cases, and, in 2 cases ~~were~~ had mild sclera dryness in bare scleral area after pterygium excision which were managed by topical steroid and artificial tear.

Conclusion: Findings of this study yielded that primary pterygium excision with amniotic membrane transplantation ~~is~~ remains a safe and effective surgical technique with minimum recurrence rate.

Keywords: Cornea, Pterygium, Amniotic membrane, Conjunctival Autograft

Introduction:

Pterygium is a wing-shaped, fibro vascular growth of the bulbar conjunctiva that crosses the limbs and extends over peripheral cornea. And may cover central parts of the cornea which causes severely visual impairment.[1] It is a common external eye condition, affecting different populations especially in tropical and subtropical regions with a reported prevalence of 2% to 7% worldwide.[2]

This invasion of the corneal surface can lead to significant visual impairments, irritation of the ocular surface, irregular astigmatism, obstruction of the visual axis and loss of corneal transparency.[3] The incidence and prevalence of this condition vary among different populations and are influenced by a variety of factors including age, sex, and geographical location.[3]

Worldwide prevalence of pterygium was found to be 10.2%.[3] With prevalence rates ranging from 2.8% to in a study [4] and 33 % in another study.[5]

The prevalence of pterygium in men was also higher than that in women, with rates of 14.5% and 13.6% respectively. Pterygium was more prevalent with increasing age.[3] Populations living in geographic latitude ranging from 20-30 also had a higher prevalence of pterygium compared with any other area.[3]

The nasal limbs are the most common site for pterygium formation. This predilection has been attributed to the focusing of light passing through the anterior chamber at the nasal limbs, causing damage to the limbal stem cell and oxidative stress.[6,7]

Many population-based studies have also revealed an association between pterygium formation and outdoor occupation and activities, most likely a result of exposure to ultraviolet (UV) radiation, the pathogenesis of which has been described.[8,9]

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Other indications are for surgical intervention including discomfort and irritation unresponsive to conservative therapy, and, restricted ocular motility difficulty with contact lens wear, anticipated Kerato-refractive surgery and unacceptable appearance.[10]

Materials and methods: -

Study Place:

Pangsha Eye Hospital, Rajbari, a South-Western district of Bangladesh which is relatively warmer and drier than other parts of the country.

Study Period:

Seven years (January 2012 to June 2019)

Study Population:

This case series of primary pterygium included 280 cases; 138 being males and 142 females. Of them, 103 patients were <35 years age-group while 59 were from >56 years. However, almost 42.1% cases were between 31 to 55 years.

Study type:

Observational study: Clinical and Surgical study on patients of primary pterygium

Clinical/ Ophthalmological methods:

The study method included a series of patients with primary pterygium extending at least 3 mm into the cornea. The history was taken and relevant investigations were done in every patient and medical data were reviewed in detail. Major systemic conditions were excluded such as severe diabetes mellitus, uncontrolled Hypertension, Collagen vascular disease and one-eyed patients.

Eye Examination/ Ophthalmological procedures:

A complete ophthalmological examination using slit lamp bio-microscopy, intraocular pressure measurements and visual acuity was performed to rule out Glaucoma, Vitreo-retinal disease, dry eye and other minor lids and ocular abnormality which may influence over the surgical procedures and operation outcome. All patients were followed up on the 1st post-operative day, after 1 week; 3rd weeks and 2 months up one year.[4]

Time of recurrence after operation:

All of 11 patients after pterygium had excision with amniotic membrane grafting within 6 months after surgery. Conjunctival grafts had a better yield in terms of pterygium recurrence as well as overall recurrence time as conjunctival grafts, including limbus stem cell grafts, inhibit the effect on the remaining abnormal tissue and help in restoration of limbal barrier with the help of limbal stem cells, resulting in reduced frequency and duration of pterygium recurrence. [11]

A study showed that, after stem grafting; recurrence of pterygium growth was only present in two cases (4.75%).[12]

Surgical procedure:

Pterygium excision was done by a single surgeon in same hospital under local peribulbar anesthesia or subconjunctival anesthesia of 2% lignocaine containing 1:10,000 adrenalines.

The head of the pterygium was first separated at the limbus and dissected toward central cornea with a pair of spring scissors. After excision of head and most of body, Tenon and sub-conjunctival fibro-vascular tissue were separated from the overlying conjunctiva, undermined and excised extensively upward and downward towards the formic and medially towards but not reaching the curuncle; caution was taken not to damage the medial rectus.

Cautery was gently applied to bleeding vessels. The conjunctiva above and below the pterygium was trimmed to create a rectangular area of bare sclera. Residual fibro-vascular tissue over the cornea was detached using toothed forceps or by gentle scraping with a 15 surgical blade. The bare sclera was covered with amniotic membrane, which was oriented with base membrane side up. The amniotic membrane was sutured through the episcleral tissue to the edge of the conjunctiva along the bare sclera border with seven to eight interrupted 10-0 silk monofilament sutures and the eye was patched. Post-operative Moxifloxacin and Dexamethasoneeye drop were administered 6 time daily and some patient complain irritation from stitches and those cases were managed by lubricants. There after eye drops were tapered as per need. Patients were following after 7 day, 3 weeks after 2 months and up to 6 months. Complications such as recurrent pterygium, epithelial defects, dullen formation and photophobia were recorded.

Result:

Total 280 eyes of 272 patients with primary pterygia of consecutive patients including 138 (49.29%)male and 142(50.71%) female subjects with mean age of 48.36 +_10.76(range 18-72) years were operated 170 (60.71%) patients had occupations with considerable exposure to actinic damage. now a day woman is also involved in outdoor work as like as male . In our study total patients received for pterygium operation majority patients were

female 142 (50.71%). The extent of pterygium invasion beyond the limbus ranged from 5.5 +- 1.6 range 3-8 mm.

On the first postoperative day, all patients had corneal epithelial defects, by one week, all epithelial defects healed completely and there was no conjunctival staining with fluorescein. None of the patients had any significant change in intraocular pressure in any time during follow up period.

Pre-operative, best corrected visual acuity for most patient 6/18 to 6/12 two or more lines of visual improvement. The recurrence rate was 4% (11patients) of 280 cases over follow up period of 6 months.

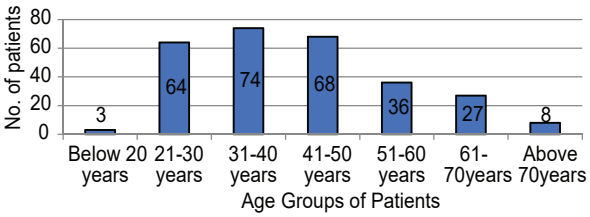
Section I: Socio-Demographic characteristics of 280 Pterygium Patients:-

Table I

Distribution of patients by their age

Patients' age	No of patients	Percentage
Below 20 years	03	1.07%
21-30 years	64	22.86%
31-40 years	74	26.43%
41-50 years	68	24.29%
51-60 years	36	12.86%
61- 70years	27	9.64%
Above 70years	08	2.86%

This above Table -I shows the age distribution of 280 pterygium patients. This reflects that younger age Groups are more affected with this disease. 19 years to 50-year age group are mostly affected 209 out of 280 (74.64%). On the study 16 year to 50 years age group 142 out of 212 (66.98%).[13]



Above two study is done in same institute and area, surgery was done by same surgeon.

In a previous study, in 2018, 18 years to 58 years age group patients was 65%. [11]

The above table shows the age specific distribution of 280 pterygium patients. The younger groups were more affected with pterygium, indicating the patients underwent amniotic surgery in infected eyes. The accompanying pie chart of the table depicts the age distribution of patients graphically.

Table II

Sex distribution of patients by gender (Amniotic membrane Grafting)

Sex	Male	Female	Total
No of patients	135	145	280
Percentage	48.2	51.8	100.0

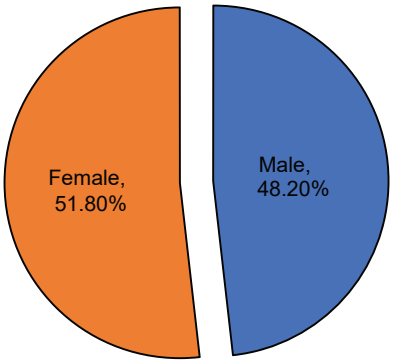


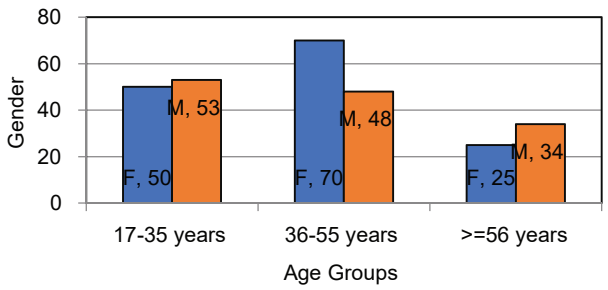
Table-II shows the gender distribution of 280 pterygium patients. This reflects that approximately 52% females were more affected with pterygium than the counterpart (48%). The accompanying pie chart depicts the same graphically as well.

Table III

Association among the age groups and genders of pterygium patients

Age Group	Gender		Statistical Association, P-value
	Female (n=145)	Male (n=135)	
17-35 years (n=103)	50	53	χ^2=5.211,
36-55 years(n=118)	70	48	P-value=.074,
>=56 years(n=59)	25	34	df=3

Table-III yields no association patients age groups with the sex of Pterygium patients (p=.074) having enough evidence not to reject any association, statistically.



The following figure below depicts the same making it obvious in bar diagram for more visibility.

Table IV

Distribution of pterygium patients by their occupations

Occupation	No of patients	Percentage
Farmer	105	37.5%
Home maker	110	39.29%
Service holder	25	8.93%
Business	18	6.43%
Teacher	12	4.28%
Student	10	3.57%

According to table IV, it had become obvious that pterygium was highest found among the home maker (~39%), followed by farmers as the next riskiest professions (37.5%) having pterygium. Female worker in outfield is increasing day by day. People today not able to depended alone single working arena due economical point of view. Teacher, business man, service holder even students are participating in outdoor work. So, now-a-days it is very difficult to differentiate occupational landmark of pterygium. The concurrent pie chart of the table-IV reflects the similar data but in a more obvious visual effect for the pterygium patients.

Section II: - Details of ophthalmological issues and surgery (pterygium) performed

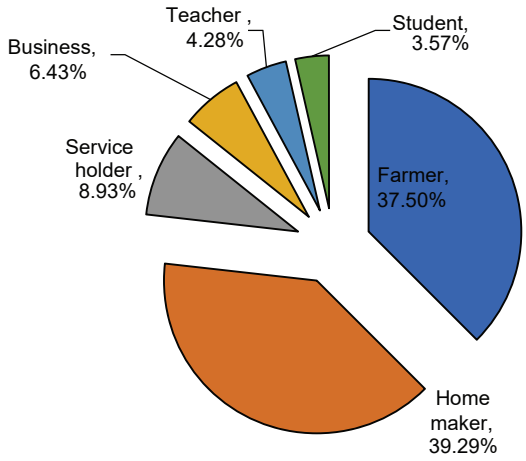


Table-V shows that the pterygium surgeries were performed most (16.4%) in 2018 followed by in 13.6% in 2019 and 14.3% in 2013 & 13.9% in 2015, and 12.5% in 2014 & 11.4% in 2017. However, a bit lower case was done in 2012 & 2016 being 9.6% & 8.2% respectively.

The figure below depicts the same data but making it more visible in graphical representation.

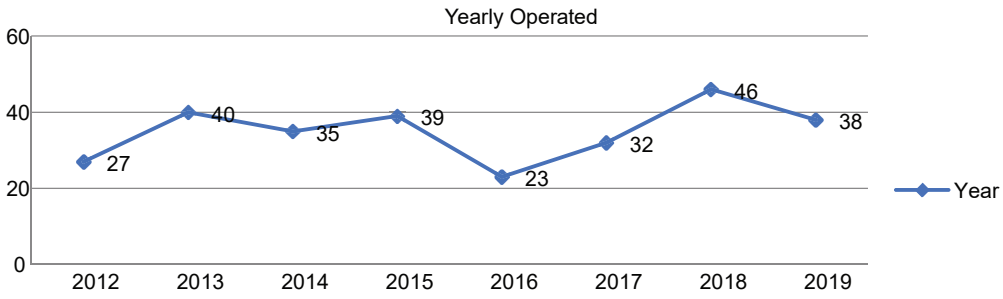


Table V

Distribution of patients by the years of operations (Amniotic membrane Grafting)

Year	2012	2013	2014	2015	2016	2017	2018	2019	Total
No of patients	27	40	35	39	23	32	46	38	280
Percentage	9.6	14.3	12.5	13.9	8.2	11.4	16.4	13.6	100.0

Table VI

Recurrence in after Amniotic membrane-graft: 11 in 280 cases

Gender	Total no	Percentage
Male	06	54.55%
Female	05	45.45%

Recurrence rate is a little high in male patients. It may early exposure of sunlight after operation as the male patients of rural area avoid black goggles and anomaly of post-operative medication may the important factors. It may need further evaluation regarding this issue.

Table VII

Distribution table of 280 patients affected eye

Affected Eye	Frequency	Percent
Left Eye	147	52.5
Right Eye	133	47.5
Total	280	100.0

Table-VII, revealed important findings that the pterygium surgery was performed most (~72%) in patient's left eye than their right one (~28%). The concurrent pie chart reflects the percentage of infected eyes with pterygium to make it more obvious on the difference of surgery done mostly in patient eyes.

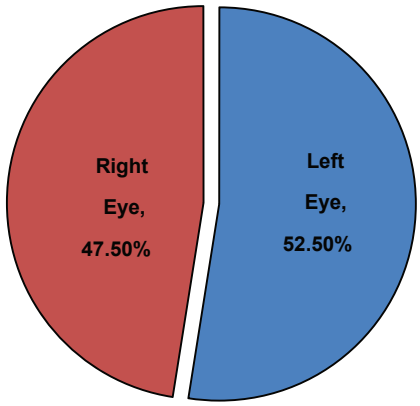


Table VIII

Association among years and age groups of pterygium patients

Year	Age Groups of Patients			Statistical Association, P-value
	17-35 years(n=103)	36-55 years(n=118)	≥56 years(n=59)	
2012 (n=27)	16	8	3	
2013 (n=40)	19	16	5	
2014 (n=35)	12	13	10	χ^2=25.324,
2015 (n=39)	12	17	10	P-value=.031,
2016 (n=23)	12	5	6	df=14
2017 (n=32)	9	13	10	
2018 (n=46)	9	27	10	
2019 (n=38)	14	19	5	

Table-VIII portrays that there is a significant association in Pterygium operation by years and age groups (p<0.03). It is also proved through seeing the data distribution between years of operations and age groups of patients. The younger groups were more operated surgery for this disease in comparison of elderly group (≥56 years (n=59). The obvious visual effect of the above table is shown through the following bar diagram.

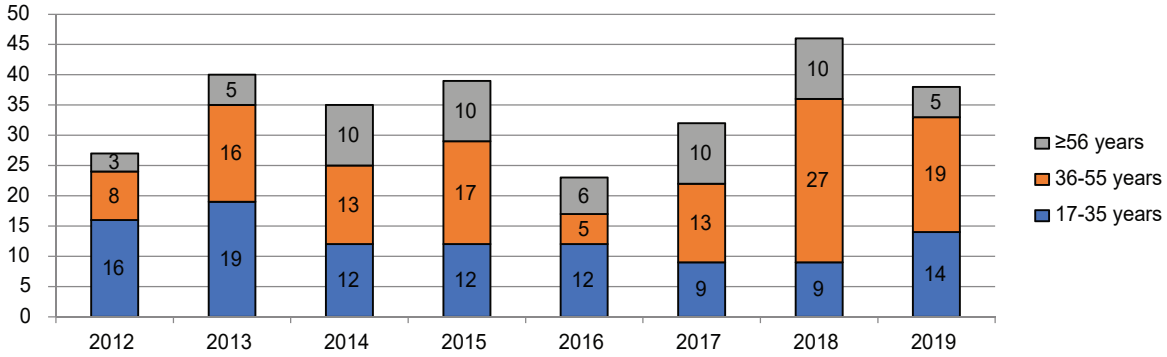


Table IX

Association table of 280 patients' between year and sex of patients

Year	Sex of Patients		Statistical Association, P-value
	Female (n=145)	Male (n=135)	
2012(n=27)	10	17	χ^2=12.519, P-value=.085, df=7
2013(n=40)	24	16	
2014(n=35)	20	15	
2015(n=39)	21	18	
2016(n=23)	11	12	
2017(n=32)	19	13	
2018(n=46)	28	18	
2019(n=38)	12	26	

Table-IX picturing that there was no association of year of operations with gender of patients as the p-value=0.085 which is greater than 0.05 providing enough evidence not to reject no association between these two variables of this study.

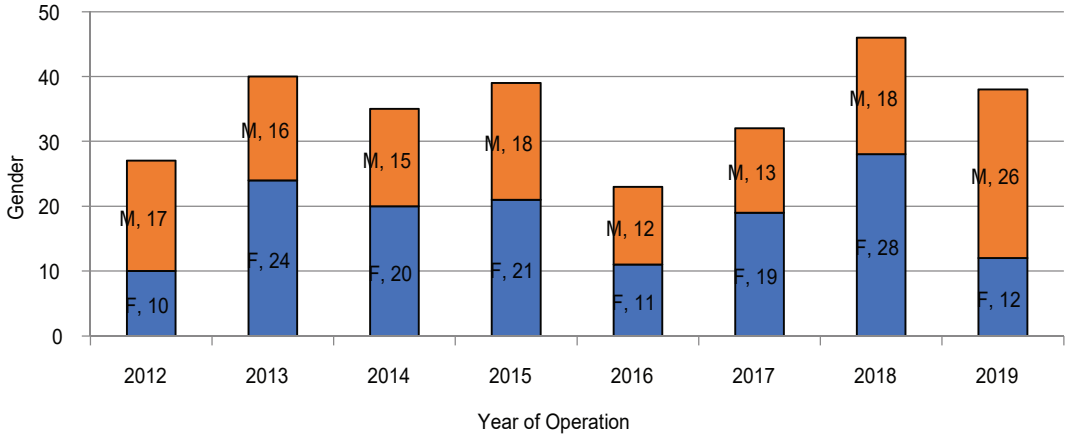
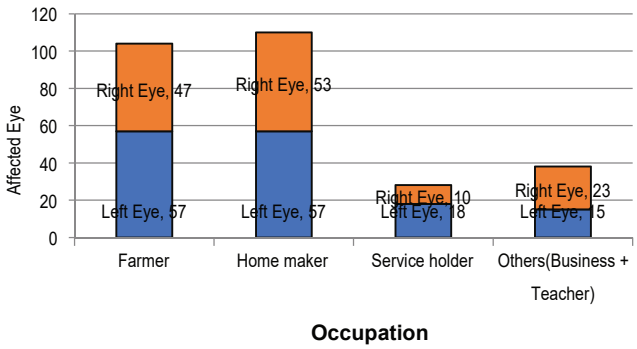


Table X

Association table of 280 patients between occupation and Pterygium of eyes

Occupation	Eye		Statistical Association, P-value
	Left Eye(n=147)	Right Eye(n=133)	
Farmer(n=104)	57	47	χ^2=4.388, P-value=.223, df=3
Home Maker(n=110)	57	53	
Service Holder(n=28)	18	10	
Others(Business + teacher + student) (n=38)	15	23	

Table-X describes there was no association of occupation of patients with infection of eyes as the corresponding p-value=0.223 which is greater than 0.05. Left eye is likely to be infected most in home maker and secondly infected most in farmer. From this table, students are less likely to be affected in right eye.



Discussion:

Pterygium is a wing-shaped, fibro-vascular growth of bulbar conjunctiva that crosses the limbus and extends over peripheral cornea- that may cover central parts of cornea causing severe visual impairment.[1] However, less studies on pterygium- a common external eye condition have not been reported among Bangladeshi population, though it affects other populations in the tropical and subtropical regions varying with a prevalence of 2%-7%.[2] But, invasion of corneal surface can lead to significant visual impairments, irritation of ocular surface, or lead to irregular astigmatism, obstruction of visual axis and loss of corneal transparency, incidence/prevalence of which may vary among different age, sex, and geographical location.3 Though worldwide prevalence of pterygium has been reported up to 10.2%,[3] ranging from 2.8%4 to 33%,5 findings of our study based on a rural district, yielded it among 50% patients: 49% in males & 51% in female patients with a mean age of 43.4±10.9 years.

Though nasal limbus, reportedly, remain commonest site of pterygium formation (due to predilection attributed to focus of light passing through anterior chamber causing damage to limbal stem cell and oxidative stress,[6-7] we observed pterygium extended on to corneas for 4.76±1.4 mm (range 3 to 8) mm in our patients.

Occupation of 37.5% of our rural patients were farmers who are to work outside in farming fields direct under the sun (UV-ray)- an observation that agrees with several population based studies revealing association between pterygium formation and outdoor occupation/activities, most likely a result of exposure to ultraviolet sradiation, as the prognosis reported by Di Giroloma N and Chui J.[8-9]

Pterygium is a multifactorial degenerative corneal disorder. Different procedures have been proposed for treatment of the condition, the main complication common to all is recurrent disease which is more difficult to control.[10] It is believed that surgical trauma and postoperative inflammation activate sub-conjunctival fibroblast and vascular proliferation, and deposition of extracellular matrix proteins, all of which contribute to recurrence of the lesion.[14] Conjunctival auto graft were superior to that of bare sclera technique.[15]

In our study, yielding lower recurrence rate and favorable safety profile of pterygium excision with AMT attested the efficacy of this treatment modality and compare favorably with previous reports due to removal of sufficient conjunctival and sub-conjunctival fibro vascular tissue, especially adjacent to the limbus- which has been elaborated, which has been elaborated in other study.[16]

On strategy of decreasing pterygium recurrence is the use of conjunctival auto grafts, that Kenyon et al reported a recurrence rate of 5.3% after fixation of pterygium with conjunctival auto grafts[17] in a randomized clinical trial, which remains similar with our findings, demonstrating only **4% eyes to have faced with recurrent pterygium.** However, Lewallen[18] reported 40% recurrence rate with the bare sclera technique versus 7% with conjunctival auto grafts, **as we followed in our patients in this study.** Intraoperative application of mitomycin C to sclera bed is another strategy which has gained increasing acceptance but entail several complications.[19-20]

The recurrence rate after amniotic membrane transplantation was initially reported to be 10.9% for primary and 37.5% for secondary pterygium, being much higher than recurrent rates of conjunctival auto grafts,[23] reducing to 3% and 9.5% respectively, after modifying the surgical technique,[24] which compared favorably with conjunctival auto grafts [14] being superior to that of bare sclera technique[25] that we have followed in our study as Fallah et al[26] performed for treatment of recurrent pterygia. Matin et al showed that amniotic membrane graft alone is effective adjunctive treatment for recurrence pterygia and the addition of intra operative mitomycin c did not further reduce recurrence rates.[27]

Nakamura [21] reported that freeze-dried amniotic membrane demonstrates excellent Biocompatibility on the ocular surface. This biomaterial may be considered as an alternative to Conjunctival grafting in the treatment of pterygium. Promotion of conjunctival epithelium wound healing suppression of fibroblasts and reduced extracellular matrix production are thought to be the major mechanism by which amniotic membrane transplantation inhibits recurrence of pterygium.[22]

To date, there has been no report of sight threatening complications following amniotic membrane transplantation. Minor complications such as conjunctival epithelial inclusion cyst formation, caused by embedded conjunctival epithelium, occur more frequently with conjunctival autografts as compared to AMT. however, amniotic membrane contamination remain a potential risk which cannot be overlooked.[11-13]

The low recurrence rate favorable safety of pterygium excision with AMT in the current study attest to the efficacy of this treatment modality and compare favorably with previous reports on mitomycin c augmented pterygium excision. We believe that the low recurrence rates were due to removal of sufficient conjunctiva and sub-conjunctival fibro-vascular tissue, especially adjacent to the limbus. coverage of a larger area by amniotic membrane in turn may promote the proliferation and differentiation of residual normal limbal epithelial cells, which may turn have an inhibitory effect on fibro-vascular ingrowth.[12] The major limitation of the study is the lack of a control group. We prefer AMT over conjunctival autografts because of faster healing time. Less discomfort and acceptable recurrence rate, and believe that amniotic membrane transplantation is an appropriate treatment modality for the surgical management of primary pterygia. This may be particularly advantageous for patients with glaucoma who require intact conjunctiva for future glaucoma procedures.

The primary objective in pterygium surgery is to remove the fibro vascular growth that will eventually produce permanent scaring in the pupillary axis and reduce recurrence. In addition, the surgeon should aim to minimize surgery related complications, increase patient comfort in post-operative period, and achieve an acceptable cosmetic outcome.[28-30] However, the various modalities used in the treatment of pterygium have focused mainly on reducing the recurrence. Currently, human fibrin glues have additional useful applications in ophthalmic surgery to minimize the use of sutures and prevent suture-related complications.[31-33]

Unfortunately, transmission of viruses (parvovirus B19, hepatitis, and human immunodeficiency virus or Creutzfeldt–Jacob agent during surgery continues to be a theoretic risk despite viral inactivation techniques.[34]

The earlier report [18] has shown the average surgical time with the use of fibrin glue as 15.5 min, which was comparable with the current study (11.2min for the fibrin glue group). Although the authors did not perform a statistical evaluation of the symptom scores. They stated that the post-operative period was generally comfortable in all patients. In our study, we used the same five-point scale and observed significantly fewer symptoms with the use of fibrin glue compared with suturing. These findings were also consistent with the study of conjunctiva auto grafts using fibrin glue, in which a number of different symptom scales have been used.[35-39]

Shortening the surgery time and improving post-operative comport may have several advantages. First, the use of fibrin glue removes the need for tedious suturing process, the learning curve may be shortened, and better results may be more consistently achieved despite differences in the surgical expertise, second, more rapid and efficient surgery may reduce the risk of infection and save the surgeon and the facility valuable operating room time. And third, from the patient's standpoint, greater comfort allows a more rapid return to their normal lifestyle and productivity.

The disadvantage, when fibrin glue is used, the retraction of the host conjunctiva or graft may result in gap formation between the grafts in the early post-operative period. It is suggested that rapid epithelialization of amniotic membrane prevents post-operative inflammation and thereby reduces the recurrence rate.**[18]** Thus, attempts of tucking in amniotic membrane under surrounding conjunctiva of pinching it together with recipient conjunctiva were tried to achieve good apposition.[40,41]

Prospective series in the literature report recurrence rate of 3-40.9% after primary pterygium surgery using suture[42] have found that single layered amniotic membrane was able to reduce the recurrence rate to 12.5% which was comparable with this study.

They stated that the addition of mitomycin C did not further reduce the recurrence rate moreover, the use of mitomycin C may result in serious complications and is commonly reserved for the recurrence cases. Study reported a lower recurrence rate (3%).[43]

When AMT was combined with intra-operative triamcinolone, depot steroid has been reported to be effective in decreasing post-operative inflammation and preventing pterygium recurrence.[44] In this study used intra-operative triamcinolone and found the recurrence rates as 9.4% in the fibrin glue group and 10.5% in the suture group.[45]

Conclusion: -

Excision of pterygium with Amniotic membrane grafting remains a good alternative and effective treatment options after conjunctival auto graft.

Conflict of interest: None.

Acknowledgement:

The authors remain grateful to the authority of Ad-din Women's Medical College and Hospital, and, Dept. of Genecology for assisting to manage amniotic membrane and dept. of ophthalmology and staff of Pangsha Eye Hospital Computer and Record Keeping Section for unconditional support and encouraging in these procedures. Thanks a lot to all patients who participate and assisted us in data collection for further analysis.

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Original Article

Comparing the Efficacy of Amoxicillin and Ceftriaxone in Clinical Management of Uncomplicated Enteric Fever in Children: A Cost-effective Approach in Bangladesh

*Md. Abdul Hye[1], Syeda Afroza[2], ARM Luthful Kabir[3], Md. Rahat Bin Habib[4], Most. Eleza Khanom[5]

Abstract:

Background: Enteric fever (EF) is a systemic and often a fatal infection caused by Salmonella enteric serotype typhi. EF poses a significant public health challenge in Bangladesh. Uncomplicated susceptibility to EF can be defined as a clinical diagnosis of typhoid or paratyphoid fever without excessive toxemia, gastrointestinal hemorrhage or perforation, shock, or neuropsychiatric complications. S. typhi, characterized by resistance to 3 (three) primary antibiotics used in typhoid treatment: chloramphenicol, ampicillin, and cotrimoxazole necessitated the search for a suitable alternative typhi susceptibility to amoxicillin, which could be a safe, cost-effective and suitable drug.

Objective: We evaluated the efficacy of amoxicillin and ceftriaxone to compare the treatment status against uncomplicated-**EF** in children thus to guide in selectivity, safety, effectiveness, readily available alternate, better therapeutic measure and potentially reduced overall treatment cost.

Methodology: In this cross-sectionally designed comparative study, we enrolled 96 children with clinically diagnosed uncomplicated-**EF** admitted at the department of Pediatrics, SSMCH. Of total 96 children, 48 were placed in the amoxicillin Group (Gp-A) and another **48** in ceftriaxone Group (Gp-B). Age, sex and socioeconomic condition of child's households/families were recorded to compare findings between A and B Group of children. Period of defervescence, hospital stay, treatment outcome, adverse effects, and cost of drugs were compared between these two Groups (A and B).

Results: Slight male preponderance was observed. Most children came from families of a low socio-economic class. A shorter defervescence period, duration of treatment and hospital stay was noted in the Ceftriaxone Group. The mean period of defervescence was 5.11 ± 1.90 days in Group A, while in the other Group it was 5.55±0.45 days - which is not statistically significant (P>0.05). In the Amoxicillin Group, the duration of treatment was 12.80 ± 1.20 days and the mean hospital stay was 12.20±1.8 days. Whereas, in the Ceftriaxone Group children received treatment for 8.70± 1.30 days on average and were inpatients for 9.13±0.87 days. Both the findings for treatment duration and hospital stay were statistically significant (p<0.05). 73% of patients receiving Amoxicillin were cured but 100% of those in Group B were cured. Treatment with Amoxicillin is significantly more cost-effective than Ceftriaxone. 63.83% and 2.13% of the isolates were resistant to Amoxicillin and Ceftriaxone respectively. No serious adverse effects were noted.

Conclusion: Ceftriaxone showed better efficacy (100% clinical sure rate) shorter defervescence period and shorter hospital stay, though no major difference was revealed. Amoxicillin remained comparable to that of ceftriaxone in treating uncomplicated EF in children yielding a high cure rate being comparable to that of ceftriaxone. Furthermore, amoxicillin appeared to be a safe choice including total treatment cost (~81% lower than that of Ceftriaxone).

Key words: Amoxicillin, Ceftriaxone, Uncomplicated Typhoid Fever, Cost-effectiveness, Bangladesh.

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Introduction

Enteric fever (**EF**) is a systemic infection, primarily caused by the bacterium *Salmonella enterica serotype Typhi,* a gram-negative bacillus.[1] It poses a significant public health challenge in the Indian subcontinent, particularly in Bangladesh[2-3] where the annual incidence rate reaches a substantial 252 cases per 100,000 people.[4] Uncomplicated-EF can be defined as a clinical diagnosis of typhoid or paratyphoid fever without overwhelming toxemia, gastro-intestinal hemorrhage or perforation, shock, or neuropsychiatric complications at the onset of treatment.

According to UK based National Health Service (NHS), the clinical features of EF range from prolonged high

fever, constipation, diarrhea and headache to severe complications, like gastrointestinal perforation, neuro-psychiatric complications and even death particularly among the vulnerable children with compromised immune systems.[5]

In 1948, the treatment landscape for typhoid fever underwent a remarkable transformation with the introduction of chloramphenicol by Theodore E. Woodward.[6] This heralded the era of modern treatment of typhoid fever, effectively transforming a once-debilitating and often fatal disease into a readily treatable one. Thus, chloramphenicol, amoxicillin, ampicillin, and cotrimoxazole emerged as the key treatment modalities for most Typhoid cases.[7] As a consequence, in 1940s, the mortality rate from EF plummeted from 26% to a mere 1%.[1] However, in 1950, Chloramphenicol-resistant *S. typhi* was reported for the first time and nearly 30 years later, the same resistance pattern was documented in Bangladesh as well.[8]

The widespread emergence of Chloramphenicol-resistant *S. typhi* and rise of multi-drug resistant (MDR) *S. typhi*, resistant to 3 three-primary antibiotics being used in typhoid treatment- *chloramphenicol, ampicillin*, and *cotrimoxazole* that posed a significant setback in the clinical management of typhoid fever (EF). So, this situation necessitated to search for a suitable alternative drug, the 3rd-generation cephalosporin (ceftriaxone). This emerged as an effective antibiotic against MDR *S. typhi.* [9-11] But, this has a big drawback: ceftriaxone is very costly and it requires parenteral administration.

Recent studies have reported a shift in the antibiotic susceptibility patterns, indicating the re-emergence of susceptibility of *S. typhi* to drugs used decades before such as chloramphenicol and amoxicillin,[12-13] where amoxicillin stands out as a safe and suitable drug and remain cost-effectiveness and suitable a drug for treating uncomplicated EF in LMICs-countries.

The promising results with amoxicillin prompted us to undertake this study to compare its efficacy against ceftriaxone in the treatment of uncomplicated EF in children. The outcome of this study may guide us in selecting a safe, effective, and readily available alternative for EF treatment, potentially reducing overall treatment costs compared to other available drugs.

Material and methods:

Study type : Cross-sectionally designed clinico-epidemiological study

Research design : Comparative study among 96 hospital admitted children with clinically diagnosed uncomplicated enteric fever-**EF**.

Study place : Department of Pediatrics, SSMCH

Study duration : 12 months (July 2013 through June 2014).

Total sample size : 96 admitted children with EF

Random distributed study Groups: 48 of total 96 randomly selected clinically diagnosed EF cases in **group-A** who received treatment with **inj. amoxicillin** and the rest **48** belonged to **group-B** who had been treated with **inj. Ceftriaxone**.

Variables studied : Age, sex and socioeconomic condition of all 96 children's households/families **Clinico-epidemiological variables**: Period of defervescence, hospital stay, treatment outcome, adverse effects, and cost of drugs were compared between these two Groups (A and B).

Data management : All double-checked data were entered into an IBM-PC using SPSS/Win.V.22.0

Data Analysis : Data of all variables (taken from filled in respective questionnaire) was analyzed using required statistical lines: Following a frequency distribution tables to yield dispersions of data to get the percentage of each variables of interest. A p-value (0.05) was taken as statistically significant, all through the analysis.

Results:

Table-I

Distribution of socio-demographic characteristics in the children (n=96)

Characteristics	Number of Patients	Percentage
Age (Years)		
2-5	46	47.92%
6-8	96	34.37%
9-12	17	17.71%
Sex		
Male	51	53.12%
Female	45	46.80%

(Male : Female = 1.13:1)

Out of the 96 cases, the majority of the patients were from the age Group of 2- 5 years (47.92%), followed by 6-8 years (34.37%). A little predominance was observed among male with female ratio of 1.13:1.

The incidence of enteric fever among the study children in relation to their monthly family income (n=96) was analyzed. More than half of patients 58 (56.25%) came from lower socio-economic households with a monthly income of less than 10,000/- BDT .

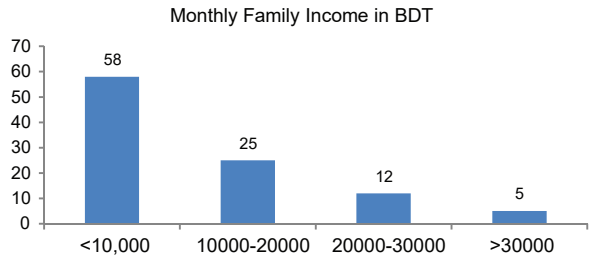

Figure-1 : *Monthly Family Income In Studied Children (n=96)*

Table-II

Distribution children with EF by physical findings (n=96)

Physical examination	Group A n (%) (n=48)	Group B n (%) (n=48)	Proportion of G-A (nA/48)	Proportion of G-B (nB/48)	p-value
Coated tongue [83 (86.5%)]	40(41.7)	43 (44.8)	0.83	0.90	0.15
Hepatomegaly [65 (67.7%)]	32(33.3)	33 (34.4)	0.67	0.69	0.41
Splenomegaly [36 (37.5%)]	17(17.7)	19 (19.8)	0.35	0.40	0.30
Toxic look [63 (65.6%)]	30(31.2)	33 (34.4)	0.63	0.69	0.26
Dehydration [17 (17.7%)]	08 (8.3)	09 (9.4)	0.17	0.19	0.39
Abd. Tenderness [74 (77.1%)]	39(40.6)	35 (36.5)	0.81	0.73	0.17
Abd. Distention [45 (46.9%)]	23 (24)	22 (22.9)	0.48	0.46	0.42
Caecal gurgling [15 (15.6%)]	09 (9.4)	05 (5.2)	0.19	0.10	0.10

On comparing all the physical examinations, like: coated tongue in 83 (86.5%), hepatomegaly in 65 (67.7%), splenomegaly in 36 (37.5%), toxic look in 63 (65.6), dehydration in 17 (17.7%), abdominal tenderness in 74 (77.1%), abdominal distention in 45 (46.9%), caecal gurgling in 15 (14.6%) among groups of A and B receiving amoxicillin and ceftriaxone respectively, but it did not differ, p-values significantly. (Table-II)[8]

Table-III

Comparison of sensitivity pattern of amoxicillin VS ceftriaxone (n=47)

	Sensitive (S) n (%)	Resistant (R) n (%)	P-value between Group A and Group B
Group A (Amoxicillin)	17 (36.2)	30 (63.8)	p<0.001
Group B (Ceftriaxone)	46 (97.9)	1 (2.1)	

The blood cultures yielded *S. typhi* spp and it's anitimicrobial sensitivity testing (AST) revealed a comparative state of both drugs (amoxicillin vs. ceftriaxone) in terms of their sensitivity 'S' and resistant 'R' pattern. While much higher percentage of 'Sensitivity' was yielded by ceftriaxone (group-B) by 98% than amoxicillin (group-A) 36%; the resistant pattern was just inversed more for amoxicillin (group-A) being more resistant to amoxicillin (64%) than that of ceftriaxone (2%), yielding a statistically valid difference in AST of *S. typhi* isolated from children with EF, (p<0.01). (Table-III)

Table-IV

Duration of treatment and clinical response to children with EF (n=96)

Clinical parameter compared (between Group-A vs. Group-B) children suffering from EF	Amoxicillin (Group- A) (Mean ± SD days)	Ceftriaxone (Group- B) (Mean ± SD days)	χ^2 test p-value
Defervescence from the day of starting antibiotics	5.55 ± 1.9	5.11 ± 0.45	0.57
Duration of treatment required	12.80 ± 1.20	8.70±1.30	<0.001
Total hospital stay	12.20 ± 1.80	9.13 ± 0.87	<0.003

P<0.05, statistically significant

Mean period of defervescence was 5.11±1.9 days for group-A children receiving amoxicillin and 5.55±0.45 days for group-B receiving ceftriaxone, which did not differ significantly (p=0.56). Contrarily, the two other clinical parameters: treatment duration and hospital stay yielded highly significant differences between the two groups: children with EF amoxicillin (group A) required 12.80±1.20 day to recover while children of ceftriaxone (group B) took 8.70±1.30 days, (p<0.01). Similarly, the mean hospital stay varied significantly: 12.20±1.80 days claimed for group-A children Inj. amoxicillin than 9.13±0.87 days for group-B (Inj. ceftriaxone) (p < 0.05). Thus, it is evident that children with EF who received ceftriaxone had a shorter treatment duration and they also had to stay in the hospital for less days, though period of defervescence between the two treatment groups (A and B) remained comparable. (Table-IV)

Table-V

Comparison in the clinical improvement (in mean days) between Group-A and Group-B suffering from EF receiving Inj. Amoxicillin vs. Inj. Ceftriaxone

Clinical Presentation	Clinical improvement in mean days of sickness		X2 test (p-value)
	Group A children of EF receiving Inj. Amoxicillin	Group B children of EF receiving Inj. Ceftriaxone	
Fever	5.19 ± 1.90	5.0 ± 0.45	0.004**
Abdominal Pain	3.15 ± 1.25	2.90 ± 0.50	0.037*
Appetite	6.30 ± 1.60	5.80 ± 1.22	0.003**
Weakness	8.30 ± 1.20	7.80 ± 1.11	0.002**
Headache	4.60 ± 1.70	3.90 ± 1.11	0.002**
Abdominal Tenderness	4.40 ± 1.20	4.06 ± 0.9	0.038*
Toxic Look	5.01 ± 1.11	4.90 ± 1.19	0.038*
Vomiting	3.10 ± 0.45	3.05 ± 0.15	0.039**
Diarrhoea	2.90 ± 1.10	2.70 ± 1.12	0.033

***Highly significant, *Moderately significant

Findings of table-V all the type of clinical improvement (in mean day) among the children suffering from EF between group-A receiving Inj. Amoxicillin and group-B receiving Inj. ceftriaxone when compared in regards to all clinical signs.

Thus all the clinical signs and symptoms, like fever, abdominal pain, appetite, weakness, headache, abdominal tenderness, toxic look, vomiting, and diarrhoea differed statistically between children of group A and group B are statistically significant (p<0.004, p<0.037, p<0.003, p<0.002, p<0.002, p<0.038, p<0.038, p<0.039, p<0.033) (Table-V).

Table-VI

Comparison of treatment outcome of studied children (n=96)

Study Group	Treatment outcome		P-Value
	Cured	Not Cured	
A (Amoxicillin) (n= 48)	35 (72.92%)	13 (27.08%)	0.03
B (Ceftriaxone) (n= 48)	48 (100%)	0 (0%)	0.14
Total	83	13	

Among the 48 cases in group A, 13 patients receiving Inj. amoxicillin did not get cured, resulting in a cure rate of 35 patients (72.92%). This difference was statistically significant ($p < 0.03$). In contrast, the Ceftriaxone group which yielded among all the children a 100% cure rate in group-B children ($p<0.14$).

Table-VII

Cost comparison between amoxicillin & ceftriaxone in treating of a patients weighing 20 kg

Drug name	Do se	Daily cost in BDT	Duration	Total cost in BDT	Proportions (total cost /8066)	p-value, z-score ***
Amoxicillin (Group A)	100 mg/ kg/ day 8 Hourly	94	14 days	1316	0.16	P<0.05
Ceftriaxone (Group B)	75 mg/ kg/ day 12 Hourly	675	10 days	6750	0.84	

As indicated in table -VII, children with EF administered with Inj. ceftriaxone group B incurred an average cost of 6,750 BDT, in contrast to Inj. amoxicillin group A spending only 1,316 BDT. Thus treatment with amoxicillin demonstrated significantly cost-effectiveness compared to that of for ceftriaxone (6750 BDT), resulting in a potential savings of approximately 5,000 BDT. Hence, treatment with amoxicillin remained 81% less costly than full treatment with ceftriaxone in children sufferinfg from complicated EF.

*** This p-value was calculated using two proportion test of unequal size using Google calculator utilizing a 1-tailed analysis. The alternative or claimed hypothesis was: Proportion of Amoxicillin≥ Proportion of Ceftriaxone. Thus, this one-tailed test was performed to prove our claim of which drug remains more effective.

Discussion:

Enteric Fever poses a significant challenge to public health in Bangladesh, often being a potentially fatal multi systemic infection. However, the 3rd generation cephalosporin (i.e. ceftriaxone) remains a costly drug with a high efficacy rate, which often evidences as potential high disease-burden in an low-middle-income country's (LMICs) like Bangladesh.[1] The wide-spread emergence of multi-drug resistant (MDR) strains has compelled us to search for an effective antibiotic.[2,3] It is spread predominantly by gram negative bacillus *Salmonella enterica serotype typhi* and less commonly Salmonella enterica serotype and para typhi A, B, and C.[1]

We evaluated and compared the efficacy of amoxicillin with ceftriaxone in the treatment of uncomplicated enteric fever (EF) among 96 admitted children at Sir Salimullah Medical College and Hospital (SSMCH). We particularly tried to determine the efficacy and cost-effectiveness between these two drugs used to match with low social economic status communities >65% of total population in Bangladesh.

Our findings yielded a little male preponderance (male to female ratio 1.13:1). Similar to that of several other studies,14 most of our children suffering from EF came out of low socio-economic strata. Half of the children's (56.25%) families had a per capita income of 10,000 BDT/month. 8,14

On clinical assessment, the common symptoms among these EF children were weakness (84.4%), followed by anorexia and/or nausea (72%) and headache and abdominal pain ranged between 61-64%, which is similarly reported by Ayamn et al from India.[13] Physical

findings in most of the children with EF showed coated tongue (86.5%), and a toxic look (65.5%)-a finding that remains consistent with that of Lakhotia M et al. from India.[15]

We observed hepatomegaly in 68% children while splenomegaly was noted in more than half of them (38%). This findings were similar to that of an Indian study[16], but it contrasted findings of Lakhotia M et al. [15] where it was 50% and 32% respectively, similar to that of Hosoglu S et al., who reported it by 42% and 20% respectively.[17]

Similar to a report from Pakistan,[18] our findings of blood culture yielded 48.9% as positive. Our finding on high yield blood culture positive cases may be due to the fact that the child having EF was brought to the hospital earlier in first week of illness and did not receive any antibiotic like amoxicillin, cotrimoxazole and chloramphenicol earlier. Blood culture of *S. typhi* isolate was sensitive to amoxicillin by 36% and ceftriaxone by 98%. The mean bacteriological R-pattern findings remain almost similar to that of another study from icddr,b, Bangaldesh,[19] and, the WHO report-2003.[20]

Based on clinical outcome the mean defervescence period was 5.55±1.9 days among group-A children receiving amoxicillin, against 5.11±0.45 days for ceftriaxone (group-B) though did not differ significantly, (p=0.57).

Efficacy of drugs was assessed, based on: i) defervescence period, ii) hospital stay and, iii) clinical cure rate, to determine the rate of "clinically cured" cases as study children started showing a positive clinical response evidenced by alleviation of clinical signs &/or symptoms. However, a study in Germany[21] contrasts our findings of mean defervescence (5.55±1.9) vs. 5.11±0.45. Their findings were 3.9±1.0 days vs 4.1±1.1 days in cases of amoxicillin and ceftriaxone, respectively.

While the duration of treatment with Inj. amoxicillin was 12.80±1.20 days, it was significantly less (8.70±1.30) days at a dose of 75 mg/kg/day for 10 days for Inj. Ceftriaxone received group B (p=0.01).

Mean duration of hospital stay of our EF children was 12.20±1.80 days who received Inj. amoxicillin (Group-A), was much less (9.13±0.87) days, who received Inj. ceftriaxone (Group-B), differing significantly, (p<0.05).

Thus, the mean period of defervescence revealed as 5.55 ± 1.90 days in group A, and 5.01±0.45 days group B yielded no statistical significant (P=0.57) difference. In the children with EF from amoxicillin group, the treatment duration was 12.80±01.20 days with a mean hospital stay of 12.20±1.8 days, in comparison to children receiving Inj. ceftriaxone (8.70± 1.3 days) on an average and, with a mean hospital stay of 9.13±0.87 days. Though findings of both the duration of treatment and hospital stay yielded a statistically significant difference (p<0.05 each), notably children receiving Inj. ceftriaxone (group-B) got faster than those receiving Inj. amoxicillin (group-A). And, children from Group-B were discharged earlier than that of Group-A.

Though the cure rate of children with EF receiving amo xicillin was good (73% cure rate), 100% children got cured who received Inj. ceftriaxone.[22] Children who did not respond to Inj. amoxicillin, even after 7 days, were then switched to receiving Inj. ceftriaxone. However, all the 96 children revealed a mean defervescence period after 5 days in both groups.

To evaluate the cost-effectiveness of these two injectable drugs in treating uncomplicated EF, we considered various factors: i) Opted for the cheapest drugs readily available in the market, ii) Per unit price of each drug was multiplied by the duration of treatment in order to account for dosing variation, iii) The mean weight of the EF children was read (~20 kg) thus, estimating the patients were cost administering Inj. ceftriaxone were projected to incur an ~cost of 6,750 BDT- while those in the Inj. Amoxicillin group it was 1,316 BDT. This evidences that treatment with Inj. amoxicillin is significantly less costly than that of with ceftriaxone. We calculated that a patient can save ~5,000 BDT. Treatment with amoxicillin is 81% less costly than treatment with ceftriaxone for complicated EF. Given that 56.25% of children with EF originated from households with family earning of <10,000 BDT/month, in the context of low- and middle-income countries (LMICs). Hence, it is reasonable that affordable treatment to treat EF children with amoxicillin will not only reduce the financial stress but also enhance treatment compliance and proper adherence among patients.

Finally, of 96 blood samples cultured from the children with EF, ~64% were resistant to amoxicillin and ~2% to ceftriaxone, respectively. With the re- emergence of sensitivity to amoxicillin against *S. typhi* and decreased

plasmid- mediated resistances, administration of Inj. amoxicillin may be effective approach of treatment as earlier data revealed.[23,24] Notably, no serious adverse drug reaction was noted in amoxicillin except slight nausea and vomiting, treating childhood EF with amoxicillin remain quite a logical and effective way to treat.

Conclusion

Though ceftriaxone showed better efficacy, shorter defervescence period and shorter hospital stay, we deduce that use of amoxicillin in treating uncomplicated children with EF may be considered as a logical option due to its high cure rate and being clinically effective when compared with ceftriaxone. Furthermore, Inj. amoxicillin appears to be a safe choice, in terms of antibiotic-related adverse effects and most notably, the cost of treatment using Inj. amoxicillin remain 81% less than that of the Inj. Ceftriaxone. This is particularly a cost-effective, safer, and, a potent antibiotic to cure children with EF, particularly in LMICs, like Bangladesh.

Limitations

1. Since this study was conducted among a relatively small sample size, we sincerely recommend further research among larger samples in multiple hospitals before refuting or accepting our findings.

2. The evaluation of cost-effectiveness should ideally include hospitalization costs, especially considering the varying hospital stay durations for the two drugs. Additionally, inpatient costs can differ based on the specific hospital where a patient is admitted. Future studies should take these factors into account to provide a more comprehensive cost analysis.

3. An essential consideration that Inj. Amoxicillin may not be suitable for children infected with EF due to probable resistance that needs to be revealed by blood culture reports.

Conflict of Interest (**COI**): None declared.

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Original Article

Histopathological Disease Spectrum of Cholecystectomy Specimen: A Retrospective Observational Study

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Abstract:

Background: Gallstone disease is a common surgical problem requiring cholecystectomy. It is known to produce diverse histopathological changes in the gallbladder ranging from acute or chronic inflammation to metaplasias and even malignancies.

Objective: The aim of this study was to emphasize the importance of a detailed microscopic examination and to study the range of histopathological lesions in cholecystectomy specimens.

Methods: This is a retrospective study of 1200 cholecystectomy specimens received in the Department of Pathology, Jahurul Islam Medical College Hospital (JIMCH) over a period of 6 years from January 2017 to December 2022. Clinical details and histopathological data were retrieved from the records. The variety of histomorphological changes in the resected gall bladder was studied.

Results: There were 1200 cases consisting of 516 (43%) males and 684 (57%) females with M;F ratio of 1: 1.33. Maximum number of patients (28.25%) being 41 to 50 years old. Most common clinical symptom were pain in the upper abdomen and right upper back (91.4%). Histopathologically, the most common diagnosis was chronic cholecystitis (66.75%), followed by acute on chronic cholecystitis (26.25%), gangrenous cholecystitis (3.25%), empyema gallbladder (1.5%), mucocele (0.75%), xanthogranulomatous cholecystitis (0.50%) and adenocarcinoma gallbladder (1%).

Conclusion: Cholecystectomy performed for a common condition like gallstone disease can result in a diverse and wide spectrum of histopathological lesions ranging from benign diagnosis to an unexpected gallbladder malignancy.

Keywords: Gallbladder, Cholecystitis, Cholelithiasis, Adenocarcinoma.

Introduction

Cholecystectomy specimens are among the most frequently accessioned specimens in general histopathology departments and account for a significant portion of the workload.[1] Histopathological examination of these specimens is primarily intended to rule out significant pathology, such as gallbladder dysplasia or carcinoma, the incidence of which varies greatly worldwide.[1]

Laparoscopic cholecystectomy is the treatment of choice done routinely for gallstone disease. Gallbladder is one of the most frequently received specimens in any histopathology laboratory. Usually, the diagnosis given in most of the cholecystectomy specimens is quite straight forward; that is, chronic cholecystitis. However, other diverse, but benign histopathological changes of gallbladder mucosa are also seen namely acute inflammation, cholesterosis, metaplasia and hyperplasia. Cholecystectomy performed with provisional diagnosis of benign diseases based on clinical, ultrasonological and computerized tomographic scanning misses a significant number of early malignant lesions of gallbladder. To avoid such blunders with bad consequences, therefore, every cholecystectomy specimen should be routinely examined histologically.[2]

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The purpose of this study was to determine the histopathological pattern of gallbladder lesions in cholecystectomy specimens in a South Delhi hospital and thus contribute in understanding of its etiopathogenesis.

Methods

Study Design: This was a retrospective study.

Study Type: This was an observational study.

Study Period: This study was conducted from 2017 to 2022

Study Place: This study conducted at Department of Pathology, Jahurul Islam Medical College, Bajitpur, Kishoregonj.

Study Population: The study was conducted on the resected cholecystectomy specimens which was operated in the Department of Surgery during a period of six years.

Sample Size: A total of 1200 cases were included in the study.

Sampling Method: Purposive.

Sampling Technique: Clinical details were retrieved from hospital records and histopathological data were obtained from the original pathology reports. Cholecystectomy specimens received in the laboratory were fixed in 10% formalin and submitted for gross examination after proper fixation. Three full thickness sections were obtained from fundus, body and neck of the gall bladder. Additional sections were taken from any grossly abnormal area if present. Sections were then stained with H and E stain and examined microscopically for a variety of morphological changes in the diseased gall bladder.

Data Analysis: All the necessary and relevant data were processed and analyzed by using the Microsoft Excel software.

Results

Table-I

Age and Sex distribution in different age groups (n=1200)

Age group (years)	Male (%)	Female (%)	Total (100%)
11-20	30 (5.81%)	15 (2.19%)	45 (3.75)
21-30	66 (2.79%)	117 (17.11%)	183 (15.25)
31-40	57 (11.05%)	150 (21.93%)	207 (17.25)
41-50	165 (31.97%)	174 (25.44%)	339 (28.25)
51-60	105 (5.81%)	105 (5.81%)	210 (17.5)
61-70	57 (5.81%)	72 (5.81%)	129 (10.75)
71-80	24 (5.81%)	48 (5.81%)	72 (6)
81-90	12 (5.81%)	03 (5.81%)	15 (1.25)

Twelve hundreds specimens of gallbladder received over a period of six years in our institution were analyzed histopathologically. Out of 1200 cases, there were 516 (43%) male and 684 (57%) female with M: F ratio of 1: 1.33. Mean age for male was 47.47 ± 15.65 yrs and for female was 45.87 ± 15.34 yrs. We found that a majority of patients of both sexes were in the age range of 41-50 yrs, with men (31.97%) predominating over women (25.44%) in that age group. The age and sex distribution are shown in Table –I.

Table-II

Presenting symptoms (n=1200)

Clinical presentation/ Symptoms	No. of Patients	Percentage (%)
Pain in the upper abdomen	1097	91.4%
Discomfort and fullness in the whole abdomen	556	46.3%
Dyspepsia, nausea, vomiting with food intake	434	36.2%
Intolerance to fatty food	140	11.7%
Feeling of mass in the right hypochondrium	109	9.1%
Non specific Incidental diagnosis	105	8.8%
Jaundice	88	7.3%

Large number of patients (85.2%) had gallstones according to the retrieved clinical data. Abdominal pain (91.4%) was the most common presenting symptom followed by abdominal discomfort (46.3%) and dyspepsia (36.2%). Table-II show clinical presentation of the patients. 88 (7.3%) patient presented with clinical jaundice. Most common clinical diagnosis was chronic cholecystitis in 972 patients (81%). 216 (18%) patients were operated for acute cholecystitis.

Table-III

Histopathological diagnosis

Clinical presentation	No. of patients with percentage
Chronic cholecystitis	801 (66.8%)
Acute on chronic cholecystitis	315 (26.25%)
Gangrenous cholecystitis	42 (3.5%)
Empyema gallbladder	15 (1.25%)
Mucocoele	9 (0.75%)
Xanthogranulomatous cholecystitis	6 (0.5%)
Adenocarcinoma	12 (1%)

All cases were examined microscopically and categorized according to their predominant microscopic pattern (Table-III). Chronic cholecystitis alone was the most common pathology reported in 801 (66.8%) cases followed by acute on chronic cholecystitis in 26.3% cases. Twelve cases of malignant lesions were found in the specimens. All were diagnosed as adenocarcinoma of the gallbladder. Eight cases of malignancy were diagnosed incidentally during microscopic examination. Table-III show histopathological diagnosis of the cases.

Table-IV

Microscopic features observed in non-neoplastic gallbladder specimen

Microscopic features	No. of cases	Percentage
Normal epithelium	112	9.3%
Ulceration / denudation of mucosa	396	33%
Perimuscular fibrosis	1128	94%
Lymphocytic infiltration	778	64.9%
Vascular congestion	510	42.5%
Rokitansky - Aschoff sinus	165	13.8%
Hypertrophic nerve bundle	212	17.7%
Metaplasia (intestinal + antral type)	86	7.2%

The non-neoplastic gall bladder microscopically was characterized by varying degrees of lymphohistiocytic infiltration along with per muscular fibrosis of the gallbladder wall, presence of Rokitansky-Aschoff sinuses, vascular congestion, metaplasia and hypertrophic nerve bundle (Table-IV).

Discussion

Gallbladder disease is one of the most common surgical disorder encountered by the surgeons which requires cholecystectomy. In our institution, all gallbladder samples collected after cholecystectomy are sent for histopathological examination. The main reason of routine pathological examination of cholecystectomy specimens is the exclusion of malignancy from the gallbladder as early diagnosis of gallbladder carcinoma is rarely achieved due to lack of specific signs and symptoms.[3]

In our study of 1200 cases, M: F ratio of 1:1.33 which was higher than other studies ranging from 1:2.6 to 1:6.4.[4, 5] Specimens with chronic cholecystitis are associated with cholelithiasis in about 95% of cases. Gallstones were seen in 85.2% cases, predominantly in women. This is consistent with the study by Mohan el al[6], who described predominance of gallstones in women. Majority of the patients was in the age group of 41-50 years. The incidence increases with age and in females possibly due to female sex hormones, sedentary habits and progressive increase in the secretion of biliary cholesterol.[7] Over ninety one per cent patients presented with pain upper abdomen, a number significantly lower than that reported by Laghari et al.[8] where all patients had upper abdominal pain.

The most common histopathological finding in our study was chronic cholecystitis; 801 (66.%) specimens were reported as chronic inflammation with filtration by chronic inflammatory and varying degrees of fibrosis. A similar study by Memon[9] also reports chronic cholecystitis as major histopathological finding, identified in 64.8% cases. Acute on chronic cholecystitis was found in 26.3% cases histologically characterized by congestion, edema, hemorrhage, acute inflammatory infiltrate and fibroblastic proliferation. Glenn et al[10] reported 6.17% acute cholecystitis cases in his study occurring more frequently in males. Xantho-granulomatous cholecystitis is a variant of chronic cholecystitis has been reported in 1.8% to 8.9% of cholecystectomy specimens .[11]

In our study, six cases were diagnosed as xantho-granulomatous cholecystitis. Empyema gallbladder is an unusual condition characterized by purulent infection of the gallbladder. The lumen is often distended with pus. Several reviews have identified empyema of the gallbladder in 2% to 11 % of patients undergoing

cholecystectomy.[11] We had 15 cases (1.25%) in this study.

Chronic inflammation to some degree is seen in most cases of chronic cholecystitis. Lymphocytic infiltration in varying degree is seen in 64.9% of the cases. However, perimuscular fibrosis of the gallbladder wall was the most consistent finding seen in 94% of cases. Rokitansky-Aschoff sinuses were seen in 13.8% of cases. Hypertrophic nerve bundles were seen in 17.7% cases. Hypertrophic nerve bundles probably occur secondary to obstruction.[4] Metaplastic changes were seen in 86 (7.2%) cases. Metaplasia of antral and intestinal type is frequently seen in gallbladders containing stones. It was presumed that prolonged irritation by gallstones and / or chronic inflammation led to metaplastic changes of gallbladder mucosa which may occasionally and eventually lead to the development of carcinoma. Khanna et al[12] reported 16% cases having metaplastic changes in their study.

Gallbladder carcinoma is a rare but fatal disease characterized by poor prognosis.[13] carcinoma constitutes 2- 4 % of all malignant lesions[14] and is the commonest malignancy of the biliary tract. Gallstones appear to be the most important risk factor, being reported in 70- 98% cases of gallbladder cancer, a far higher prevalence than that in age matched general population. Despite the strong association between carcinoma and presence of gallstone, the casual relationship between gallstone disease and carcinoma has not been established. Only 1- 3% of patients with gallstones go on to develop carcinoma and many patients without gallstones develop carcinoma.[13] In our study there were 12 cases of adenocarcinoma, all of which were associated with gallstone.

Conclusion

The histopathological spectrum of gallbladder after cholecystectomy is extremely variable. . Incidental diagnosis of carcinoma gallbladder is not rare; we discovered evidence of malignancy in 12 (1.0%) cases on subsequent histopathological examination of gallbladder specimen. The utility of submitting all routine cholecystectomy specimens for histopathological examination should be critically appreciated.

Conflict of interest: None

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Original Article

Surgical Site Wound Infection Following Caesarian Section at Ad-din Women's Medical College and Hospital, Dhaka: Rates and Microbiological Profile

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Abstract:

Background: Surgical site infection (SSI) occurs within 30 days of post-surgical procedure involving skin, subcutaneous tissue, soft tissue or any other parts of anatomy. According to the CDC. SSI is a significant cause of post-surgical morbidity and mortality. The objectives of this study were to determine the occurrence, the risk factors for infection following caesarean section (C/S) and to analyze its microbiological pattern.

Method: This prospective hospital-based study was conducted at the OBG Dept. of Ad-din Women's Medical College and Hospital. Dhaka, from 6 months period (January to June 2021). Total 5199 caesarean sections were performed at the OBG, AWMCH among women who developed surgical site infections (SSI) within 30 days of CS performed. Suspected SSIs were confirmed clinically by the surgeon, attested, by bacteriological culture.

Results: Of 5199 caesarean deliveries, 136 cases developed SSI (2.6%). The highest incidence of SSI was documented among women aged 20-30 years (63.2%), of who 54.4% were multiparous. The majority women were originally from rural areas (5 1.5%) women, 76.5% of women which were due to not attending for an antenatal care (ANC) checkup. Of them 90 cases (66.2%) belonged to middle class family. The incidence of infection was higher in obese women (47.8%) having BM1 > 30. and 33% in those with a BMI of 25-29.9. Of all associated comorbidities Premature Rupture of Membranes (PROM) were 25%, Gestational Diabetes Mellitus (GDM) in 14.7%, anemia in 14.7% and Gestational hypertension (GHTN) in 1 1%. Majority emergency caesarean deliveries 77.9% cases. Of total 52.2% cases had prolonged operation. On bacteriological culture growth. 26% which were *S. aureus,* followed by 25% *P. Aeruginosa,* 12.5% *S. Epidermis's* and 1 1.5% *E. coli*. However, 60 cases (44.1%) revealed as Multi-drug Resistant (MDR).

Conclusion : Surgical site infection in patients of caesarean delivery may be reduced by maintaining a normal BMI, ensuring proper and regular ANC to identify and treat comorbidities, limiting the preoperative hospital stay, improving surgeon's operative skill and technique and to reduce the operating duration and also informing the patients about the risk of SSI associated with elective C/S.

Key words: Body mass index, Caesarean Section, Hospital Stay, Hypertension, Diabetes Mellitus, Surgical Site Infection. Gestational Hypertension, Gestational Diabetes Mellitus.

Introduction:

The caesarean section (CS) is one of the most common obstetrical surgical procedures. It is performed when clinically indicated to facilitate delivery in complicated cases, hence prevents maternal and perinatal morbidity and mortality.[1]

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Among surgical complications, surgical site infection (SSI) rates range from 3-15% worldwide[2-4] and is defined as the infection which occurs within 30 days of post-surgical procedure involving skin, subcutaneous tissue, soft tissue or any other part of the anatomy, according to the Centers for Disease Control and Prevention (CDC).[5] Surgical site infection (SSI) following caesarean section is a major cause of morbidity and mortality, increasing both the duration of hospitalization and hospital cost.[6-9]

To reduce this complication, it is imperative to identify the risk factors and manage these factors. Multiple factors are related to SSI. Host related factors include- maternal age, obesity, personal hygiene, and immune-compromised status, presence of other medical comorbidities like hypertension, Diabetes Mellitus, anaemia, premature rupture of membrane (PROM), prolonged labor, and previous surgeries. Some procedural factors include- preoperative preparation, duration of surgery, the skill of operating surgeon, the type of suture material used and the prophylactic use of antibiotics.

The objectives of this study were to determine the incidence, & other factors for infection following caesarean section and to analyze its microbiological pattern.

Materials and methods:

The study was conducted at Ad-din Women's Medical College and Hospital (AWMCH), Dhaka, which is a 700 bed facility with multiple medical and surgical specialties, including Obstetrics and Gynecology. The study period was from January 2021 to June 2021. The data were collected from the post-operative ward, on a day to day basis and the risk factor profile was analyzed for those patients who had developed SSI following their caesarean delivery at the AWMCH.

Patients with SSI were identified as per the following criteria:

1. Infection occurring in the first post- operative week (Within 30days>)
2. Involving skin and subcutaneous tissue at surgical site with any one of the following :
    a. Purulent discharge.
    b. Organism isolated from fluid / tissues of superficial incision.
    c. At least one sign of inflammation (indurations/ erythema/local rise of temperature).
    d. Wound deliberately opened by the surgeon for drainage.
    e. Surgeon declares that the wound is infected.

The Exclusion Criteria is as follows:

1. Patients who required obstetric hysterectomy or had any other surgical complication
2. Caesarean deliveries that were not performed at the AWMCH.

Patients presenting with the symptoms and signs of wound infection following caesarean delivery were identified as per the CDC (Centers for Disease Control and Prevention) definition and criteria. As part of the risk factor profile analysis, patients' maternal age, parity, socio-economic class, area of residence, Body Mass Index (BMI), Antenatal care (ANC) attendance was recorded and patients were also assessed for hypertensive disorders, diabetes mellitus, anemia, hypothyroidism, bronchial asthma, etc. These aforementioned factors may contribute as the socio-demographic and obstetric risk factors along with the particulars of the surgery and labor pain. Details of the microbiological profile and antibiotic sensitivity were recorded from the wound culture and sensitivity reports.

Statistical analysis:

Out of 5199 caesarean deliveries, 136 patients met the inclusion criteria for SSI and were sampled in this study. The occurrence of surgical site infections were documented in percentage, and its distribution among the socio-demographic factors, associated comorbidities, type of caesarean section, surgery duration, and wound culture reports, was tabulated.

Result:

A total of 5199 pregnant women underwent caesarean section during the study period. Out of these, 136 were documented cases of SSI and this puts the incidence of SSI in AWMCH at 2.6%.

The following observations were noted in our study:

Table I

Distribution of surgical site infection among maternal socio-demographic obstetric characteristics

Variables	No. of Patients (n=136)	Incidence of SSI (%)
Age Range		
Less than 20 years	18	13.2%
20-30 years	86	63.2%
Years	22	16.2%
>35 years	10	7.4%
Parity		
Nulliparous	62	45.6%
Multiparous	74	54.4%
Location of Residence		
Rural	70	51.5%
Urban	66	48.5%
ANC attendance		
Regular	32	23.5%
Irregular	54	39.7%
Did not attend	50	36.8%
Socioeconomic status		
Lower	34	25%
Middle	90	66.2%
Higher	12	8.8%
Body Mass Index		
18.5-24.9 (Normal wt.)	26	19.1%
25-29.9 (Overweight)	45	33%
≥ 30 (Obese)	65	47.8%

Table I shows that the highest incidence of SSI was documented in women aged 20-30 years (63.2%), and 54.4% of multiparous women developed SSI. The majority were originally from rural areas (51.5%). A large number of patients did not have regular ANC attendance, 39.7% of which had irregular antenatal care (ANC) attendance, or not undergone any antenatal checkup at all (36.8%). of them 90 cases (66.2%) belonged to a middle class family. Their Body Mass Index (BMI) typically fell within the range of 18.5 to 24.9, but of 47.8% who had infection had a BMI of ≥ 30, and other 33% had a BMI of 25-29.9.

Table II

Prevalence of co- morbidities among patients with SSI

Associated Comorbidity	Number of of SSI (n=136)	Incidence (%)
Hypertensive disorder	15	11%
Eclampsia	5	3.7%
Gestational diabetes mellitus (GDM)	20	14.7%
Bronchial asthma	6	4.4%
Hypothyroidism	8	5.9%
Anaemia	20	14.7%
Premature Rupture of Membranes (PROM)	34	25%
PROM < 6 hours	25	18.4
PROM >6 hours	9	6.6
Urinary Tract Infection (UTI)	6	4.4%
IUFD (Intrauterine fetal death)	4	2.9%
Other (Obstetric cholestasis/ Hepatitis/Cholecystitis)	8	5.9%
No known comorbidities	10	7.4%

Table-II showed that, among 136 patients, 34 had suffered from PROM (25%), 20 had GDM (14.7%), 20 were anemic (14.7%), 15 had GHTN (11%). Only 7.4% of infected patients had no known comorbidities.

On analyzing the particulars of surgery, it was determined that emergency deliveries accounted for 106 cases (77.9%), and the frequency of SSI escalated with surgeries exceeding of a duration of 45 minutes (52.2%). (Table-III)

Table III

Relation between particulars of the surgery and incidence of SSI

Type of caesarean section	Number of Patients (n=136)	Incidence of SSI (%)
Emergency	106	77.9%
Elective	30	22.1%
Duration of surgery		
30-45 minutes	65	47.8%
>45 minutes	71	52.2%

Table IV

Relation between the labor status and number of per vaginal examinations (PVEs) and incidence of SSI.

Duration of labor pain	Number of Patients (n=136)	Incidence of SSI (%)
< 6 hours	15	11%
>6 hours	35	25.7%
6-12 hours	19	14%
Number of PVEs before CS		
< 3	29	21.3%
> 3	40	29.4%
Was not in labor	67	49.3%

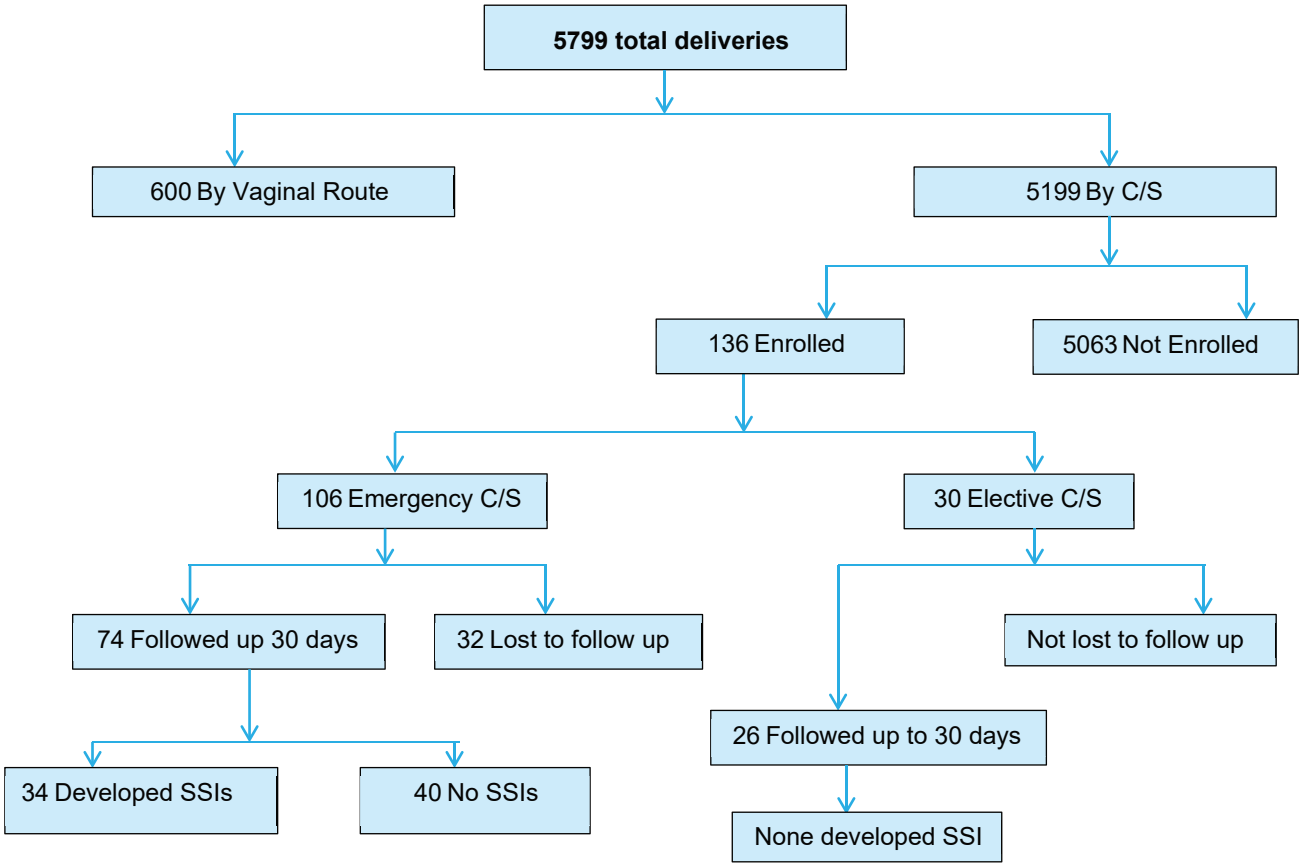
Of 69 patients who had labor pain (51%), 54 had labor pain for more than 6 hours (39.7%). We observed that repeated >3 PVE had been performed on 29.4% of patients who developed SSI. (Table-IV)

Table V

Microbiological characteristics of infected patient

Days to infection	No. of Patients (n=136)	Incidence of SSI (%)
< 15 days	102	75%
≥ 15 days	34	25%
Nature of the wound discharge		
Purulent	48	35.3%
Bloody	30	22.1%
Serous	58	43%
Wound culture		
Positive growth	96	70.6%
No growth	40	29.4%
No MDRO (Multidrug resistant organism)	76	55.9%
MDRO	60	44.1%
Organism detected		
Staphylococcus aureus	25	26%
Pseudomonas Aeurigonsa	24	25%
Staphylococcus epidermidis	12	12.5%
Actinobacter	10	10.4%
E.Coli	11	11.5%
Proteus	6	6.3%
Diphtheroid	5	5.2%
Nocardia	3	3.1%

Flowchart:



Among the 136 SSI cases, 102 developed infection within 15 days post-operatively (75%), 43% had serous discharge, while pus was present in wounds of 35.3% cases. Out of 136 wound swabs collected, 70.6% (96 cases) showed a growth of an organism, while 29.4% did not. Multidrug resistant organisms (MDRO) were found in 60 cases (44.1%). Among the 96 cases, 26% yielded growth staphylococcus aurous 25% pseudomonas aeruginosa 12.5% S. epidermidis 10.4% Actinobacter, 11.5% E.Coli, 6.3% Proteus, 5.2% Diphtheria and 3.1% Nocardia (Table-V).

Discussion:

As per the National Nosocomial Infection Surveillance (NNIS) system, SSI (surgical site infection) is the second most common post-operative infection following caesarean deliveries, with an incidence ranging from 3 to 15%. In India, as per a study conducted at Lady Hardinge Medical College New Delhi, the infection rate was 24.2%. In a study showed that, at a tertiary care center, Tamkur in Karnataka, the SSI rate following a lower segment caesarean section (LSCS) was 16%.[10] In our study, the incidence of SSI was 2.6%.

Multiple factors have been shown to contribute to post –CS SSI. In our study, the majority of cases, 76.8% of SSI, were above 20 years of age. This was similar to studies conducted by Anjum and Wloch C, et al (2012), while a study in Nigeria showed 75% SSI cases were below 25 years of age, replicating the outcomes of a study in rural India.[11-14] In our present study, we observed a high incidence of SSI in with a BMI of ≥ 30 (47.5%). Similar results were found in other studies. (BMI >35kg/m,[10-12] multiparty was found to be a major factor in our study.[15,16] Majority of our patients were multiparous, and a large number of patients had no antenatal checkup or had it irregularly. Majority of the patients when developed SSI belonged tomiddle class families.

Patients with pre-existing illness, such as anemia, hypertensive disorders, and diabetes mellitus were seen to be more prone to yield infection. It is generally agreed

that anemia diminishes resistance to infection and is frequently associated with puerperal sepsis. Pre-operative anemia is an important predictor of infection as provedm in several other studies.[17, 18] Hypertensive disorders were present in 14.7% of our cases. Hypertension, pre-existing or pregnancy induced, and related comorbid states have been associated with SSI in several studies.[19-21] Hyperglycemia has several deleterious effects on host immune function, most notably on neutrophil function. Poor control of glucose during surgery and in the perioperative period increases the risk of infection. The disease state, inductions, hypo-albuminuria, edema-all can contribute to the development of SSI. A high proportion of SSI (25.5%) has been reported in emergency CS when compared to the 7.6% in elective cases[22], in our study. Asthma and hypothyroidism also predisposed to wound infection in our study.

A study conducted at Bugando medical center, showed repeated per vaginal examinations was a risk for post cesarean section surgical site infection; this study show that, women who had 3 or more PVEs were more likely to develop post cesarean section surgical site infection as compared with the counterparts who have less than 3.[22] This may be due to ascending infection to the surgical site.

Longer durations of surgery, exceeding more than 45 minutes, carried a significant association in our study. A study revealed that an operative period longer than the 75th percentile increased the risk of SSI by 1.84times, [24] with the probable etiologies for this increased SSI risk being: complicated surgery, inadequate tissue concentration of antibiotic, tissue trauma, breach of sterile technique, increased blood loss and prolonged exposure to environmental pathogens.

Wound infections represent the most common nosocomial infections in patients who underwent surgery and are often caused by a limited range of opportunistic pathogens.[23-25] In our study, 96 cases (70.6%) yielded microbial growth. Among which, 26% showed growth of Staphylococcus aureus, the other organisms isolated included Pseudomonas Aeruginosa (25%), S. epidermidis (12.5%), Actinobacter (10.4%), E.Coli (11.5%), Proteus (6.3%), Diphtheroid (5.2%) and Nocardia (3.1%). Multidrug resistant organisms (MDRO) were found in 60 cases (44.1%).

Preoperative hospital stay significantly increased SSI in this study. The stay in hospital premises increases patient susceptibility to hospital acquired infection. These infections increase the chance of puerperal sepsis and wound infection in these patients.

Women opting for a caesarean section for non-medical reasons should be discouraged and informed of the risks of SSI as a complication. For reducing the prevalence of SSI following CS we should take measures in the pre-, intra- and post- operative phases. In the preoperative phase, maintenance of a patient's personal hygiene, antibiotic prophylaxis and proper antiseptic preparation of the surgical site and the use of sterilized instruments all contribute to suppressing postoperative infection.

Conclusion:

By maintaining a normal BMI, ensuring proper and regular ANC attendance to identify and treat any comorbidities, limiting the preoperative hospital stay, improving surgeon operative skill and technique to reduce the operating duration, informing about the risk of SSI associated with elective cesarean section, we may be able to reduce SSI in patients of caesarean delivery.

In view of the increasing rates of CS being performed without a clear medical indication, new practice protocols should be implemented to reduce the rate of caesarean deliveries as a CS surgery has a 5-20 times higher risk of postpartum infection as compared to vaginal deliveries. Surgical site infections has increased the morbidity significantly in the postoperative period, thus requiring a prolonged hospital stay and surgical intervention. Multiple factors are responsible for SSI. Identification of risk factors should be done and management accordingly is one of the preventable measures to reduce SSI. Emergency CS and improper antibiotic prophylaxis are important risk factors in the development of SSI, and given the proliferation of multidrug resistant organisms. To reduce the infection rate, we should implement a revised prophylactic antibiotic policy.

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Original Article

Comparison of Effectiveness Between Nebivolol and Bisoprolol in Treating Hypertensive Patients

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Abstract:

Hypertension is the leading cause of cardiovascular disease. Beta blockers are prescribed for hypertension, heart failure, angina pectoris or a history of myocardial infarction. In this study, we have compared the effectiveness between two beta blockers, i.e. Nebivolol and Bisoprolol in hypertensive patient.

A randomized prospective study was conducted from 1st January to 31st July 2022 at Jashore Medical College Hospital, Jashore in the outpatient department of medicine after maintaining all ethical issues. Five hundred twenty eight hypertensive patients without other comorbidities were studied after informed written consent. Patients were followed up for three months.

Out of 528 patients 264 were received Nebivolol. In this case group 40 patients were missed in follow up. And among 224 patients, 198 patients were found optimum reduction of blood pressure which was 88.39% out of 224. Rest 264 were received Bisoprolol. In this case group 58 patients were missed in follow up. And among 206 patients, 176 patients were found optimum reduction of blood pressure which was 85.43% out of 206.

In this study Nebivolol showed superiority in reduction of blood pressure in comparison to Bisoprolol that is 2.95%. Large scale trials along with comorbidities, mortality and hospital stay reduction as well as strict follow up are needed to compare various beta blockers.

Keywords: Beta blockers, Bisoprolol, Nebivolol

Introduction:

Beta blockers differ with respect to their mechanisms of action, especially in terms of beta-1 adrenoceptor selectivity and vasoactive effects[1]. First generation beta blockers are non-cardio selective (Propranolol) whereas second generation beta blockers are more beta-1 selective (e.g. Metoprolol, Atenolol etc). Third generation agents have not only beta adrenoceptor blocking properties but also vasodilating properties (e.g. Carvedilol, labetalol, nebivolol)[2-3]. Beta blockers are choice of drug in controlling hypertension, angina, heart failure and ischaemic heart disease. Many data explained that nebivolol has some special effects on endothelial dysfunction, aortic stiffening and central venous pressure. Nebivolol shows no significant increase risk on new onset diabetes mellitus as compare to other beta blockers[4]. In Bangladesh these two drugs have been used for a decade but there is no suitable data in comparison to their effectiveness. So, this study showed their effectiveness in controlling hypertension.

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Materials and methods:

This randomized prospective study was conducted from 1st January 2022 to 31st July 2022 at Jashore Medical College Hospital, Jashore. Five hundred twenty-eight (528) participants were studied after informed written consent. Group-A was given Nebivolol and group-B was given Bisoprolol. Patients age, gender, smoking, family history and duration of hypertension were noted in self structured questionnaire. Their blood pressures were measured in outdoor medicine department and follow up were counted in every month up to 3 months. All collected data were analyzed by using SPSS (Statistical Package for Social Science) version-22. Frequency and

percentage for categorical variables, *M(±SD)* and Chi-square test were used among categorical variable to determine the association between outcome and independent variables. A *p* value less than .05 were considered as significant all through.

Ethical Approval:

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

Results:

Out of 528 patients 264 received nebivolol. Of which 40 patients dropped out of were missed in following up. In this group of 224 patients, 198 had optimum reduction of blood pressure (88.39%). Of 264 were receiving Bisoprolol, 58 were missed in follow up. Thus 206 patients, 176 patients had an optimum reduction of blood pressure.

This findings demonstrates that study nebivolol showed superiority in reduction of blood pressure by 2.9% in comparison to that of Bisoprolol had.

Table I

Association between age groups and genders of patients (n = 528)

Age Group	Gender		Statistical Association, P-value
	Female (n=289)	Male (n=239)	
25-45 years(n=90)	56	34	χ^2=4.97
46-65 years(n=365)	188	177	P-value=.08,
66-85 years(n=73)	45	28	df=2

Majority of the respondents both male and female belong to the age group of 46-65 years. Here the statistical association between age groups and gender was not found significant (P=0.08) (Table I).

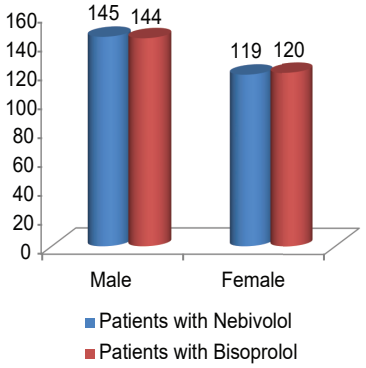

Table 2: *Gender specific distribution of hypertensive patients receiving Nebivolol and Bisoprolol of the patients (n=528)*

Out of total 528 patients, 264 received Nebivolol and majority (145 respondents) in this case group were men. The remaining 264 patients received bisoprolol, with majority of 144 male patients.

Table-II

Association between age groups and family history of patients

Age Group	Family history		Statistical Association, P-value
	Yes (n=27)	No (n=501)	
25-45 years(n=90)	3	87	χ^2=0.70
46-65 years(n=365)	20	345	P-value=0.70
66-85 years(n=73)	4	69	df=2

The majority of patients, from (46-65) years, reported no history of hypertension in their families which was not statistically significant (P=0.70).

Table III

Age of the patients (n=528)

Age of the patients	Patients with Nebivolol (n=264)	atients with PBisoprolol (n=264)
(Mean±SD)	54±9	55±9
25-45years	51 (19%)	39 (15%)
46-65 years	176 (66%)	189 (72%)
66-85 years	37 (14%)	36 (14%)

Mean age of patients with Nebivolol and Bisoprolol were (54±9) and (55±9) respectively. Patients aged (46-65) years make up 66% of Nebivolol patients and 72% of Bisoprolol patients.

Table IV

Distribution of Antihypertensive Drug (n=528)

Blood Pressure (mmHg)	Patients with Nebivolol (n=264)	Patients with Bisoprolol (n=264)	P-value
Systolic blood pressure, mmHg	145±7	146±7	0.47
Diastolic blood pressure, mmHg	90±2	91±2	0.83

In comparison between Nebivolol and Bisoprolol patient's Systolic (P=0.47) and Diastolic blood (P=0.83) pressure, there had no difference.

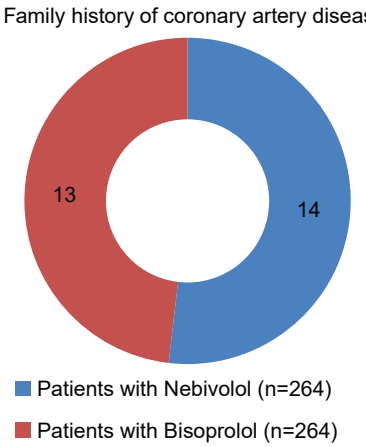

Figure-2: *Family history of coronary artery disease (n=528)*

Family history of coronary artery disease had been identified in 14 and 13 patients, respectively, out of 264 patients using nebivolol and bisoprolol.

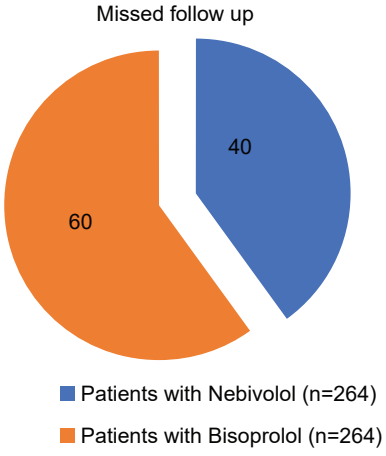

Figure-3: *Missed patients during follow up (n=528)*

The number of patients missed during follow-up among those using nebivolol and bisoprolol was 60 and 40, respectively.

Table-V

Association between age groups and drugs

Age Group	Drugs		Statistical Association P-value
	Nebivolol (n=264)	Bisoprolol (n=264)	
25-45 years(n=90)	51	39	χ^2=2.07
46-65 years(n=365)	176	189	P-value=0.35
66-85 years(n=73)	37	36	df=2

In both cases integrating nebivolol and bisoprolol, the majority of patients were found to be between the ages of (46 - 65) years and no statistical significance was found (P= 0.35).

Table-VI

Association between gender and drugs

Age Group	Drugs		Statistical
	Nebivolol (n=264)	Bisoprolol (n=264)	Association, P-value
Male (n=289)	145	144	χ^2=0.08
Female (n=239)	119	120	P-value=0.93, df=1

Male patients accounted for a larger proportion of those using Nebivolol and Bisoprolol than female patients and gender and drugs were not statistically not associated (P=0.93).

Table-VII

Association between drugs and missing patient

Drugs	Follow up		Statistical
	Missed (n=100)	Follow up (n=428)	Association, P-value
Nebivolol (n=264)	40	224	χ^2=1.35
Bisoprolol (n=264)	60	204	P-value=0.02, df=1

In Nebivolol and Bisoprolol case group 40 and 60 patients respectively were missed in follow up (P=0.02).

Table VIII

Comparison between Nebivolol and Bisoprolol patient's Systolic blood pressure (mmHg) (n=528)

	Systolic blood pressure, mmHg before medicated	After Systolic blood pressure, mmHg after medicated	P-value
Nebivolol	144±7	122±4	<0.001
Bisoprolol	144±7	143±7	0.23

In comparison between Nebivolol and Bisoprolol patient's Systolic blood pressure, Nebivolol case was more significant (P<0.001) than Bisoprolol case (P=0.23)

Table IX

Comparison between Nebivolol and Bisoprolol patient's Diastolic blood

	Diastolic blood pressure, mmHg before medicated	Diastolic blood pressure, mmHg after medicated	p-value
Nebivolol	90±2	82⊠4	<0.001
Bisoprolol	91±2	90⊠4	0.33

In comparison between Nebivolol and Bisoprolol patient's Diastolic blood pressure, Nebivolol case was more significant (P<0.001), than Bisoprolol case (P=0.33)

Discussion:

Hypertension is a globally reported risk factor developing ischemic heart disease (IHD), heart failure, stroke, atrial fibrillation, peripheral vascular disease etc. Blockers remains the first-line treatment against hypertension reported to be beneficial in primary and secondary prevention of coronary artery disease (CAD).[5, 6] Nebivolol, a third-generation (profoundly) β1-selective blocker is primarily been utilized for mild and moderate essential hypertension or combined with standard therapeutic drugs as some studies yielded. [5, 7-8]

Nebivolol and bisoprolol are highly selective β 1-adrenoceptor antagonists having clinical indications in many countries for the treatment of heart failure with reduced left ventricular ejection fraction (HFrEF), ischemic heart disease (IHD), and hypertension.[9]

Nebivolol and bisoprolol had similar impact on the mean change of diastolic blood pressure (DBP) and systolic blood pressure (SBP), according to a previous study, showing no difference in the overall incidence of AEs. Findings of a meta-analysis reported that nebivolol, compared to other blockers had no discernible difference with other second-generation β blockers in reducing blood pressure, SBP, and DBP.[10]

Findings of this study showed a clear-cut superiority of nebivolol over bisoprolol in reducing/ controlling blood pressure. Another study on bisoprolol showed that it reduces cardiovascular events too. [10] While a different study showed that nebivolol reduces mortality and cardiovascular hospitalization compared to that of placebo.[11, 12]

Due to super selectivity and unique mechanisms of nebivolol it protects more CVD cases since it has greater affinity on human cardiac beta-1 than beta-2 receptors, being more selective.[13] Nebivolol is 3.5 times more beta -1 adrenoceptor selective than that of bisoprolol and nebivolol not only decrease nitric oxide (NO) but also inhibits proliferation of human coronary endothelial cells and aortic smooth muscle cells via NO delivery. [14, 15]

This study therefore evidence that nebivolol remains superior to that of bisoprolol, but needs to be follow up uses of β- blockers, strictly.

Conclusion:

Our findings attest that, nebivolol and bisoprolol remains quite good in controlling of hypertension irrespective of patients' age and sex. In comparison to bisoprolol, nebivolol showed superiority in reduction of blood pressure by 2.95%. However, large scale clinical trials are needed to be conducted on the comparison of nebivolol and bisoprolol involving comorbidity, mortality, hospital stay including other beta blockers specially these two (nebivolol and bisoprolol).

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Original Article

Association of Epilepsy in Children Experiencing Febrile Seizure: Findings from National Institute of Neuroscience, Bangladesh

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Abstract

Background: Febrile seizure-(FS) remains the commonest benign convulsive childhood event. Prolonged-FS may have long-term consequences, including increased risk of subsequent-epilepsy.

Objective: To assess if there is any association among epilepsy and epilepsy syndrome with FS.

Methodology: This cross-sectional study was conducted in Epilepsy Clinic, National Institute of Neurosciences, Bangladesh, from January-June, 2021 involving one hundred 1-18 years-old-children diagnosed as epilepsy without secondary causes (intracranial space occupying lesion, head-trauma, CNS-infection, stroke). Patients were clinically evaluated thoroughly and were divided into two groups (Gp): Gp-A having a history of (H/O) FS and Gp-B, without FS. Demographically, clinical profile and electrophysiological-parameters were compared between the two groups for association with H/O FS. Pre-checked/cleaned-data were analyzed using SPSS.V.22.0 for proportional differences, taken p<.05 as significant (95%-CI). It was distributed nearly equally among both sexes, irrespective of FS. Although generalized epilepsy was common in both 12/14 (85.71%) Gp-A Vs. 54/86 (62.79%) Gp-B; epilepsy syndrome (infantile spasm, LGS, JME, JAE) revealed significantly more among non-FS-children than genetic epilepsy FS+ was more in FS group (p = 0.04). On EEG, generalized slowing [2/14 (14.28%)], generalized discharge [3/14 (21.42%) and features of encephalopathy [3/14 (21.42)] was observed more in patients with H/O FS, than non-FS.

Conclusion: In contrast to other types of epilepsy, our study revealed that genetic epilepsy febrile seizures + was associated with epileptic children who had H/O FS.

Key Word: Epilepsy, Febrile seizure, generalized epilepsy; Association

Introduction:

Febrile seizures (FS) are defined as seizures occurring in childhood accompanied by a temperature of 38°C or higher without evidence of an intracranial infection or defined seizure. It is the most common seizure type in children from 5 months to 5 years with a frequency of 2 to 5%, being higher in the second year of life.[1] The growth and development usually remain unaffected in children with a history of FS. Although FS are considered to be benign, recent evidence suggests that a small number of children with FS may develop recurrent FS or epilepsy. The prevalence of FS does not vary in different studies.[2,3] Variation of prevalence of FS depends on geographic location and is higher in Japan and Guam.

Although FS are not epilepsy, it may be the first presentation of subsequent epilepsy. It is difficult to predict who will develop epilepsy in future having FS in children. Epilepsy after FS was found to be 2% to 7%, four to five times more than general pediatric population. Published data are limited on the prevalence of epilepsy in association with FS in Bangladeshi children. Thus, this study was conducted on children at Epilepsy clinic, National Institute of Neurosciences, (NINS) Dhaka, to give an impression of the problem among children. This

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study aimed to highlight the characteristics of epilepsy in children with history of (H/O) FS. In the present study, we evaluated the association between FS and epilepsy and also a possible association between FS and any specific type of epilepsy/ syndrome.

Methodology:

Hospital set-up and patient population:

This cross-sectional study was conducted from January to July, 2021 at Epilepsy Clinic, National Institute of Neurosciences (NINS), Dhaka, being the only national level hospital on neurology in Bangladesh.

Detailed methodology, clinical evaluation and neurological investigations:

After taking informed consent, 100 children aged 1 to 18 years diagnosed as Epilepsy according to international league against epilepsy (ILAE) were enrolled for this study. However, secondary causes of seizure (intracranial space occupying lesions, head trauma, CNS infection and stroke) were excluded. All children were evaluated by the pediatric-neurologists, when detail history, clinical examination and necessary investigations, like, EEG, CT/MRI of Brain were performed. The criteria proposed by the International Classification of febrile Seizures (FS) and Epilepsy & Epilepsy Syndromes were considered to classify FS and epilepsy in our study.

Randomized grouping based on clinical symptomatology and neurological investigations:

Clinico-epidemiological history related to age at onset of FS, duration, type, frequency of FS, age of onset of epilepsy, its type, family history of FS/epilepsy, consanguinity, developmental history, birth and vaccination history were noted. As the children were clinically evaluated thoroughly, they were divided into two groups (Gp): Gp-A having a history of (H/O) FS and Gp-B, without FS. Demographic, clinical profile and electrophysiological-parameters were compared.

Data management and statistical analysis:

All the demographic status, clinical profile and electrophysiological-parameters from both FS- and non-FS groups were compared for the existing association these 2- groups. Pre-checked/cleaned-data were analyzed using SPSS.V.23.0. Analysis was performed to find out the association of epilepsy among the children who had H/O FS and who had no H/O of FS. Continuous data with normal distribution were analyzed in mean, standard deviation and the data those were non-normally distributed used, median and inter-quartile range with minimum and maximum ranges. Categorical or discrete data was summarized in frequency distribution (counts and percentages). For end points analysis, chi square test was used for categorical variables (comparing proportions) and an analysis of variance (one-way ANOVA Test) for continuous outcomes. Finally, multiple logistic regressions were performed to understand the independent association of epilepsy with FS. In the regression model, epilepsy was the dependent variable and significant associated factors with epilepsy were considered as the independent variables. A two-sided P value of less than 0.05 was considered to indicate statistical significance. Odds ratios and their 95% confidence intervals were calculated to evaluate strength of the association.

Ethical Clearance:

The institutional/ Ethical review committee of National Institute of Neurosciences and Hospital approved the study prior to launching. Before enrolling parents were explained about the purpose of the study and written informed consent was sought from the participant's guardian.

Result:

A total of 100 children aged 1 to 18 years diagnosed as Epilepsy (ILAE) without any secondary causes (ICSOL, head trauma, CNS infection, stroke) were enrolled. Among the study cases mean age was 9.98 ± 5.75 years, most of them were female 58 (58%), 33 (33%) cases had developmental delay and 3 (3%) had family history of epilepsy. The mean age of epilepsy onset was 5.44 ± 5.26 years and generalized epilepsy were common epilepsy type 66 (66%) followed by focal 30 (30%), unknown 4 (4%) and 10 (10%) had epilepsy syndrome. Infantile spasm 4(4%), LGS 2 (2%), JME 2(2%), GEFS+ 1(1%), JAE 1 (1%) were common epilepsy syndrome here **(Table I).**

Majority of the cases had no history of FS, except 14% who had FS **(Figure 1).** All cases who had history of FS, mostly (85.71%) experiencing simple FS with tonic-clonic (50%) in nature, and 57% facing recurrent episodes with an average frequency of > 2 FS **(Table II).**

Mean (± SD) age was 8.20 ± 4.77 years in children having history of FS and 10.28 ± 5.86 years who had no FS, the male female ratio was 1:1. Epilepsy was observed more in children belonging to middle class parental families in both FS and non-FS groups. Developmental delay was higher in FS-children (33.7%) than non-FS (28.57%). On both groups most of the cases had full term delivery, Group A: 13/14(92.85%)) and Group B 80/86 (93.02%). While the mean age of epilepsy onset was 4.87± 3.97

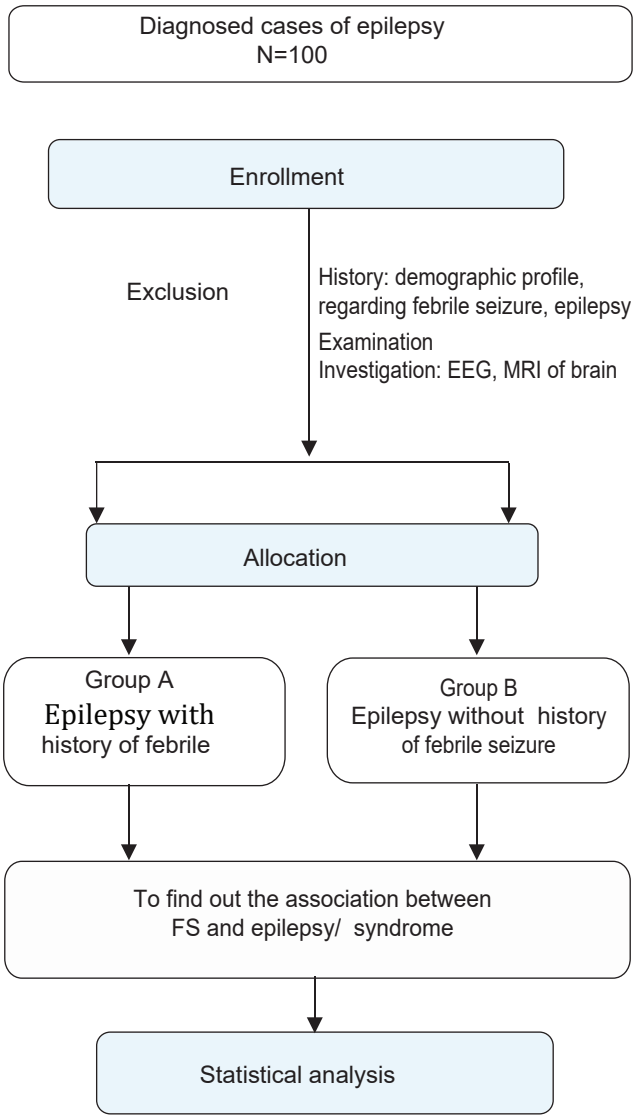

Figure 1: *Enrolment of epileptic children with or without FS*

years it was 5.54 to 5.48 years with or without FS, respectively. Generalized epilepsy was higher in both groups FS Group 12/14 (85.71%) and non FS group 54/86(62.79%), epilepsy syndrome (infantile spasm, LGS, JME, JAE) were significantly higher Non-FS group with the exception of GEFS+, and, for those, who had FS (p=0.04) more commonly. EEG revealed more focal epileptiform discharge in patients without H/O FS (48.83%) than not (35.71%), and, more generalized slowing 2/14 (14.28%), generalized discharge 3/14 (21.42%) and features of encephalopathy 3/14 (21.42) was observed in patients with H/O FS. MRI was done among 4 cases and found cerebral atrophy in 3 cases and 1 case had hippocampal sclerosis and all were in non-FS group **(Table III).**

Table I

Clinico demographic profile among the study cases (N=100)

Clinico-demographic profile	Frequency (%)
Age (Years) mean ±SD	9.98 ± 5.75
Sex	
Male	51 (51%)
Female	58 (58%)
M:F	
Socio-economic status	
Poor	35 (35%)
Middle	58 (58%)
Good	7 (7%)
Family History of epilepsy	3 (3%)
Developmental delay	33 (33%)
Epilepsy	
Age of onset	5.44 ± 5.26
Epilepsy type	
Generalized	66 (66%)
Focal	30 (30%)
Unknown	4 (4%)
Epilepsy syndrome	10 (10%)
Infantile spasm	4 (4%)
LGS	2(2%)
Juvenile myoclonic epilepsy	2(2%)
Genetic epilepsy febrile seizure plus (GEFS+)	1(1%)
Juvenile absence epilepsy	1 (1%)

Table II

Characteristics of febrile seizure among the study cases (n=14)

Febrile seizure (14)	n (%)
Types of febrile seizure	
Simple	12 (85.71)
Complex	1 (7.14)
Status epilepticus	1 (7.14)
Phenomenology	
Tonic	4 (28.57)
Clonic	1 (7.14)
Tonic-clonic	7 (50)
Version	2 (14.28)
Single febrile seizure	6 (43)
Recurrent febrile seizure	8 (57)
Frequency of febrile seizure, Mean ± SD	2.42 ± 2.20 (1-9)

Table III

Clinic demographic factors among the study cases (n=100)

Variable	Epilepsy		P-value
	Group A H/O Febrile seizure (n=14) n (%)	(Chi-Sq)Group B No H/O Febrile seizure (n=86) n (%)	
Age, Mean ± SD	8.20 ± 4.77	10.28 ± 5.86	0.212
Gender			
Male	7 (50)	44 (51)	
Female	7 (50)	42 (49)	0.565
M: F	1:1	1.04:1	
Socioeconomic status			
Poor		30 (34.88)	
Middle	5(35.71)	49 (56.97)	0.758
good	9 (64.28)	7(8.13)	
	0		
Birth history			
Preterm	1(7.14)	6(6.97)	0.545
Term	13(92.85)	80 (93.02)	
Family H/O epilepsy	1(7.14)	2 (2.32)	0.370
Developmental delay	4 (28.57)	29 (33.72)	0.470
Age of Epilepsy onset (mean± SD)	4.87± 3.97	5.54± 5.48	0.664
Duration of epilepsy, Mean ± SD	3.06 ± 2.85	4.36 ± 3.81	0.282
Epilepsy type			
Generalized	12 (85.71)	54 (62.79)	
Focal	2(14.28)	28 (33.55)	0.251
Unknown	0	4 (4.65)	
Epilepsy Syndrome			
Infantile spasm	0	4(4.65)	
LGS1	0	2(2.32)	0.04
JME2	0	2 (2.32)	
GEFS3+	1(7.14)	0	
JAE4	0	1(1.16)	
Abnormal EEG (n= 62)	9 (64.28)	53 (61.62)	0.674
Focal slowing	1 (7.14)	2(2.32)	
Generalized slowing	2 (14.28)	5 (5.81)	0.708
Epileptiform discharge			
Focal epileptiform discharge	5(35.71)	42 (48.83)	
Generalized discharge	3 (21.42)	14(16.27)	
Epileptic encephalopathy	3(21.42)	15(18.60)	0.691
MRI of brain (n= 4)			
Cerebral atrophy	-	3 (3.30)	
Hippocampal sclerosis	-	1(1.16)	-

1Lennox Gastaut syndrome, 2Juvenile myco-clonic epilepsy, 3Genetic epilepsy FS+ and 4Juvenile absence epilepsy.

Discussion:

To our knowledge this is the first from Bangladesh evidencing association of development of epilepsy with febrile seizure. However, few epidemiological studies were conducted on FS among Bangladeshi children, in addition to a number of important observations on FS that we pioneered to conduct it at the Bangladesh child Hospital and institute. Most of those cases were simple FS and their onset was below 1 year. Another study was carried out in Dhaka medical College Hospital on adult-onset epilepsy with a previous history of (H/O) where they found 29.34% epilepsy cases who had a H/O febrile seizure.

Inherent lower seizure threshold genetically predisposes child with FS for the development epilepsy. In the present study 14% of the epilepsy patients had H/O FS. A retrospective study by Sardar et al in Bangladesh found a frequency of FS of 33.7%.[9] On the other hand a prospective cohort study by Neligan et al. from United Kingdom found the incidence of subsequent epilepsy after FS to be 2-10%.[6] Similar results were found in other studies as well.

The risk of unprovoked seizure was more with children with complex FS. In the current study, most (85.71%) of the FS were found to be simple type and almost consistent to other studies.[10] However study by Almojali et al. from Saudi Arabia found a higher frequency (52.3%) of complex FS among the children who presented with their first febrile seizure. Although the frequency of simple FS is more in the present study, it revealed no significant association between the FS-type and subsequent epilepsy.

The mean age of onset of epilepsy in the present study was 4.87± 3.97 years and 5.54± 5.48 years with/without FS respectively. Some studies reported a late onset of 20 years and 18 years.[10 12] The age-related discrepancy is probably due to inclusion of patients of different ages. Generalized epilepsy was the most frequent type of epilepsy in both groups (85.71% and 62.79% respectively). This is somewhat contradictory to the findings of other studies where focal epilepsies were the most frequent type.[10 12] However, Annegers et al found equal number of generalized and focal epilepsy in their study.[5] The study on the prevalence of epilepsy in Bangladesh by Mohammad et al. found generalized epilepsy as the commonest type (67.2%).[6]

Epilepsy syndromes were significantly higher (p= 0.04) among patients without H/O FS with the exception of GEFS+ which was more common (7.14%) in children with H/O FS. Generalized epilepsies with febrile seizures plus (GEFS+) are a genetic syndrome characterized by heterogeneous epilepsy phenotypes including FS &generalized epilepsies.[17,18] Focal epilepsies can occur rarely in this syndrome.

Generalized slowing (14.28 % Vs 5.81%) and generalized discharges (21.42 % Vs 16.27%) in EEG were more frequent in patients with H/O FS which did not correlate with the study by Lee et al where focal discharges were more common.[9] According to literature focal seizure are the most common seizure disorders in adult.[19] In Bangladesh and India, however, generalized seizures outnumbered other types of seizures both in children and adult.[11,17,20] In this light of findings of this study we are further planning a prospective study to be launched soon for further clarifications.

In this study, none of the parameters of demographic profile (age, gender, prematurity, socioeconomic status and family history of epilepsy) yielded any association with the risk of subsequent development of epilepsy in children irrespective of FS status, a finding being consistent with a report by Almojali et al. Moreover, findings from several other studies reported early FS-onset, prematurity and a family history of epilepsy as risk factors for subsequent unprovoked seizures following FS.[11-13, 21-22] We assume that such differences might have occurred due to dissimilarity in study design.

Conclusion:

In contrast to other types of epilepsy, our study revealed that genetic epilepsy febrile seizures + was associated with epileptic children who had H/O FS, a large-scale prospective study will better establish the causal association between FS and epilepsy and may also denotes the risk features of FS that may predict the progression to epilepsy.

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Review Article

Primary Ciliary Dyskinesia (PCD)- A Disease in Disguise: Latest Situation Analysis in Bangladesh

Nabila Tabassum[1], Md Abid Hossain Mollah[2]

Abstract

Primary ciliary dyskinesia (PCD) is a rare autosomal recessive genetic condition due to dysfunction of cilia, the microscopic organelles in child's respiratory system. This results in defective functioning of cilia, leading to chronic sinu-pulmonary infection, situs inversus, dextrocardia, and congenital heart abnormalities, ultimately leading to subfertility and infertility.

Alike other low-income countries, lack of awareness on PCD remains one of the existing challenges associated with PCD diagnosis, in Bangladesh (BD), particularly in its primary care-phase, since it's non-specific symptoms mimic other conditions. Basically, absence of a single, "gold standard" genetic-based diagnostic test is fatefully missing in BD. The test in itself remain highly expensive and requires certain sophisticated steps, hi-fi equipment and a highly-trained professional team to run and maintain those appropriately.

Although management predominantly remains supportive it is not based on high-level evidences, *per se*. This updated review aims to discourse the importance of early, accurate and available diagnosis of PCD and its management particularly in countries like BD where it is prevalent but often remains under-cover.

Introduction

PCD is a rare autosomal recessive, genetic disorder resulting from mutations in genes coding for ciliary protein "dynein" which is involved in the ultrastructure, transport and function of cilia. Mutation leads to abnormalities in ciliary motility (dyskinesia), cilia function and impaired mucociliary clearance and chronic sino-pulmonary infection, bronchiectasis and infertility. Kartagener's syndrome (KS) is a subset of primary ciliary dyskinesias (PCDs) comprising a triad of situs inversus, bronchiectasis and sinusitis.[1] The term "primary" means it is an integral problem of cilia and not a 'secondary' problem caused by inflammation and infection.

Similar to many low-income countries, Bangladesh faces the challenge of limited awareness about Primary Ciliary Dyskinesia (PCD), especially during its initial phases of diagnosis. This is primarily due to the fact that the symptoms of PCD are nonspecific and can be easily mistaken for other medical conditions. In Bangladesh, there is a notable absence of a single definitive, "gold standard" genetic-based diagnostic test for PCD. Furthermore, the available tests for PCD are costly and require sophisticated equipment and a highly skilled professional team to administer and maintain properly.

While the management of PCD primarily focuses on supportive care, it lacks a strong foundation of high-level evidence. This updated review seeks to emphasize the importance of early, accurate, and accessible diagnosis of PCD, especially in countries like Bangladesh where the condition is prevalent but often goes undetected

The aim of the updated review is to provide a latest scenario- a '*status-quo*' on the clinico-epidemiological characteristics in Bangladesh, it's currently available diagnostic modalities and the latest management capabilities of childhood-PCD in BD.

This would facilitate our clinicians' in adding values towards:

- Increasing broader understanding of our clinicians/ pediatricians on PCI in Bangladesh
- Building boarder awareness to address this life-threatening yet manageable genetic disorder

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- Getting optimistic in characterizing & early-diagnosing such serious lie threatening cases
- Thus, to add values in child's life with better prognostic approaches and higher survival rates through increased detection and outcome in Bangladesh.

Clinico-Epidemiological Characteristics:

A large international survey on pediatric PCD, including 1,192 children by Kuehni et al. concluded that the prevalence of PCD ranged from 1:10,000 to 1:20,000.[2] However, the actual prevalence is thought to be much higher since PCD is often underdiagnosed due to poor knowledge of the disease, symptoms resembling other respiratory conditions and the lack of diagnostic facilities.[3]

The mode of inheritance is autosomal recessive, making it more common in populations with high prevalence of consanguineous marriages such as those reported in British Asian population.[4,5]

Etiological and patho-physiological features:

PCD is inherited in an autosomal recessive manner, however some cases of autosomal dominant and X-linked recessive inheritance has also been reported.[5,6]

Pathogenesis and pathognomonic characteristics:

Normally the respiratory epithelium is lined by ciliated columnar cells. The axoneme of motile cilia is composed of nine peripheral doublet microtubules with attached inner and outer dynein arms (IDA and ODA, respectively) and radial spokes, surrounding a central pair complex (CC) consisting of two central microtubules surrounded by the central sheath(so called 9 + 2 structure).[6]

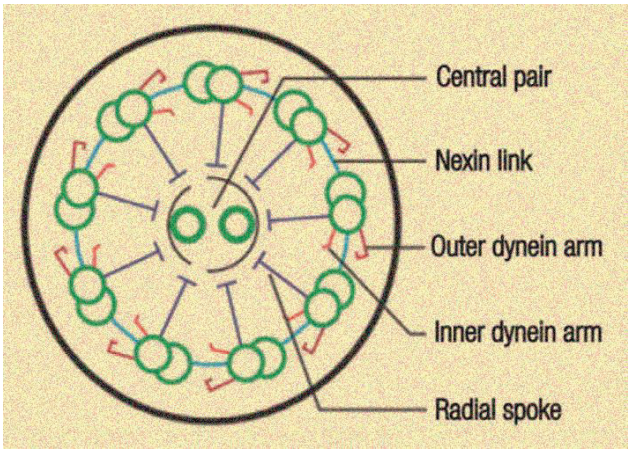

Fig: *Ciliary Ultrastructure*[2]

Cilia beat in a coordinated fashion, at 10–15 Hz, transporting mucus, trapped particles and pathogens towards the nasopharynx and out of body, (muco-ciliary clearance).[7] In PCD, mutation of gene coding for ciliary ultrastructure leads to abnormalities in ciliary structure, (loss of ODA or IDA), ciliary motility (dyskinesia) and impaired muco-ciliary clearance. As a result, there is buildup of respiratory secretion and the affected child suffers from lifelong chronic airway infection, recurrent pneumonia, chronic rhino sinusitis, glue ear and subsequently bronchiectasis.

In addition, subfertility or infertility is seen in male PCD patients caused by sperm dysmotility. Moreover, dyskinesia of cilia results in situs inversus as motile nodal cilia are crucial for normal situs development during embryogenesis.[8,9]

Clinico-epidemiological Features

Early warning features of PCD that should make clinicians suspect this disorder are-

Neonatal period:

- Unexplained neonatal respiratory distress in an otherwise healthy full-term baby and requiring long term O_2 therapy[10]
- Early onset persistent and recurrent rhino sinusitis and wet sounding cough

Infants and children:

- a persistent, daily "wet sounding cough" that has always been there, never completely clears even with treatment
- chronic and persistent rhino sinusitis is the most common feature.6,11
- chronic or recurrent otitis media with effusion, with hearing and speech impairment
- situs abnormalities (around 50% of cases).[6,12]
- Recurrent pneumonia and infective exacerbations
- Bronchiectasis and respiratory failure.[6,12]

Adults

- Subfertility /infertile due to dyskinetic sperm.[8,9]

Examination findings may include-

- Dextrocardia and situs inversus, asplenia, nasal polyps, rhinitis and conductive deafness.
- Features consistent with chronic lung disease and bronchiectasis, bilateral wheeze and crackles.
- Extremities may exhibit digital clubbing.[6,9,11]

Indications of referral for diagnostic testing

- Neonatal respiratory distress requiring prolonged oxygen of unknown cause.[10]

- History of consanguinity and sibling with PCD, particularly if symptomatic
- Situs inversus plus respiratory or sinu-nasal symptoms
- Recurrent sinu-pulmonary infection, serous otitis media in association with lower and upper airway symptoms.[6,9,12]
- Daily lifelong "wet cough that does not seem to go away"
- If considering testing for cystic fibrosis (CF), also consider testing for PCD particularly if rhinitis, sinusitis or glue ear with dextrocardia are present
- Unexplained bronchiectasis.[13]

Required Investigations and Accurate Diagnosis:

The diagnosis of PCD remains challenging due to a lack of awareness by general practitioners and pediatricians, symptoms overlapping other respiratory conditions and a lack of a gold standard investigation.[13,14]

Diagnosis is usually made by conducting a combination of five PCD-specific tests [3, 13] where laboratory setup is available *e.g.*

- Measurement of nasal nitric oxide (nNO) concentration: It involves breathing in nitric oxide and then measuring the level during exhalation through the mouth or nose with a chemiluminescent analyzer. It is found to be low in patients with PCD (10–15% of normal values) due to reduced ciliary clearance in the para nasal sinuses.[15] It used to be a moderately accurate and immediate screening tool for patients >5 years of age. However, the ERS guidelines argue that nNO should not be used as a screening test, since low levels are found in nasal obstruction and CF.[15] and there are no age-related cut-off values.
- High-speed video microscopy (HSVM): Ciliary function is assessed by ciliary beat pattern (CBP) and ciliary beat frequency (CBF) less than 10 Hz/second. It can be quantified by highly magnified and high-resolution video images of cilia recorded by a digital camera attached to a microscope.[16]
- Immunofluorescent (IF) antibody staining of ciliary proteins: Involves visualization of fluorescence- labeled antibodies specific for cilia proteins in epithelial cells.[17]
- Transmission electron microscopy (TEM): TEM is used to visualize respiratory cilia ultrastructure defect in electron microscope at high magnification (>60 000×).[18]
- Genetics: Genetic mutation analysis to detect genes associated with PCD.[19]

Other required investigational approach

- Saccharine test: Saccharin is placed in the nose and the speed of transport to the nasopharynx is measured. However, it is technically difficult to perform in young children & thus no longer used.[6,9,20]
- X-ray chest: Show dextrocardia, lung over-inflation, bronchial wall thickening, peri-bronchial infiltrates and atelectasis.3,6,9,11,21
- HRCT scan: Bronchiectasis and involvement of paranasal sinuses (poorly aerated mastoids ± absence of frontal sinuses.3,6,12,21
- Pulmonary function tests: Spirometry reveals an obstructive picture with a reduction in the FEV1/FVC, FEV1 and a reduction in respiratory flow of 25-75%.[22]

Diagnosis:

Based on the above clinical features and investigation findings.

In the UK, diagnosis is based on consistent clinical history plus at least two abnormal tests (TEM, HSVM and low nNO; repeating nNO and HSVM if TEM is normal) [23] whilst in North America, genetic testing is given more importance.[24,25]

According to European Respiratory Society (ERS) guidelines, diagnosis of PCD include.[2,3]

➢ **Definitive PCD**
- Patients with a supportive history of PCD with
- Non ambiguous bi-allelic mutation OR
- Hallmark ciliary ultrastructure defect

➢ **Highly likely PCD**
- Compatible history, And
- Very low nasal nitric oxide (nNO), And
- Either highly abnormal ciliary beat pattern on high-speed video microscopy on 3 occasions OR
- Highly abnormal ciliary beat pattern on high-speed video microscopy analysis on cell culture

➢ **Extremely unlikely PCD**
- Modest on non-suggestive history And
- Normal or high nNO And
- Normal ciliary ultrastructure

In countries with limited resources, Neonatologists, Pediatricians and ENT specialists should keep a high index of suspicion for PCD as clinical diagnosis. **PICADAR** (Primary Ciliary DyskinesiA Rule) is a recent validated predictive tool based on clinical characteristics that can help identifying patients with PCD to refer for further testing.[26]

The score is based on analysis of 7 clinical questions of a patient who has been suffering from a daily wet cough, started since early childhood. However, PICADAR is not designed for patients without a wet cough.[26]

Was the patient born pre-term or full term?	Term	2
Did the patient experience chest symptoms in the neonatal period (e. g. tachypnea, cough, pneumonia)?	Yes	2
Was the patient admitted to a neonatal unit?	Yes	2
Does the patient have situs abnormality (situs inversus or heterotaxy)?	Yes	4
Does the patient have a congenital heart defect?	Yes	2
Does the patient have persistent perennial rhinitis?	Yes	1
Does the patient experience chronic ear or hearing symptoms (e. g. glue ear, serous otitis media, hearing loss or ear perforation)?	Yes	1

The score demonstrates good sensitivity and specificity. Patients with a PICADAR score ≥10 have more than 90% probability of testing positive for PCD, while a score ≥5 indicates more than 11% chances of being diagnosed as PCD. In countries with no diagnostic testing, PICADAR could potentially be used to estimate the diagnostic likelihood of patients.[26]

In addition, centers where TEM is not available should consider collaborating with a PCD service with electron microscopy capacity. An advantage of TEM is that samples in fixative blocks may be sent by land or air to specialist centers.[18]

Differential diagnosis:

PCD may be confused with the following condition-[2,3,6]

- Allergic rhinitis
- Conditions linked to bronchiectasis e. g.
    - Acquired obstruction- foreign body aspiration
    - Tuberculosis
    - Congenital obstruction - bronchomalacia, pulmonary sequestration
    - Immunodeficiency
- Cystic Fibrosis
- Miscellaneous disorders e. g. alpha-1 antitrypsin deficiency, Interstitial lung diseases

PCD situation in Bangladesh

There is very little awareness as regards to PCD in children of Bangladesh. Moreover, the confirmation of diagnosis is very difficult. The facilities for the investigation are lacking here including the provision for measurement of nasal nitric oxide concentration, high speed video microscopy (HSMV), immune-fluorescent antibody, transmission electron microscopy to visualize respiratory cilia ultrastructure defect in electron microscope at high magnification. There is documentation of cases of PCD with presentation since early infancy with chronic wet-sounding cough, massive and long standing productive sputum, sinusitis and bilateral bronchiectasis [6,9,21] but the cases were diagnosed clinically and could not be subjected to genetic test.

Management

PCD is difficult to diagnose, thus are often labeled as difficult-to-treat asthma/ Cystic Fibrosis/ immunodeficiency [25] and is treated accordingly. Although sometimes patients respond to such treatment "by chance", the daily wet cough and rhino sinusitis never completely clears. Such a label often delays the diagnosis, it is thus very important to correctly label the disease and treat it specifically to improve outcome. Evidence-based medicine protocols for PCD is very limited and management protocols have largely been deduced from treatment programs for CF bronchiectasis.[27]

Management should be undertaken by multidisciplinary team and families should be counseled about the genetic basis of disease. The mainstay of treatment for PCD involves-

Airway mucus clearance

- Mucolytic therapies (first line): Nebulized inhalation of hypertonic saline /N-acetyl cysteine. It moistens and dilutes viscous airway secretions, and thereby facilitates muco-clearance techniques.[28]
- Muco-clearance techniques (second line): Manual chest physiotherapy, postural drainage, active cycle breathing, and manual devices like positive expiratory pressure (PEP) valves, and mouthpiece or chest wall oscillating devices.[28]

Infection control and prevention:

- Systemic antibiotics (indicated for respiratory exacerbation marked by changes in cough quality, sputum production, increased respiratory rate, and work of breathing, or a decline in FEV_1%). Duration of treatment is 14–21 days.[29] The commonest pathogen found in sputum of patients with PCD is H influenza.[30] Others include S pneumoniae, S aureus, M catarrhalis and P aeruginosa.[30] The selection of antibiotics should be based on most recent sputum culture results and colonization history of individual patient. Macrolides is a good choice. Regular inhaled or oral antibiotics *e. g.* Azithromycin should be considered in patients where eradication strategies fail. Inhaled Tobramycin should be reserved for P. aeruginosa infection.[30]
- Vaccinations against pneumococcus & Influenza are recommended on an annual basis.[29]

Other supportive treatment

- ENT disease including recurrent otitis media with effusion may require tympanostomy tube placement and endoscopic sinus surgery.[27]
- Elimination of exposure to inflammatory triggers and passive smoke
- **Pulmonary surgical resection** (i.e., segmentectomy or lobectomy) in diffuse lung disease and severe hemoptysis despite medical management of bronchiectasis.[27]
- Lung transplant.[27]

Follow up

- Routine clinical visits (2-4 visits per year) for spirometry monitoring, respiratory culture surveillance through sputum or oropharyngeal cultures [27] and chest radiography reserved for acute episodes

Complications

Bronchiectasis, pneumonia, empyema, conductive deafness, infertility and communicating hydrocephalus.[3]

Prognosis:

There is no reliable estimate of life expectancy for children with PCD. It is a life altering, life shortening, multi-system condition, with progressive decline in lung function progressing to develop bronchiectasis during childhood, reducing quality of life. Careful and routine follow-up to monitor symptoms and manage chronic lung disease and bronchiectasis can help improve patient outcomes

Summary

Primary Ciliary Dyskinesia, although common, are seldom diagnosed in children especially in countries with limited resources due to a lack of awareness and confirmatory tests. In such cases, high index of clinical suspicion, scoring systems e.g. PICADAR and cost-effective alternatives should be considered. Features that might increase suspicion of PCD include consanguinity, recurrent and chronic upper & lower respiratory symptoms along with sinusitis, middle ear infection and dextrocardia or situs inversus. Investigations are costly, time consuming and requires technical expertise and countries like Bangladesh fall short of such resources. However, it is important to setup international networks and collaborations with neighboring countries to widen the accessibility of diagnostic tests and develop standardized protocols to correctly label and manage the disease.

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Case Report

Abdominal Pain in Dengue Hemorrhagic Fever in children: What it May Indicate?

Mahmuda Hassan[1], Jannatul Ferdous Sonia[2], Masuma Khan[3], Afsana Mukti[4]

Background:

Dengue fever (**DF**), a major public health concern globally, particularly in it's southern part of tropical and subtropical countries. DF caused by flavivirus- the most common mosquito borne viral infection.

There is a wide range of clinical presentation of dengue syndrome. It ranges from non-specific infections (influenza-like illness- as self-limiting diseases up to life threatening dengue hemorrhagic fever (**DHF**), dengue shock syndrome (**DSS**) and Expanded dengue syndrome (**EDS**). Due to increased spread of disease and 2nd or 3rd attack in same person may remain as the ground of atypical presentations. This may be potentially serious resulting in increased morbidities, often being life threatening. It is, therefore, crucial for a pediatrician to monitor a child with dengue (DEN) being aware of and alert to notice atypical manifestations, chiefly. Here, we report a case of DF presenting with severe acute abdominal pain due to acute pancreatitis, which is infrequently reported complication of DEN infection in children.

Though, abdominal pain is a commonly reported symptom in children with DF including hepatitis, acidulous cholecystitis and peptic ulcer disease, pancreatitis has not been reported in children so far (if not rarely) but is reported among adults[1] in the form of case reports.[2]

The case

A 8 years old female child admitted at a tertiary care hospital with a history of high grade fever of about 104°F, headache, myalgia, nausea and vomiting for 5 days followed by diffused abdominal pain being more marked in the epigastrium region with abdominal tenderness.

On examination she was febrile with cold extremities and her appearance was toxic. Her pulse was 126/min, rapid and thready, blood pressure 60/40 mm of Hg with pulse pressure of 20mm/Hg and her respiratory rate was increased due to hypovolemic shock (28/min). Abdominal examination revealed diffuse tenderness without any point of definite area or region of tenderness, abdomen was soft and bowel sound was present**.** Findings of respiratory and central nervous system examination were unremarkable except tachycardia.

Laboratory investigations were performed just after arrival at the hospital before crystaloid infusion and which showed hemoglobin 12.2gm%, total leucocyte count 3600/cmm. polymorphs 64% and lymphocytes 36%, hematocrit 41% and platelet count 66000/cmm. Also blood was send for sepsis screening which showed negative result subsequently.

After sending the baseline investigations, we started I/V infusion of 0.9% NaCl at the rate of 20ml/kg over 30 minute as per DEN guideline and subsequent blood pressure was 90/60mm of Hg. Pulse 110/minute with good pulse volume. Then fluid had been continued at the rate of 7ml/kg/hr for the next 5-6 hours. Thereafter, 6 to 7 hours of admission, CBC was repeated where HCT showed 39% with a platelet count of 44,000/cmm. Platelet went on its nadir on 4th hospital day with gradual rise of HCT. But the child was very irritable for her abdominal pain. Ultra-sonogram of whole abdomen was done on the 2nd day of admission due to having severe abdominal pain, but revealed no evidence of intestinal perforation as free intraperitonial air.

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Liver was normal in size with edematous gall bladder. Head and body of her pancreas appeared normal, but it's tail appeared to be swollen with hypo echoic area measuring about 3.4 cm-which was suggestive of focal pancreatitis.

The biochemical parameters of liver enzymes were within normal limit, AST and ALT 40 and 21 IU/L**.** Blood glucose was 5.6mmol/ dl and calcium 8.2 mg/dl. Total protein was 6.3gm/dl. Serum electrolytes showed mild hypernatremia (Na 133 mmol/L).

Pancreatic enzyme determination disclosed an amylase level of 259U/L (normal 20-95) and lipase levels 280U/L (normal 3-40). Her CRP was 20mg/dl. D - dimer was 4.23µg/ml.

Her NS1 antigen for dengue was negative on 5th day of fever.

But her dengue serology (IgM using ELISA) was positive while viral markers for hepatitis were negative. However, due to COVID pandemic, RT-PCR was done but yielded negative, chest x-ray was normal.

The girl was managed as per national protocol of dengue syndrome and including using proton pump inhibitor, and she got improved without any other complication. Before discharge platelet count came to more that 100000/µl and hematocrit level came down to normal. Thus, she was discharged on 8th day after hospitalization.

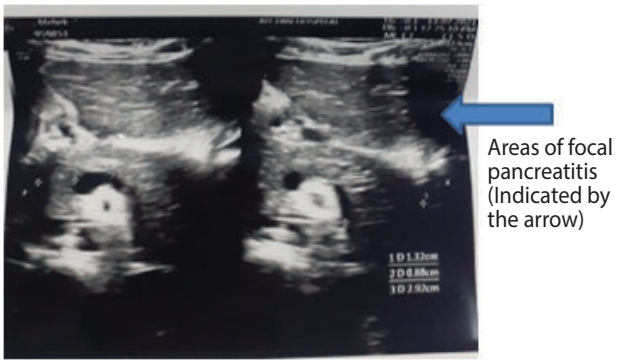

Fig 1: *Ultra sonogram of the abdomen shows below yielded as acute pancreatitis.*

She was advised for follow up after 48 hours of her discharge with follow up report of serum amylase which came down to almost normal level. But serum lipase level took 2 weeks to become normal. So, this as a ease of DHF with acute pancreatitis. Finally we diagnosed this case as expended dengue syndrome.

Discussion

In dengue fever, abdominal pain can be caused by hepatitis, acalculous cholecystitis, peptic ulcer disease or may be due to pancreatitis.[3,4]

Majority of the reported cases of pancreatitis in dengue fever were from Southeast Asian countries like India, Bangladesh, Taiwan and Indonesia as dengue is widely prevalent in these regions. Of these 17 cases, 11 were males (64.7%). The average age of the patients in these reports was 37.68 years, that is in the adult group.[5]

Acute pancreatitis is a rare complication of dengue fever that has been reported very infrequently. [5,6]

Further, some observational studies documented the occurrence of pancreatitis and lipase/amylase elevation in patients with underlying dengue fever and studies were from adults. [7,8,9,10,]

Acute pancreatitis may be under diagnosed because of diffuse abdominal pain, and we think about acidulous cholecystitis, peptic ulcer and the rarely we think about pancreatitis in children. Therefore, clinicians might not request serum amylase or lipase or suspect the diagnosis despite patient having abdominal pain or vomiting. In patients with dengue fever who develops abdominal pain, it is helpful to estimate and monitor serum lipase and amylase levels and to perform abdominal imaging to rule out acute pancreatitis.

The exact pathogenesis of pancreatic involvement in dengue infection is very rare.[2] It may be due to direct viral invasion, secondary to host immune reactivity or the result of hypotension that remains to be established.

But a study was done by the ultra-sinologists where included few children with dengue hemorrhagic fever and abdominal pain to assess the pancreatic involvement. The majority of patients with DHF and epigastric pain do not have enlarged pancreas.11 Serum levels of amylase and lipase were raised in patients with severe DHF. In our case both the pancreatic enzyme and sonographic evidence of focal pancreatitis were present.

Conclusion

Dengue infection can have wide range of clinical presentations and multi system involvement which might remain unrecognized and unreported. Acute pancreatitis is uncommon in children and a life-threatening complication of dengue hemorrhagic fever. Meticulous observation of children during dengue illness, prompt diagnosis and management of dengue related complications including acute pancreatitis is necessary to avoid serious morbidity and reducing mortality.

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Mini Review

Culture-bound Syndrome: The Enigmatic Contingency in Clinical Epidemiology

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Introduction:

In medical science, particularly in medical anthropology, 'Culture-bound Syndrome (**CbS**)' remains a culture-bound syndrome- which is also dubbed as 'Folk Illness'. CbS constitutes a blended entity of psychiatric & somatic symptoms that are considered/recognized as 'occurrence of diseases' among &/or within a specific society or in a defined cultural unit, only. The term *culture-bound syndrome* **(CbS)** has been included in 4th version of *Diagnostic & Statistical Manual of Mental Disorders* (Am Psychiatric Assoc., 1994) adding a list of common culture-bound conditions. But, there are no objective biochemicals or structural alterations of body organs &/or functions, and CbS is essentially centered within some cultures that is not recognized by other cultures/communities. Broadly, an endemic disease attributing to certa in behavior pattern within specific culture/community refer to as 'potential behavioral epidemic'.

The aim of this mini review is to bring out **CbS** into recent light in our medical arena to judge if some of such issues do suits to our country perspective since use of drugs, or alcohol abusing, smoking and disease transmission are being determined by communal reinforcement via person-to-person interaction. Though **CbS** often remains difficult to get those diagnosed properly just based on etiological grounds, yet it must remain distinguishable based on causal contribution of community/culture specific prevailing diseases staying apart from other environmental factors like toxicity.[1]

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The term '**CbS'** is not familiar in Bangladesh, *Am Psychiatric Assoc.,* signifies it as recurrent, locality-specific patterns of aberrant behavior/troubling-experiencing symptoms plausibly linking to particular DSM-IV diagnostic category, where some of such indigenously considered 'illness or affliction' with local names.[2] We, thus, wanted to bring into light if such culture-bound syndrome or community-based societal practices exist in our local areas/tribes/ religious groups, in Bangladesh that might be in vogue in some traditional communities/ spiritual practices, may open newer horizon in the disease epidemiology of Bangladesh towards adding values as plausible clue(s) in our country's re/emerging infectious diseases issues much more.

Culture-bound syndrome is identified based on the following characteristics:1-2

- Categorized such CbS/disease which neither remain voluntary behavior nor false claiming
- How widely CbS are spread out in communities having a definite basis in a given culture
- Are those lacking in familiarity or misunderstood the condition to community/cultures
- CbS mostly has no objective-based proofs of biochemical or tissue abnormalities (signs)
- Mostly recognized and treated by the community-derived or culture-based folk medicine

CbS/culture-specific syndrome is not similar to geographically-localized disease with specific,

identifiable yet causal tissue abnormalities. One of such is 'Kuru' (sleeping sickness), or certain genetic conditions. Nevertheless, condition originally assumed as culture-bound behavioral syndrome based on biological cause must have certain medical perspective to be redefined into another nosologically categorized.

Of its wider perspectives, some CbS involves somatic symptoms, like, pain, disturbed body function, while others remain behavioral/features of trans-cultural communities, with locally specific traits, viz., penis panics.

Medical Perspectives:

According to *Am Psychiatric Assoc.,* the term *culture-bound syndrome* (CbS) signifies recurrent, locality-specific patterns of aberrant behavior and troubling-experiencing symptoms might be linked to particular DSM-IV diagnostic category, though many of such patterns are indigenously considered as 'illness or affliction' with local names.[2] Though presentations conforming to such DSM-IV categories exists throughout the globe, the particular symptoms, course, and social response are often influenced by locally-followed cultural factors. In contrast, CbS are generally limited to specific societies/community-areas having definite culture remain localized, folk, diagnostic categories that frame coherent meanings for certain repetitive, typical/patterned, and clumsy/troubling sets of experiences and observations.

Controversies and Arguments:

The term *culture-bound syndrome* often seems to be controversial since it reflects different opinions of anthropologists and psychiatrists.[3] Anthropologists have a tendency to emphasize the relativistic and culture-specific dimensions of the syndromes, while physicians tend to emphasize the universal and neuropsychological dimensions.[4,5]

In 1999, psychiatrists like, Guarnaccia & Rogler, argued in favor of investigating **CbS** on their own terms since the syndromes have enough cultural integrity to be treated as independent objects of research.[6] They demonstrated that such issues occurring on diagnosing **CbS** to be used DSM-IV. They referred that 'one of key problems remains the "subsumption of culture bound syndromes into psychiatric categories",[6] which ultimately creates a medical hegemony and places the western perspective above that of other cultural and epistemological explanations of disease. So, Guarnaccia and Rogler felt the urgency for further investigation or reconsideration of the DSM-IV's authoritative power is emphasized, as the DSM becomes an international document for research and medical systems abroad. They provided two research questions that must be considered, "firstly: how much do physicians know about **CbS** to be able to fit those into any standard classification; and secondly: whether such a standard and exhaustive classification in fact exists".[6]

Earlier, in 1991, Latour, Bruno from USA opined DSM (Diagnostic and Statistical Manual of Mental Disorders) as problematic in nature and that, the 'DSM has been evident when viewed as definitively conclusive'. He further posed questions: if **CbS** can be treated as discrete entities, or, more importantly, if their CbS-symptoms remain generalized to perceive it as an merger of previously diagnosed illnesses'. If yes, then DSM may be, what Bruno defined as "particular universalism" which Western medical system may view to have a privileged insight into the true intelligence of nature, in contrast to the model provided by other cultural perspectives.[7]

Some studies on childhood diseases/disorders suggest **CbS** as an acceptable way within specific cultural context among certain vulnerable individuals (i.e. an *ataque de nervios* at a funeral in Puerto Rico) to express distress in the wake of a traumatic experience,[8] a similar manifestation of distress pertaining to childhood trauma when displaced into US culture leading to different way including adverse outcome in individuals and family.[9] Thus, history &/or etymology of such cases, like, 'Brain-Fag Syndrome', also reattributed to 19th Century Victorian Britain rather than West Africa.[10] Judging all these options and opinions, the term *culture-bound syndrome* **(CbS)** was dropped from the DSM 5 to replace it anew with **"cultural concepts of distress"**.[11]

Cultural Collusion with Medical Perspectives:

A study published by the Epilepsy Foundation reported that within the traditional among culture, epilepsy (qaug dab peg) is directly translated into "the spirit catches you and you fall down" meaning an evil spirit called a dab that captures soul to make one ill. In such culture, individuals with seizures are thought to be blessed with gift; as an access into spiritual realm than anyone.[12]

Contrarily, to that, in Western society, epilepsy is recognized as a serious long-term brain condition that might cause major impairment in one's life. The way the illness is dealt with in Hmong culture is vastly different due to the high-status epilepsy in their culture, compared to individuals who have it in western societies.

Individuals with epilepsy within the Hmong culture are a source of pride for their family.[13]

Another type of culture bound illness remains neurasthenia- a vaguely described medical ailment in Chinese culture that presents as lassitude, weariness, headaches, and irritability and is mostly linked to emotional disturbance. Aback in 1942 a report revealed 87% of such patients diagnosed by Chinese psychiatrists as having neurasthenia. So this has been reclassified as having major depression according to the DSM-3 criteria.[14] In Hong Kong, Cheung, Fanny M et al, reported in a study in 1982 & later on in 1985 that most patients selectively presented symptoms accordingly what they perceived as appropriate and tended to focus on somatic suffering only than their emotional issues that had been facing.[15,16]

An abridged test DSM-IV & DSM-V

The following 26 diseases have been listed out in the 4th edition of *Diagnostic and Statistical Manual of Mental Disorders* classifing those as culture-bound syndromes (**CbS**) , as shown, below:[17]

1. **Running amok**: It is an aggressive dissociative behavioral pattern derived from Indonesia and Malaysia that led to the English phrase, running amok. The word derives from the Malay word *amuk*, traditionally meaning "an episode of sudden mass assault against people or objects, usually by a single individual, following a period of brooding, which has traditionally been regarded as occurring especially in Malaysian culture but is now increasingly viewed as psychopathological behavior.

2. **Ataque de nervios & 3. Bilis, cólera:** It is a psychological syndrome mostly associated, in the United States, with Spanish-speaking people from the Caribbean, although commonly identified among all Iberian-descended cultures. *Ataque de nervios* translates into English as "attack of nerves", although it is used in its common cultural form to refer to a specific pattern of symptoms, rather than being a general term for feeling nervous.

3. **Bouffée délirante:** It is a uniquely French psychiatric diagnostic term. It is "an acute, brief nonorganic psychosis that typically presents with a sudden onset of fully formed, thematically variable delusions and hallucinations against a background of some degree of clouding of consciousness, unstable and fluctuating affect, and spontaneous recovery with some probability of relapse."

4. **Brain Fog syndrome:** It is characterized by confusion, forgetfulness, and a lack of focus and mental clarity. This can be caused by overworking, lack of sleep, stress, and spending too much time on the computer.

5. **Dhat syndrome:** It is a condition found in the cultures of South Asia (including Pakistan, India, Bangladesh, Nepal, and Sri Lanka) in which male patients report that they suffer from premature ejaculation or impotence, and believe that they are passing semen in their urine.

6. **Falling-out:** It is reported in Latin America and the Caribbean and usually brought on by stress.

7. **Ghost sickness:** It is more a socio-cultured being traditional incertion indigenous peoples in North America, notably the Navajo, and some Muscogee and Plains cultures, as well as among Polynesian peoples. People who are preoccupied and/or consumed by the deceased are believed to suffer from ghost sickness. Reported symptoms can include general weakness, loss of appetite, suffocation feelings, recurring nightmares, and a pervasive feeling of terror. The sickness is attributed to ghosts or, occasionally, to witches or witchcraft.

8. **Hwabyeong:** It is a Korean somatization disorder, a mental illness which arises when people are unable to confront their anger as a result of conditions which they perceive to be unfair.

9. **Koro:** Also known as shrinking penis, is a culture bound delusional disorder in which individuals have an overpowering belief that their sex organs are retracting and will disappear, despite the lack of any true longstanding changes to the genitals.

10. **Khyâl cap:** It is a syndrome of PTSD specific to Cambodian refugees. Symptoms are similar to the ones of common panic attacks and include palpitations, dizziness and shortness of breath. This Cambodian term directly translate to wind attacks.

11. **Latah:** It is a condition in which abnormal behaviors result from a person experiencing a sudden shock or other external stressor almost exclusively having been observed in persons from Southeast Asia. When induced, the affected person typically engages in such behaviors as screaming, cursing, dance movements, uncontrollable laughter, mimicry and command obedience.

12. **Locura:** Which translates to "insanity" in Spanish, is a mental disorder characterized as severe chronic psychosis. The term refers to a culture-bound syndrome, found mostly in Latin America and Latin Americans in the United States. Also referred to as *ataques de locura* (meaning "madness attacks"), it is categorized as a more severe form of *nervios ataque de nervios* with symptoms appearing similar to those of schizophrenia.

13. **Mal de pelea:** It is an aggressive dissociative behavioral pattern derived from Puerto Rico. It is like running amok.

14. **Evil eye:** The evil eye is a supernatural belief in a curse brought about by a malevolent glare, usually inspired by envy. It is found in many cultures in the Mediterranean region, the Balkans, the Middle East and Central Asia, with such cultures often believing that receiving the evil eye will cause misfortune or injury,] while others believe it to be a kind of supernatural force that casts or reflects a malevolent gaze back upon those who wish harm upon others (especially innocents).

15. **Piblokto:** Also known as pibloktoq and Arctic hysteria, is a condition most commonly appearing in Inughuit (Northwest Greenlandic Inuit) societies living within the Arctic Circle. Piblokto who has culture-specific hysterical reaction in Inuit, especially women, who may perform irrational or dangerous actsevents suffering from amnesia.

16. **Pa-leng** (**frigophobia):** It is a phobia pertaining to the fear of becoming too cold. Which is mainly in the Chinese culture. Sufferers of this problem bundle up in heavy clothes and blankets, regardless of the ambient air temperature.

17. **Zou huo ru mo** (**Qigong** psychotic reaction): Also known as qigong **deviation** is a Chinese-culture concept traditionally used to indicate that something has gone wrong in spiritual or martial arts training.

18. **Rootwork/Hoodoo:** Hoodoo is a set of spiritual practices, traditions, and beliefs that were created by enslaved African Americans in the Southern USA taken from various traditional African spiritual. Christianity and from healers indigenous botanical background including Hoodoo rootworkers, conjure doctors, conjure man and woman (Regional synonyms conjure).

19. **Sangue dormido: Sangue dormido** (lit. 'sleeping blood'): It is a psychological syndrome reportedly affecting Cape Verdeans and members of the Cape Verdean diaspora who believe infak. The patient described Cape Verdean folk beliefs in which traumatic injury would cause living blood (sangre vivo) to leak out and coagulate as sleeping blood (sangue dormido) or dead blood (sangue morto), resulting in loss of circulation to affected area and thus gets more potentially serious symptoms (”backing up" behind the obstruction).

20. **Shenjing shuairuo/Neurasthenia:** Neurasthenia (from the Ancient Greek νεῦρον neuron "nerve" and ἀσθενής asthenés "weak") is a term that was first used as early as 1829[6] for a mechanical weakness of the nerves. The condition was explained as being a result of exhaustion of the central nervous system's energy reserves, which Beard attributed to modern civilization. As a result as the increasingly Physicians in the Beard school of thought physicians associated neurasthenia suffering from stresses of urbanization. This commonly occurs elite people and with professionals sedentary occupations that incluude any one living within the monetary system.

21. **Shenkui, shen-k'uei:** It is a traditional Chinese medicinal term in which the individual suffers withdrawal like symptoms including chills, nausea, and even flu-like symptoms with anxiety, believed to be caused by an orgasm and loss of semen. The symptoms may last weeks to months after a single orgasm.

22. **Shinbyeong:** Also called "self-loss", is the possession from a god that a chosen *mu* (shaman) goes through in the Korean shamanic tradition. It is said to be accompanied by physical pain and psychosis. Believers would assert that the physical and mental symptoms are not subject to medical treatment, but may only be cured through acceptance of and full communion with the spirit only.

23. **Susto:** It is a cultural illness primarily among Latin American cultures. Inhibiting condition of "chronic somatic suffering stemming from emotional trauma or from witnessing any/some traumatic experiences that others may have had.

24. **Taijin kyofusho:** This Japanese team significant culture-specific syndrome that translates into the disorder (sho) of fear (kyofu) of interpersonal relations (taijin) suffering among these feel

extremely embarrassed to fearful displeasing their bodies or their appearances to others.

25. **Zār:** In the cultures of Horn of Africa and adjacent regions of the Middle East, Zār denotes a demon spirit assumingly to possess in women, causing discomfort illness. The so-called zār ritual or zār cult remains the practice of exorcising such spirits from the possessed individual.
26. **Uqamairineq:** Is a curse and a demonic possession,[1] seen in Zulu- and Xhosa-speaking communities in Kenya S. Africa that it is refer to saka. anxiety state attributed to magical effects (given to them by rejected lovers), or spirit demonic possession commonly seen in Zulu people.

Other Relevant Examples associated with culture-bound syndromes (CbS):

Reportedly, though "the ethnocentric bias of Euro-American psychiatrists has led to the idea that **CbS** are confined to non-Western cultures",[18] within the contiguous United States, the consumption of kaolin, a type of clay, was proposed as CbS observed in Afro-Americans communities in the rural south, of mining of kaolin being common.[19]

Among the South African Xhosa community, the syndrome of amafufunyana is commonly used to describe possessed by demons/other malevolent spirits. Traditional healers, there, usually perform exorcisms in order to drive off these spirits. Upon investigating the phenomenon, researchers found those cases affected by the syndrome exhibited traits and characteristics of schizophrenia.[20]

Moreover, researchers have suggested that both premenstrual syndrome (PMS) & severe premenstrual dysphoric disorder (PMDD) which have currently unknown physical mechanisms,[21,22,23] which remain Western culture-bound syndromes.[24,25] Nevertheless this still remains controversial.[24] Tarantism is an expression of mass psychogenic illness documented in Southern Italy since the 11th century.[26]

Morgellons is a rare self-diagnosed skin condition reported primarily in white populations in the United States.[27] It has been described by a journalist as "a socially transmitted disease over the Internet".[28]

In former Soviet Union countries, Vegetative-vascular dystonia can be considered an example of somatic condition formally recognised by local medical communities in former Soviet Union countries, but not in Western classification systems. Its umbrella term nature as neurological condition also results in diagnosing neurotic patients as neurological ones,[29,30] in effect substituting possible psychiatric stigma with culture-bound syndrome disguised as a neurological condition.

Likely Swedish refugee children known to fall into coma-like states on knowing their families will be deported a condition, called *uppgivenhetssyndrom*, or resignation syndrome, existing among the refugee population in Sweden. This has been prevalent since the 21st century. In 2006, a team of psychologists, political scientists, and sociologists hypothesized that it was a culture-bound syndrome.[31]

Further startle disorder similar to latah, called *imu* [ja] (sometimes spelled *imu:*), is found among Ainu people, both Sakhalin Ainu and Hokkaido Ainu.[32,33]

In Siberia, condition piblokto, called *menerik* [ru] (sometimes *meryachenie*), is found among Yakuts, Yukaghirs, and Evenks living in Siberia.[34]

Finally, the trance-like violent behavior of the Viking age berserkers – behavior that disappeared with the arrival of Christianity – has been described as a culture-bound syndrome as well[35]

The term culture-bound syndrome (CbS) has been included in 4th version of Diagnostic & Statistical Manual of Mental Disorders (Am Psychiatric Assoc., 1994) adding a list of common culture-bound conditions. But, there are no objective biochemicals or structural alterations of body organs &/or functions, and CbS is essentially centered within some cultures that is not recognized by other cultures/communities. Broadly, an endemic disease attributing to certain behavior pattern within specific culture/community refer to as 'potential behavioral epidemic'.

Highlights and Rundown

A thorough literature search failed to yield any information on "Culture-bound Syndrome: CbS' (Folk illness) in our Bangladeshi medical literature &/or anthropological database.

- CbS constitutes a blended entity of psychiatric and somatic symptoms that are considered as 'occurrence of diseases' among/ within a specific society or in a defined cultural unit.
- CbS is only to judge if it suits to any country

perspective (drugs/ alcohol abusing, smoking, disease transmission etc.) that are determined by communal reinforcement via person-to-person interaction

- Since CbS remains difficult to diagnose properly just based on etiological grounds, so it must be distinguished based on causal contribution of community/culture-specific prevailing diseases including environmental factors.
- Though the term 'CbS' is not familiar in Bangladesh, Am Psychiatric Assoc., signifies it as recurrent, locality-s pecific patterns of aberrant behavior/ troubling-experiencing symptoms plausibly linking to particular DSM-IV diagnostic category, where some of such indigenously considered 'illness or affliction' with local names.
- That is why we wanted to highlight this issue if CbS or associated community-based societal practices that are existed in local communities, tribal areas, religious/spiritual groups, in Bangladesh that might contribute significantly in our disease epidemiology that may add plausible values in country's re/emerging infectious diseases and public health per se.

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Short Communication

Rationale to achieve Critical View of Safety in Laparoscopic Cholecystectomy

Prof. Dr. Sardar Md. Rezaul Islam

Introduction

Bile duct injury (BDI) is the most serious iatrogenic complication in Laparoscopic Cholecystectomy (LC). The incidence of major BDI is 0.1 to 0.5%. The most common cause of serious BDI is misidentification. A method of identification of cystic structures was first introduced by Steven Strasburg in USA in 1992. Later he named it Critical View of safety (CVS) in 1995. Three criteria are needed to achieve CVS. 1. Calotte's triangle was cleared of fat and fibrous tissue, 2. Lower third of the gall bladder (GB) is dissected off the cystic plate.3. Two and only two structures are seen entering the GB which are cystic duct and cystic artery. Some surgeons have adopted this CVS method of dissection. Others use classical infundibular (IN) method or both. We studied the efficacy and safety of CVS technique as sole method of dissection in laparoscopic cholecystectomy.

Fig-1: *Professor Steven Strasburg*

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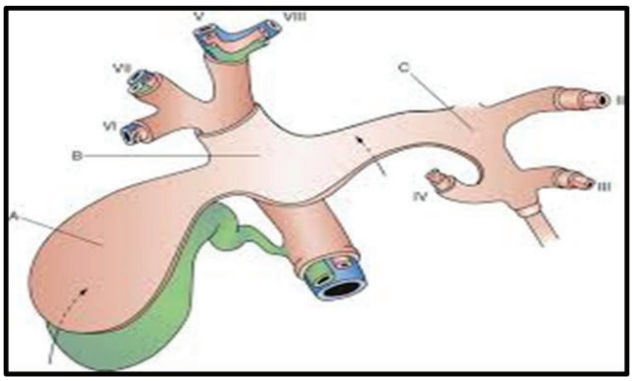

Fig-2: *Hilar Plate system of liver*

Methods

1647 cases of LC were done between January 2012 and January 2022 in two hospitals. All were operated by CVS dissection technique and none by infundibular technique. All operations were carried out by a single surgeon. Data were collected in a retrospective manner. Cases included acute cholecystitis, mucocele, empyema, chronic cholecystitis and simple cholelithiasis. Conventional 4 ports were used. In the CVS technique, complete incision of the serosa is performed both in the medial and lateral aspect of the infundibulum and extended upwards almost to the fundus. Dissection of Calot's artery (which connects the cystic artery to the cystic duct) lateral to the anterior branch of cystic artery permits access to the critical safety triangle. The critical safety triangle is defined as a triangle between the gallbladder wall on the right, the cystic duct inferiorly, and the cystic artery on the left. The entire fatty dissection of this triangle and mobilization of the infundibulum, both anteriorly and posteriorly, permits visualization of the liver surface through the triangle, well above Ruviers' sulcus. The cystic artery and the cystic duct are clipped separately and divided. Afterwards retrograde dissection of the gallbladder completes the operation.

Results

Average operating time was 42 minutes and range being 13 to 80 minutes. All 3 criteria of CVS were achieved in 1515 (92%) cases out of 1647 cases. Two criteria were achieved in remaining 132 cases. There was no postoperative death in our series. Our rate of conversion was 4.3%. There were two incidence of post operative bile leak, which required drainage and stenting of the CBD (0.12%).

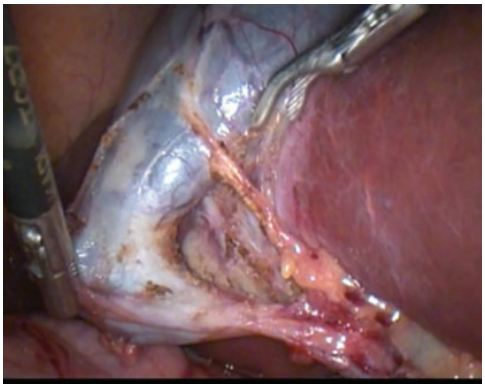

Fig-3: *Anterior view of CVS*

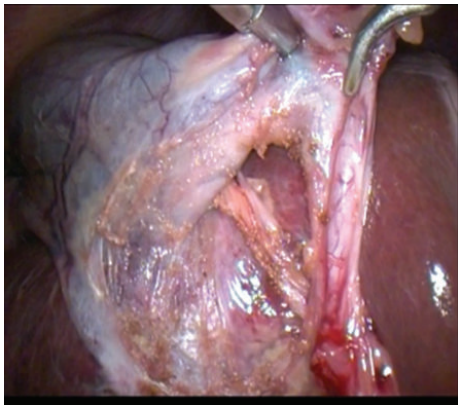

Fig-4: *Posterior view of CVS*

Discussion

Surgeons have long strived to make LC the safest and complication free procedure. This effort has been made successful to some extent by the introduction and application of CVS.(1,2) In our study the operative time is significantly reduced for patients with CVS technique, which is 42 minutes. Vettoretto et al. and Viswanathan V also found significant reduction in operating time (51.5 min), which is comparable to our study. [3,4]

Another important aspect as pointed out by Lam T and Manatakis DK in separate studies is that there is negligible difference in achieving adequate CVS scores with operator experience (consultant vs. trainees) without adding significant operative time in the hands of trainees. Thus advocating this technique for teaching is largely safe regardless of surgeons experience.[5,6] Although CVs technique may have a little more chance of bleeding as involves dissection of the lower third of the GB while cystic artery supply is still intact.

There was no mortality in our series. Morbidity including minor leaks were only 0.12%. But there was no incidence of major bile duct injury requiring bile duct reconstruction. This finding is superior to many published series, where rate of major BDI in LC was 0.1% to 0.5%.[3,10,11,12]

Currently, the CVS technique is accepted as a Gold Standard for reduction of morbidity and mortality associated with LC by the European Association of Endoscopic Surgery (EAES).[7,8,9] There are no randomized controlled trials published up-to-date to give us level-1 evidence that CVS prevents bile duct injuries.[1,2] However, if we look at the large case series [1,2] published so far, we believe that major BDI can be prevented by strictly adhering to all the three criteria of CVS. The reason is, it helps give reliable exposure to identify important structures of calot's triangle.

Conclusion

Although the "critical view of safety" requires more dissection as compared to infundibular technique, but once learnt and mastered, it is faster and safer identification technique during laparoscopic cholecystectomy. To prove that CVS dissection method prevents bile duct injury required randomized trial involving a large number of sample. Low rate of complication of this technique probably makes the surgeon feel more secure both with inflamed and uninflamed anatomy. Excellent outcome of our study forecasts that CVS method is the gold standard technique in the dissection of the gallbladder in LC. A further dissemination of the technique is necessary to improve safety in LC.

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News and Views

Presentation on Impact of Climate on Public Health: Emerging/ Re-emerging Infectious Diseases in Bangladesh

Dr. Kazi Selim Anwar, Engr. Ahmed Arif Rashid

A presentation on public health titled '**Impact of Climate on Public Health: Emerging/Re-emerging Infectious Diseases in Bangladesh'** was presented at a national seminar on World Meteorological Day on 23 March 2023**,** with the theme **'The Future of Weather, Climate & Water Across Generations**' by Dr. Kazi Selim Anwar**,** Head, Medical Research Unit (MRU), Ad-din Women's Medical College.

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It goes without saying how climate change impacts human health eminently by disrupting eco systems and societal systems. Disruption to eco systems brings about allergies, food & water borne diseases, asthma etc. while malnutrition, work capacity conflict and mental health illness are caused by the disruption to societal systems, by and large give rise to sickness, injuries, deaths from extreme events and storm surges.

When the host and agent are in an unbalanced state, we had been around epidemic to pandemic catastrophe.

Glimpse on Climate Change Global Warming: Where do we stand!

According to American Public Health Association (APHA) climate change affects human health by worsening air quality, spreading vector-borne diseases**,** devastating lower SES communities. Drought, flood, storm, and thunderstorm are manifestations of extreme weather events. To fight against these environmental disasters, strong climate change adaptation strategies and interventions to safeguard public health is profoundly needed.

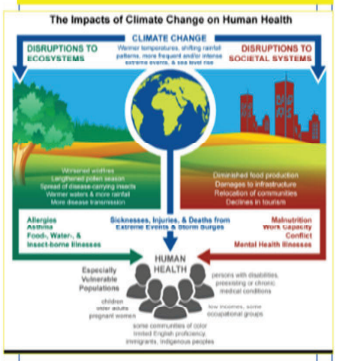
In this presentation, the American Public Health Association's (APHA) provided illustrations were used to show how climate change affects health through air quality, extreme weather and vector borne diseases.

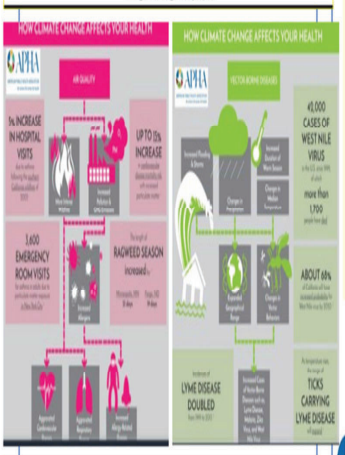
Most emerging infectious diseases of our country is associated with few/some types of climate/weather issues, particularly with its spatiotemporal variations. Since no full-fledged epidemiological research on EID exists in Bangladesh involving meteorological variables, so far, it is imperative that public health experts be tie up in a team with BMD meteorologists to shape up this crucial task prudently towards predicting EID based on Weather forecasts/ epidemic control activities. We have enough data base on dengue, COVID-19, Hand Foot Mouth (HFMD) Disease.

Details of this poster has been delineated below in two sections:

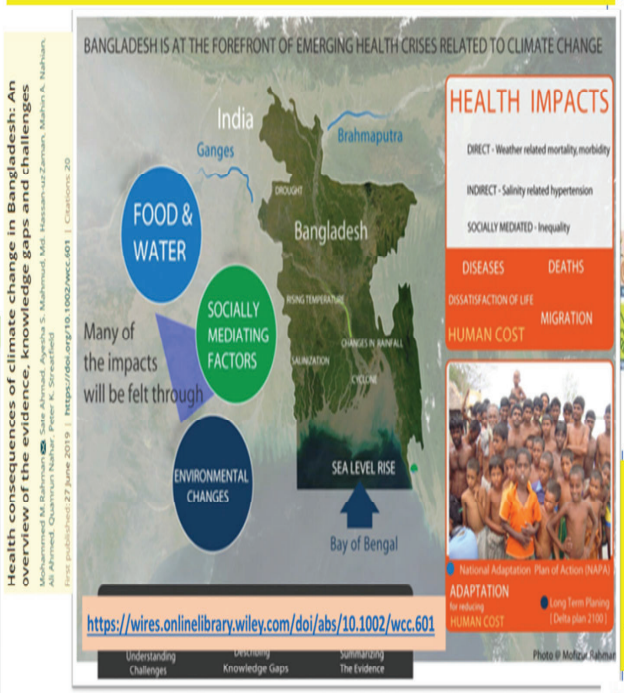
National Seminar on World Meteorological Day: 23 March 2023
Theme: 'The Future of Weather, Climate & Water Across Generations'

The Impacts of Climate Change on Human Health

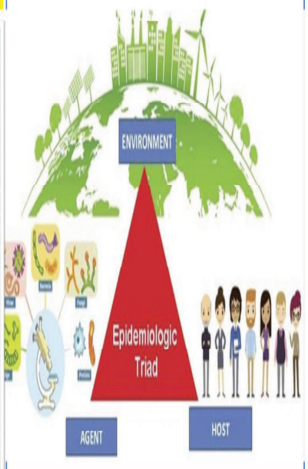




Impact of Climate on Public Health:
Emerging/Re-emerging Infectious Diseases in Bangladesh



Epidemiological Triad Model



Glimpse on Climate Change Global Warming:
Where do we stand !

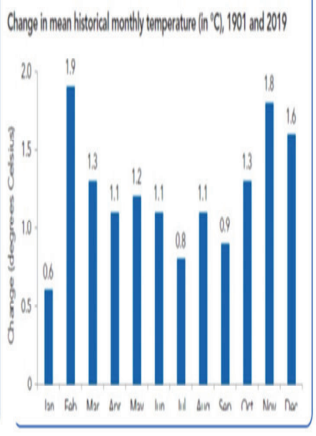
Bangladesh's Climate Refugees:
Can They Fight The Rising Sea? *Insight | Climate Change In Asia*

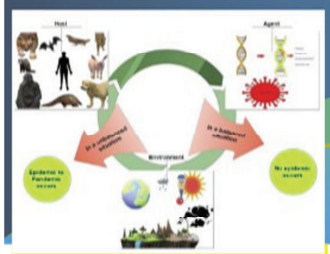
American Public Health Association
How Climate Change Affects Human Health

- Worsened air quality
- Spreading vector-borne diseases
- Devastates Lower SES communities

Extreme Weather Events:
Drought, Flood, Storm, Thunderstorm
→Needs strong climate change adaptation strategies
→Interventions to safeguard public health

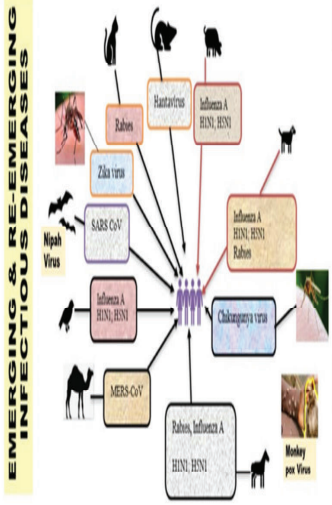
THE WORLD BANK
Climate Change in Bangladesh: Impact on Infectious Diseases and Mental Health





EMERGING & RE-EMERGING INFECTIOUS DISEASES

The emerging viruses of the 21st century



PARIS, June 10, 2022 (BSS/AFP) - The recent explosion of monkeypox cases

Climate & Public Health/ Re/Emerging Infectious Dis (EID)

>2500 years ago, Hippocrates termed 'Epidemics' to describe diseases propagation through populatn, in a seasonal fashion,[1-2]

His thesis: 'Air-Water-Place' proved environment & seasonal influence → Direct physicians/public health scientists towards our community-health but focusing sun, soil, elevation, geography, climate.[1-3]

EFFECT OF GLOBAL WARMING IN BANGLADESH: status quo

Impact of Climate change on Agriculture in Bangladesh *Byomkesh Talukdar, Fri Sep 28, 2007*

Bangladesh Health National Adaptation Plan (HNAP) (Pending approval) *Ministry of Health and Family Welfare, WHO Country Office, Bangladesh*

National Strategy for Water Supply and Sanitation December, 2014 *Local Government Division, Ministry of Local Government, Rural Development and Cooperatives, Government of the People's Republic of Bangladesh*

VULNERABILITY & ADAPTATION ASSESSMENTS (V&A)

Assessment of Health Vulnerability Reduction to Climate Change in Bangladesh Final Report June, 2014 *WHO Country Office for Bangladesh*

Vulnerability and Adaptation to Climate Change in Coastal and Drought Prone Areas o Bangladesh: Health anc WASH August, 2015 *WHO Country Office for Bangladesh*

Concluding Part

Knowing climatic patterns to assist public health planners, for diagnosing based on forecasting weather depended issues (heat/ cold waves: *El-Nino, La Nina*), towards:

- ❑ Early forecasting of probable EID-outbreak
- ❑ Proper assessment of spatiotemporal variation

for any upcoming EID-outbreaks.

Combating Severe Dengue in Children in Ad-Din Hospital Utilizing WHO-2009 Classification: Insight on a Rapid Appraisal of Pocket Outbreak in Urban Dhaka, Bangladesh

*[1] Dr. Kazi Selim Anwar, *MD (Moscow, USSR), M. Phil. (Liverpool Univ., England)*

[2] Prof. ARM Lutful Kabir, *MBBS (Dhaka), FCPS (Bangladesh CollegePhy Surg, Bangladesh)*

[3] Dr. Sudipta Roy, *MBBS (Raj MCH), FCPS (Bangladesh CollegePhy Surg, Bangladesh)*

How Weather → Climate associates with Pub Health/ EID

What Our Study Yields in Bangladesh

Here are some climate dependent EIDs

How our scientific effort add values in associating Weather/Climate & Public Health/ EID in Bangladesh

We report here few EIDs those were climate dependent

Dengue (DEN),[5A] (Mosquitoes: *Aedes aegypti / albopictus*)

Chikungunya,[5] (Mosquitoes: *Aedes aegypti / albopictus*)

HFMD (Hand, Foot, Mouth Dis.),[8A] *Virus EV-71,Coxsackie A16*

COVID-19,[9] *Coronavirus' SARS-CoV-2*

These EIDs: associated with climatic (ambient air, drinking H_2O, toxic/contaminated food; with weather components (T°, humidity, wind velocity, Xrainfall) causing EID.[10]

❑ Malaria,[4] (Mosquitoes: *Anopheles- Plasmodium*)

❑ Cholera,[7A] (Bacteria: *Vibrio cholerae/ V. chol 0139B*

❑ Typhoid, (Bacteria: *Salmonella typhi , Para A, B*

These EIDs: associated with climatic (ambient air, drinking H_2O, toxic/contaminated food; with weather components (T°, humidity, wind velocity, Xrainfall) causing EID.[10]

Bottomline:

Most Emerging Infectious Diseases our country is associated with few/some types of climate/weather issues → particulaly with its spatiotemporal variations

Since no full fledged epidemiological research on EID exists in Bangladesh involving meteorological variables, so far, it is imperative that public health experts be tie up in a team with BMD meteorologists to shape up this crucial task prudently towards predicting EID based on Weather forecasts/ epidemic control activities.

We have enough dBase on DEN, COVID-19, HFMD

Dr. Kishor Kumar Paul, Fumiki Dhar Chowdhury, Emdadul Haque, et al. 2018. Risk Factors for the presence of dengue vector mosquitoes and determinants of test prevalence and larval site selection in Dhaka, Bangladesh. PLoS ONE 13(6): e0199457. 1-19.

News and Views

Presentation on Molecular Genetic Approach in Diagnosing Childhood Primary Immunodeficiency Disease (PID) Attending Six Major Hospitals in Bangladesh

Dr. Sudipta Roy, ARM L Kabir and Dr. Kazi Selim Anwar

Background

PIDs are a heterogeneous group of adaptive and innate immune system inherited disorders. However, these disorders remain under-recognized and under-reported in several developing countries due to a lack of awareness among physicians and the non-availability of diagnostic facilities.

Abstract

On this ongoing study 42 cases were enrolled, PID screening positive-31, clinical exome sequencing was done in 13 cases yielded pathogenic mutations were found in 3 cases, likely pathogenic in 2 cases and significance in 7 cases. Genetically of three pathogenic genes one each of SCID Gene- IL2RG (-), X-Linked agammaglobulinemia GeneBTK (-) AND immunodeficiency-8 Gene-CORO1A (+) . Two of likely pathogenic are Severe congenital neutropenia-2 Gene-GFI1 (-) and Vici syndrome, Gene-EPG5 (-).

Objective:

To confirm the diagnosis of clinically suspected screening-positive PIDs in Bangladeshi children using molecular genetics.

Methodology

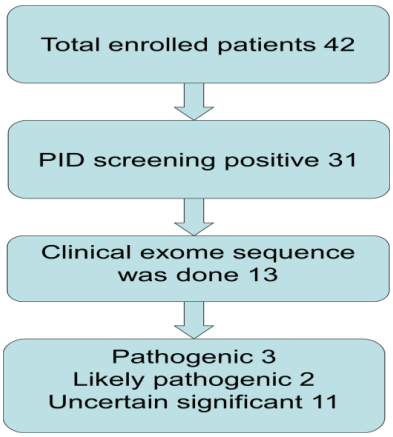
This is an ongoing longitudinal observational multicenter study in the pediatric department of 6 hospitals in Dhaka city funded by integrated health science research and development fund activity, Ministry of health and family welfare, Bangladesh over 2 years (September 2022 to August 2023). Study population -50. Children under 18 years with recurrent or persistent infections (3 or more) were enrolled. Exclusion criteria: chronic steroid ingestion, AIDS, PEM, NS, Leukemia etc.). PID screening tests (CBC, Serum antibody IgA, IgG, IgM, IgE and Lymphocyte Subset analysis), infection screening (CXR, MT, Gastric lavage etc.) were done. Clinical exome sequencing was performed in selected screening positive PID cases in Med Genome Labs Ltd., Bangalore, India for genetic analysis. Interim analysis was done after six months of study.

Result

Distribution of preliminary selected patients (42) fulfilling the inclusion criteria:

Conclusions

In the literature review, very few studies on PIDs have been published from Bangladesh and no molecular genetic analysis has been conducted yet. Our study shows 38% of clinically suspected patients have genetically confirmed PID. Large scale study is required to understand the molecular basis of PIDs in Bangladeshi children.



Variable	Frequency
Age (Months)	31.29 ± 39.35
Sex	
Male	20 (71%)
Female	9 (29%)
M: F	2.2:1
Consanguinity	16 (51.6%)
H/O Sib death	5 (16.1%)
Affected Sib	4 (12.9%)
Mean age of onset (Months)	7.41 ± 9.25
Mean age of Diagnosis (Months)	30.56 ± 39.69

Table 1. Demographic profile of the study cases.

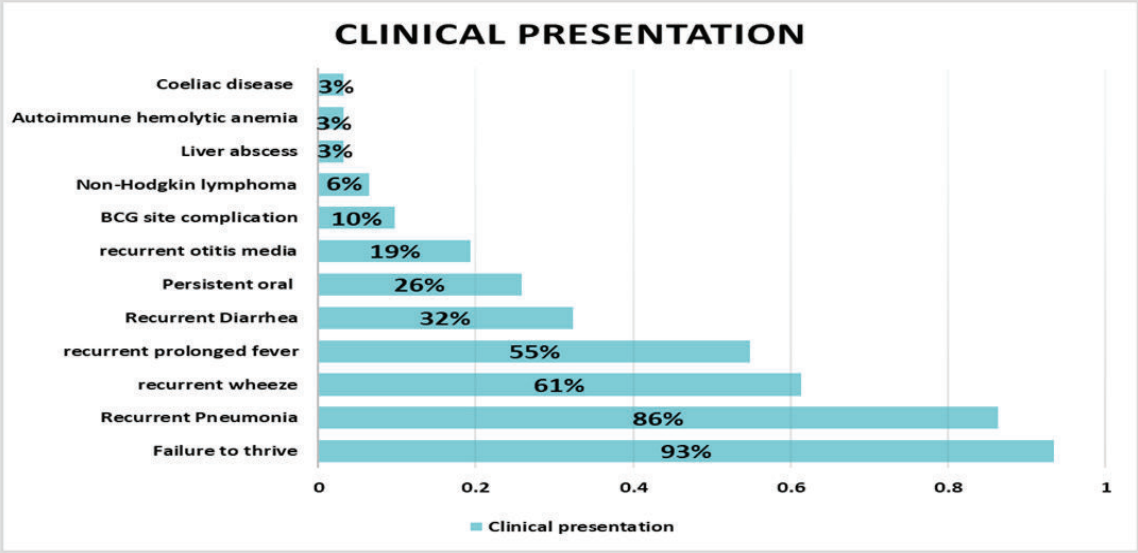


Chart 1 : The clinical presentation of PID patients

Ad-din Foundation

Molecular Genetic Approach in Diagnosing Childhood Primary Immunodeficiency Disease (PID) Attending Six Major Hospitals in Bangladesh

Sudipta Roy; ARM Luthful Kabir; Kazi Selim Anwar

ABSTRACT

On this ongoing study 42 cases were enrolled, PID screening positive -31, clinical exome sequencing was done in 13 cases yielded pathogenic mutations were found in 3 cases, likely pathogenic in 2 cases and uncertain significance in 7 cases. Genetically of three pathogenic genes one each of SCID Gene-IL2RG(-), X-linked agammaglobulinemia GeneBTK(-) and Immunodeficiency-8 Gene-CORO1A(+). Two of Likely- pathogenic are Severe congenital neutropenia-2 Gene-GFI1(-) and Vici syndrome, Gene-EPG5 (-)

BACKGROUND

PIDs are a heterogeneous group of adaptive and innate immune system inherited disorders. However, these disorders remain under -recognized and under -reported in several developing countries due to a lack of awareness among physicians and the non-availability of diagnostic facilities.

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RESULTS

Distribution of preliminary selected patients (42) fulfilling the inclusion criteria:

Total enrolled patients 42

↓

PID screening positive 31

↓

Clinical exome sequence was done 13

↓

Pathogenic 3
Likely pathogenic 2
Uncertain significant 11

RESULTS

Variable	Frequency
Age (Months)	31.29 ± 39.35
Sex	
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Female	9 (29%)
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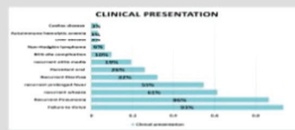

Chart 1. Bar Chart showing the clinical presentation of PID patients.

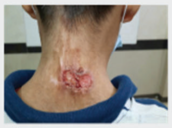

Figure 1. Chronic Nocardia infection in Hyper IgE syndrome.

Figure 2. BCG site abscess in SCID.

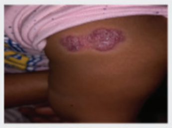

Figure 3. Exaggerated BCG response in NK cell deficiency.

Figure 4. Subcutaneous emphysema.

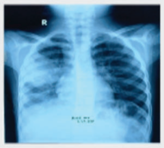

Figure 4. CXR showing consolidation (rt. Lung) in Hyper IgE syndrome.

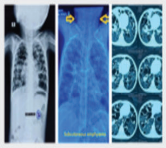

Figure 5. Bilateral cystic lesions & subcutaneous emphysema & Multiple cystic lesions in severe congenital neutropenia.

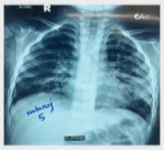

Figure 6. CXR showing bilateral consolidation in Bruton's agammaglobulinemia(X-linked).

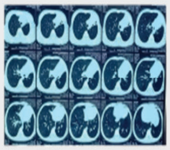

Figure 7. CT scan showing left-sided extensive bronchiectasis in Bruton's agammaglobulinemia (X- linked).

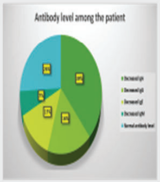

Chart 2. Pie chart showing antibody levels among the patient.

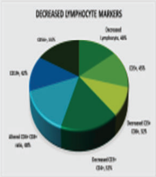

Chart 3. Pie chart showing the status of T cell, B cell, NK cell.

Findings of Clinical Exome Sequencing

SN	Gene(Transcript) & Location	Variant	Zygosity	Disease(OMIM)	Inheritance	Classification
01	IL2RG (-) (ENST00000374202.7) Exon 8	[illegible]	Hemizygous	Severe combined immunodeficiency (OMIM#300400); Combined immunodeficiency (OMIM#312863)	X-linked recessive	Pathogenic
02	BTK (-) (ENST00000308731.8) Exon 9	[illegible]	Hemizygous	X-linked agammaglobulinemia (OMIM#300755)	X-linked recessive	Pathogenic
03	CORO1A(+) ([illegible]) Intron 7	[illegible] (3' splice site)	Homozygous	Immunodeficiency 8	Autosomal recessive	Pathogenic
04	EPG5 (-) ([illegible]) Exon 37	[illegible]	Homozygous	Vici syndrome (OMIM#242840)	Autosomal recessive	Likely Pathogenic
05	GFI1 (-) ([illegible]) Exon 4	[illegible]	Heterozygous	Severe congenital neutropenia 2 (OMIM#613107)	Autosomal dominant	Likely pathogenic

Table 2. Table showing Pathogenic or likely pathogenic mutation in 5 patients.

Sl no	Name of gene & location	Variant	Zygosity	Disease	Inheritance	Classification
01	TCF3 (-) ([illegible]) Exon 7	[illegible]	Heterozygous	Agammaglobulinemia-8A; Agammaglobulinemia -8B	Autosomal recessive	Uncertain Significance
02	LIG1 (-) ([illegible]) Exon 11	[illegible]	Heterozygous	Immunodeficiency -96	Autosomal recessive	Uncertain Significance
03	DNAH11 (+) ([illegible]) Exon 40	[illegible]	Heterozygous	Primary ciliary dyskinesia-7	Autosomal recessive	Uncertain Significance
04	JAK3 (-) ([illegible]) Exon 19	[illegible]	Heterozygous	T cell-negative (T-), B cell-positive (B+), natural killer cell-negative (NK-) severe combined immunodeficiency	Autosomal recessive	Uncertain Significance
05	MCM4 (+) ([illegible]) Exon 14	[illegible]	Heterozygous	Immunodeficiency 54	Autosomal recessive	Uncertain Significance
06	ZAP70 (+) ([illegible]) Exon 9	[illegible]	Heterozygous	Infantile-onset multisystem autoimmune disease-2	Autosomal recessive	Uncertain Significance
07	IL12RB1 (-) ([illegible]) Exon 5	[illegible]	Heterozygous	Immunodeficiency 30	Autosomal recessive	Uncertain Significance
08	CD40LG (+) ([illegible]) Exon 5	[illegible]	Heterozygous	X-linked immunodeficiency with hyper IgM type1	X-linked recessive	Uncertain Significance
09	C7 (+) ([illegible]) Intron 15	[illegible] (5' splice site)	Heterozygous	C7 deficiency	Autosomal recessive	Uncertain Significance
10	LRBA (-) ([illegible]) Exon 22	[illegible]	Heterozygous	Common variable immunodeficiency 8 with autoimmunity	Autosomal recessive	Uncertain Significance
11	TAP1 (-) ([illegible]) Exon 9	[illegible]	Homozygous	Bare lymphocyte syndrome type I	Autosomal recessive	Uncertain Significance

Table 3. Table showing mutation of uncertain significance in 11 patients.

CONCLUSIONS

In the literature review, very few studies on PIDs have been published from Bangladesh and no molecular genetic analysis has been conducted yet. Our study shows 38% of clinically suspected patients have genetically confirmed PID. Large scale study is required to understand the molecular basis of PIDs in Bangladeshi children.