Original Research Article

A FIVE YEARS RETROSPECTIVE STUDY ON ETIOLOGY AND CLINICAL ANALYSIS OF MENINGITIS IN ST.PAUL'S HOSPITAL MILLENNIUM MEDICAL COLLEGE PEDIATRIC WARD IN 2012-2016.

Abstract

Meningitis is one of the most serious CNS suppurative infections in infants and childhood. Ethiopia is endemic for bacterial meningitis with frequent meningococcal epidemics occurring every few years particularly in the dry season from December to June.

To main aim of the study is to assess determinants and clinical analysis of meningitis in pediatrics ward which were admitted to St.Paul's hospital millennium medical college pediatrics wards in 2012-2016.

A retrospective study on etiology and clinical analysis of meningitis admitted in pediatrics ward. The study population was all pediatric patients admitted with meningitis that presented in ward during the study period and fulfilling the mentioned inclusion criteria was included. The data were collected on prepared format in September, 2016.

Out of 95 cases, 64 were males and 31 were females making a male to female ratio of 2.06:1. The most marked seasonal variation was observed for *N. meningitidis* which had a high incidence in the 2nd quarter (April to June). During the dry season (April to June) 18 cases were confirmed by culture results. The culture results showed the highest incidence of *S. pneumoniae* among the common agents of bacterial meningitis. The most common symptom was fever. High grade fever (>38^{o}C) was recorded in 84 cases (88.4%). The most common outcome of the treatment was

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complete recovery which was observed in 55 (65.5 %). Death was the second most common outcome with 17(20.2 %) cases recorded as fatal cases. Neurological or other sequelae were present in 9(10.7 %) cases.

Key words: Bacterial meningitis, Etiology, Pediatric, Meningitis sequelae, Neisseria meningitides.

1. INTRODUCTION

1.1Back ground of the study

Bacterial or pyogenic meningitis is an inflammation of the arachnoids layer of the meninges and the fluid that circulates in the ventricles and sub-arachnoids space (CSF) Caused by bacterial infection. The commonest causative agent during infancy is E.Coli, Group b streptococcus and listeria monocytogenus, but beyond the neonatal period the most important one are hemophilus influenzae, streptococcus pneumoniae and neisseria meningitidis. The common manifestation of bacterial meningitis in childhood are fever, nausea and vomiting, headache, alteration of mental status which varies from lethargy to coma , neck stiffness, Brudzinski,'s sign and kerning's sign for older children, but for neonates and infants ,difficulty of feeding, vomiting, fever, lethargy are the common manifestations. The treatment is mostly with appropriate parentral antibiotics (1, 2).

Bacterial meningitis is one of the most serious CNS suppurative infections in infants and childhood. The infection is associated with high rate of acute complication and chronic morbidity.

Bacterial meningitis is a serious infection and is associated with considerable mortality and morbidity in various parts of the world. It has a global epidemiology but sub-Saharan Africa bears the highest burden of the disease. Located in the eastern horn of Africa, Ethiopia is also endemic for bacterial meningitis with frequent meningococcal epidemics occurring every few years particularly

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in the dry season from December to June. Although it is generally considered a disease of the childhood, no age group is exempt from the infection. In the developing countries the fatality rate associated with bacterial meningitis can often be very high. In the absence of proper treatment,

bacterial meningitis is known to cause serious neurological complications which may persist throughout the life (3).

Despite the general consensus of the importance and seriousness of bacterial meningitis in children in Ethiopia, there are no adequate hospital based studies, especially in St.Paul's Hospital millennium medical college, to describe the prevalence, etiologies, age and sex distribution, clinical manifestations, and case fatality rates of meningitis in children.

1.2 Statement of the problem

The highest burden of bacterial meningitis occurs in an area of sub-Saharan Africa known as the "meningitis belt", described by Léon Lapeyssonnie in 1963. The area of meningitis belt that stretched from Mali to Sudan in 1963 gradually extended in the past decades. The meningitis belt that we know today stretches from Senegal in the west to Ethiopia in the east and includes 400 million people and 21 nations. This area is characterized by high prevalence of bacterial meningitis. Marked seasonal fluctuations occur in the prevalence of meningococcal meningitis which rises during the dry season from December to June with incidence as high as 1000 cases per 100,000 populations during an epidemic. The incidence then falls steeply on the arrival of the rainy season. The mechanism by which the dry season affects the incidence of meningococcal disease may be multifactor. Although dry climate and harsh winds may have an effect of propagation of meningococcal disease by droplet spread, the more widely accepted view is the effect of the dry climate on the integrity of the mucosal surface of nasopharynx. The breaks in the mucosal barrier lead to the progression of the carrier state to the invasive infection. The nasopharyngeal carriage rates of *N. meningitides* in the area of meningitis belt are estimated

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to be as high as 30 %.(4) Studies done in Kenya, shows that the important causes of death and neurological squeals in children in developing countries are acute bacterial meningitis.

Half of all childhood deaths from meningitis worldwide occur in sub-Saharan Africa. In this study 2% of admission had meningitis and 0.7% had possible meningitis, and there were 32% deaths in meningitis cases representing 10% of inpatient deaths aged $\geq$ 60 days during the study (8, 9).

Meningitis is a public health problem in Africa including Ethiopia, which causes epidemic meningitis in Africa meningitis belt areas. The most affected part of the population is children and young adults, and the attack rate can be as high as 1%. Epidemic meningococcal meningitis occurs everywhere in the world, but it is particularly severe in countries of the meningitis belt in sub-Saharan Africa including Ethiopia. Severe epidemics have occurred in this belt country in the past decades. The most serious epidemic report in this belt was in 1988 and 1989.There was reported cases of 70, 000, and more than 40,000 of them were reported from Ethiopia. Major epidemics occurred outside this epidemic belt and it has also occurred during the wet and rainy season in Ethiopia, Addis Ababa, in 2000 (7).

In the absence of laboratory facilities the diagnosis of bacterial meningitis largely depends upon the clinical signs and symptoms at the time of presentation. The most common clinical symptoms that were recorded from the clinical records of Awassa Referral Hospital include high grade fever (88.9% of the cases), neck rigidity (74.8%), headache (69.6%) and nausea and vomiting (59.3%). Altered mental state was present in more than half of the patients. Various outcomes were recorded including complete recovery (56.7%), partial recovery with sequelae (9.2%) and death which was recorded in 23.5% of the cases.(5)

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Out of all pediatrics admission in GUH, 2.2% were with bacterial meningitis and 13.2% of the meningial admissions were died. Most the deaths (65%) occurred in the first 72 hours of hospital admission. Out of all pediatrics admission 31.1% of them were infants below the age of 12 months and children under the age of 5 which accounts 58.3% of all admission and the median age is 3.8 years. A higher case fatality rate 46.2% was observed in infants below the age of 6 months. Majority of the admission were males, with male to female ratio of 2:1, and 62.3% of them were from rural areas whereas 37.7% of them were from urban areas High admission of meningitis was recorded from April to July in 2001 in Gondar. (3, 7)

1.3 Significance of the study

The study will help to show the magnitude of the disease as well as analyzing the nature of the disease with emphasis on how a better outcome is achieved. The study result also serves as a base line data for future investigations on the same topic in future.

Although the true incidence of bacterial meningitis is not well known in Ethiopia, it is believed to be a common disease in this country as elsewhere, but statistics regarding this disease are mostly done in limited areas (in Awassa and Gondar).

Additionally, the study result will help as a source of information to update the knowledge of health professionals.

2.1 LITRATURE REVIEW

Globally, apart from epidemics at least 1.2 million cases of meningitis are estimated to occur every year with 135,000 deaths, and about half of the cases and deaths occur in Africa (3). The prevalence of bacterial meningitis in United States in 2010 is 3 per 1000 persons. In Canada, there are at least 150 to 170 cases of bacterial meningitis in children younger than 5 years of age each year (10).In Brazil estimates that the prevalence of meningitis is 22 cases per 100, 000 persons (2).

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Out of all admissions aged ≥ 60 days during the study in Brazil, 22% of which had LP (lumbar puncture), and 2% admissions had meningitis and 0.7% had possible meningitis. A bacterial Pathogen was cultured from CSF. In 58 (64%) of meningitis cases; streptococcus pneumoniae (n= 31), Homophiles influenza (n=24), non typhoid salmonella (n=2), and pseudomonas aeruginossa (n=1). Neonate with bacterial meningitis had a higher mean CSF protein value (2.67 g/1 vs. 1.97 g/1) and a significantly higher mean CSF white cell count 21 cells /ml vs. 7 cells/ml (8,13).

Neisseria meningitis and streptococcus pneumoniae each causes about 40% of the cases of bacterial meningitis, with other pathogens causing the remainder of cases, Homophiles influenza type b (Hib) is a rare causes of meningitis, with just 2 cases identified in Canada children in 2002, 14 years after the 1st vaccine was licensed (10) .

Among proven bacterial meningitis, which is done in Logus University Hospital, streptococcus pneumoniae was the most common organisms responsible for bacterial meningitis 48% followed by Hib 35%, and neissaria meningitis and salmonella species accounts 6% each. Beyond the neonatal period the most common organisms that cause acute bacterial meningitis are streptococcus pneumonia, Hib and neisseriae meningitides. The rate of pneumonia meningitides has declined 59% since the introduction of conjugate pneumococcal vaccine in 2002. The incidence of disease caused of streptococcus pneumoniae is highest in children aged 1 to 23 months and in adults older than 60 years streptococcus pneumoniae and neisseria meningitides cases are accounts 6-5, and 4 cases per 100, 000 children aged 1 to 23 months respectively (11, 14) .

The aim of early diagnosis of acute bacterial meningitis is a reduction in death and neurological sequelae by timely administration of appropriate antibiotic therapy and supportive care. The 1st line treatment of acute bacterial meningitis in most developing world is intravenous penicillin with chloramphinicol (CAF) because of their low cost. However, increasing antimicrobial resistance of Hemophilus influenzae and streptococcus pneumoniae challenges the 1st line use of penicillin with chloramphenicol in this setting. The benefit of dexamethasone to prevent hearing loss and acute

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neurological complications were more apparent over all for hemophilus influenza, meningitis than for streptococcus pneumonial meningitis, with a benefit for streptococcus pneumonial meningitis being apparent only when dexamethasone was given with or before the 1st dose of antibiotics.

High level of resistance to B-lactamase among strep.pneumoniae necessitates the addition of vancomycin to 3rd generation cephalosporin. In many developing countries the problems are fundamentally increase resistance of strep. pneumoniae to penicillin and CAF, and Hemophilus influenza to CAF means that only children with bacterial meningitis receives ineffective treatment, as 3rd generation cephalosporin are often unavailable or unaffordable (15,16) .

Research done in Gondar University Hospital beyond neonatal age shows that the most common symptoms presentation are fever and vomiting which accounts 89.2% and 74.6% respectively. The other symptoms are stiff neck 66.9%, difficulty of breathing 19.9%, seizure 18.4 %, and respiratory distress 28.5 %. The prevalence of stiff neck varies in different age to 11 mores 50.0%, less than or equal to 12 months 91.3%,and the prevalence of level of consciousness are alertness 49,7%, lethargic 34.2%, stuporous 5.4% , and comatious 10.7 % (12) . On the other hand, studies done in GUH showed that 91.4% were treated with a combination of crystalline penicillin and CAF, Dexamethasone was used in 36.6% of the patients. It was mainly used for children under the age of five 46.0%. Out of patients with seizure, 73.9% were treated with phenytoin and 34.9% with Phenobarbital, but 8.7% of them were given the combination of the two drugs (12).

Studies done by focusing Africa children showed that nearly one-fifth of bacterial meningitis survivors experienced in hospital squeals. About one-fourth of children surviving from pneumococcal meningitis, and Hemophilus meningitis has neurological squeals by the time of hospital discharge a risk higher than meningococcal meningitis cases (median= 7%) Serious long term neurological squeals further increase the population impact of pediatrics meningitis. The squeals comprise a range of findings with implication for child development and functioning include such defects as hearing loss, cognitive delay speech or language disorder, behavioral

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problems, motor delay or impairment and seizures, neurological squeals occur in one third of survivors. Meningitis squeals can present a long term serious hardship for families with limited means to care for disabled child, especially in resource poor settings (15, 17).

Bacterial meningitis is a serious often disabling and potentially fatal infection resulting in 170,000 deaths worldwide each year. Young children are potentially vulnerable to bacterial meningitis, and when they exposed, poor out comes may occur do to immaturity of their immune systems.In Africa; pneumococcal meningitis case fatality ratio attains 45% compared to 29% for Hemophilus influenza meningitis and 8% for meningococcal meningitis (17, 18).

Studies done in Tikur Anbessa Hospital shows that the 2nd commonest causes of all pediatrics admission , and death is bacterial meningitis accounts 7.2 %,and 10.3% following severe pneumonia accounting 38.6% , and 41.9% respectively (6) .

3. OBJECTIVES OF THE STUDY

3.1 General objective

★ To assess etiology and clinical analysis of children with meningitis who are admitted to SPHMMC pediatrics wards in the previous 5 years from 2012-16.

3.2 Specific objectives

- To determine the magnitude of patients with meningitis admitted to pediatrics ward
- To identify etiology of meningitis
- To analyze the laboratory findings of the patients with meningitis
- To determine the outcomes of the treatments

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4. METHODS AND MATERIALS

4.1 STUDY AREA AND PERIOD

Study was done in St. Paul's Hospital pediatric ward. The hospital was built in 1969 (was named St Paul General Specialized Hospital until 2008) by Emperor Haile Selassie in collaboration with the German Evangelical Church, as a source of medical care for underserved populations. It currently has more than 392 beds, with an annual average of 200,000 patients and a catchment population of more than 5 million. Approximately 75% of the patients receive medical services free of charge. There is over 1300 clinical and non-clinical staff in over 13 departments, most recently launching its new hemodialysis unit. The study will be conducted in October 12 to 30 in 2016.

4.2 STUDY DESIGN

The study involves a retrospective collection of clinical and laboratory data in SPHMMC to provide a quantitative assessment of the recent epidemiological trends of meningitis.

4.3 STUDY POPULATION

All pediatric patients with meningitis that presented in SPHMMC during the study period and fulfilling the mentioned inclusion criteria were included in the study and defined as the study population.

4.4 SAMPLE SIZE

No predefined sample size was set. The study was including all the cases of meningitis that presented in SPHMMC during the defined study period and fulfilled the inclusion criteria which is a total of 95 cases..

4.5 VARIABLES

4.5.1 INDEPENDENT VARIABLES

Socio-demographic variables

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4.5.2 DEPENDANT VARIABLES

- Presence of complications
- Treatment outcome
- Duration of symptoms before admission

4.6 INCLUSION AND EXCLUSION CRITERIA FOR CASES:

Inclusion criteria

The patients fulfilling the following criteria were selected for the study:

- Positive CSF culture or Gram staining results suggestive of meningitis
- Clinically diagnosed cases of meningitis by a medical specialist in the cases where a CSF culture or Gram staining were not performed.

Exclusion criteria:

The patients exhibiting the following characteristics were included in the study:

- Simultaneous infection with another form of meningitis such as tuberculosis.
- Presence of another CNS infection that can present with symptoms similar to meningitis such as cerebral malaria or any other CNS lesion.

4.7 DATA SOURCES:

The clinical and laboratory data were collected from the available clinical and laboratory records. The potential cases was identified by the hospital log books present in the emergency wards, pediatrics and

neonatal in-patient wards and also the out-patient registers. Once the cases were identified from any of these sources the original hospital clinical records were accessed with the help of the main record room staff. The records were traced using the patient hospital registration number from the log books. The original laboratory result slips were attached inside these clinical record forms was also accessed.

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4.8 DATA COLLECTION:

The information obtained from the above mentioned sources was entered into pre-defined data collection forms. Among the clinical details, the signs and symptoms at presentation such as stiff neck, headache, fever, altered mental state, seizures, etc and the treatment outcome was recorded. Demographic details such as age, sex and the month of presentation was also record. Similarly laboratory findings from the laboratory log book such as results of CSF cultures, Gram staining, CSF cell count, proteins and glucose level, depending upon their availability was recorded on the data collection forms. On identification of cases, each participant was given a code number that was used throughout the research to avoid confidentiality issues. The data was recorded by six data collectors.

4.9 DATA HANDLING:

Data entry:

The data from the filled-in data collection forms were entered into SPSS version 18.0.0 and later converted to Excel sheets for convenience during discussions.

4.10 Operational Definition

- **Bacterial or pyogenic meningitis**:- is an inflammation of the arachnoids layer of the meninges and the fluid that circulates in the ventricles and sub-arachnoids space(CSF) Caused by bacterial infection the cause of bacterial meningitis vary with age.
- **Clinical analysis**: the use of laboratory data and checking clinical manifestations.
- **Etiology**:- the set of factors that contributes to the occurrence of a disease

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4.11 ETHICAL CONSIDERATIONS:

Ethical clearance was obtained from the SPHMMC research director to request grant on ethical approval. Once these ethical reviews was sought and the approval granted from the above mentioned a final administrative order directing the commencement of the study were issued to the office of the medical service director directorate and Hospital record officer.

4.12 QUALITY CONTROL MEASURES

The data collectors were trained on how to collecting data, handling data and over all sequence of data collection and was supervised on how to collecting the data. Data was checked for its completeness by principal investigator.

5. EXPECTED OUTCOME OF THE STUDY

The study is intended for the host population as being the sole beneficiaries. The retrospective data collected from SPHMMC will prove helpful in establishing the current magnitude of meningitis in these particular settings. The effect of seasonal variability on various types of bacterial meningitis and the age wise and gender wise distribution of disease burden will provide useful estimates on the recent trends of meningitis. Therefore, the results obtained from the study will also prove helpful for other hospitals in Ethiopia working in similar settings. Special emphasis has been laid to ensure the validity of the clinical and laboratory data. This 5-year retrospective study component may provide valuable data that can be used for further research and formulation of preventive strategies.

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5. RESULTS AND FINDINGS

The clinical record files from the hospital's in-patient and emergency wards and the laboratory records identified 95 cases of bacterial meningitis at St.Paul Hospital Millennium medical college from September 2012 to the end of December 2016. These 95 cases include the laboratory diagnosed cases as well as the cases that were clinically confirmed based on the signs and symptoms. The data collected from the clinical record files of these patients were used to study the demographical trends of bacterial meningitis as well as the clinical features and the outcome of treatment.

Age wise and sex wise distribution of bacterial meningitis:

Out of 95 cases, 64 were males and 31 were females making a male to female ratio of 2.06:1. The trend was uniform in all age groups with more case occurring among males. The highest number of cases was in the between the age 15 to 18 years. In this age group 38 cases (39.5 %) of bacterial meningitis were observed. 32 cases (33.7%) were children less than 4 years of age, half of which were infants less than one year of age.

Age wise and sex wise distribution of cases at St.Paul Hospital Millenium Medical College during 2012-2016.

		GENDER		**TOTAL**
AGE GROUP		MALE	FEMALE	
Infant (0-12 months)	No. of cases (N)	12	4	16
	Percentage (%)	75 %	25 %	100 %
1-->4 years	No. of cases (N)	8	8	16
	Percentage (%)	50 %	50 %	100 %
5-->9 years	No. of cases (N)	9	3	12
	Percentage (%)	75 %	25 %	100 %
10-->14 years	No. of cases (N)	8	5	13
	Percentage (%)	61.5 %	38.5 %	100 %
15-->18 years	No. of cases (N)	27	11	38
	Percentage (%)	61.5 %	38.5 %	100 %
TOTAL	No. of cases (N)	64	31	95

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	Percentage (%)	67.4 %	32.6 %	100 %

Effect of seasonal variation of the incidence of bacterial meningitis:

The bacterial cultures were used to interpret the effect of seasonal variations on the prevalence of the organisms causing bacterial meningitis. The whole calendar year was broken down into 4 quarters to assess the effect of change in weather conditions on the common agents of bacterial meningitis. The most marked seasonal variation was observed for *N. meningitidis* which had a high incidence in the 2nd quarter (April to June). During the dry season (April to June) 18 cases were confirmed by culture results as compared to very few cases in other quarters. When the cases were split according to the time of presentation the highest incidence was observed in the month of June where culture from 8 CSF specimens revealed *N. meningitidis*. The incidence of *N. meningitidis* dropped drastically during the winter months from October to December. The seasonal variation on the incidence of bacterial meningitis is shown in the figure 1.

Organisms of bacterial meningitis:

The organisms causing bacterial meningitis was identified in 95 cases. Bacterial cultures were performed on 66 cases out of these 95 patients and 50 patients were confirmed on the basis of Gram staining results. Both culture results as well as Gram staining results were carried out to diagnosis 21 cases.

Table 2: Laboratory confirmation of cases of bacterial meningitis in SPHMMC during 2012-2016.

Cases confirmed by both by culture and Gram Staining	21
Cases confirmed by only by culture	45

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Cases confirmed only by Gram staining	29
TOTAL	**95**

The culture results showed the highest incidence of *S. pneumoniae* among the common agents of bacterial meningitis. *S. pneumoniae* was isolated from the CSF cultures of 32 patients (33.7%). *N. meningitidis* was isolated from 24 cases (25.3%) and *H. influenzae* from 12 cases (12.6%).

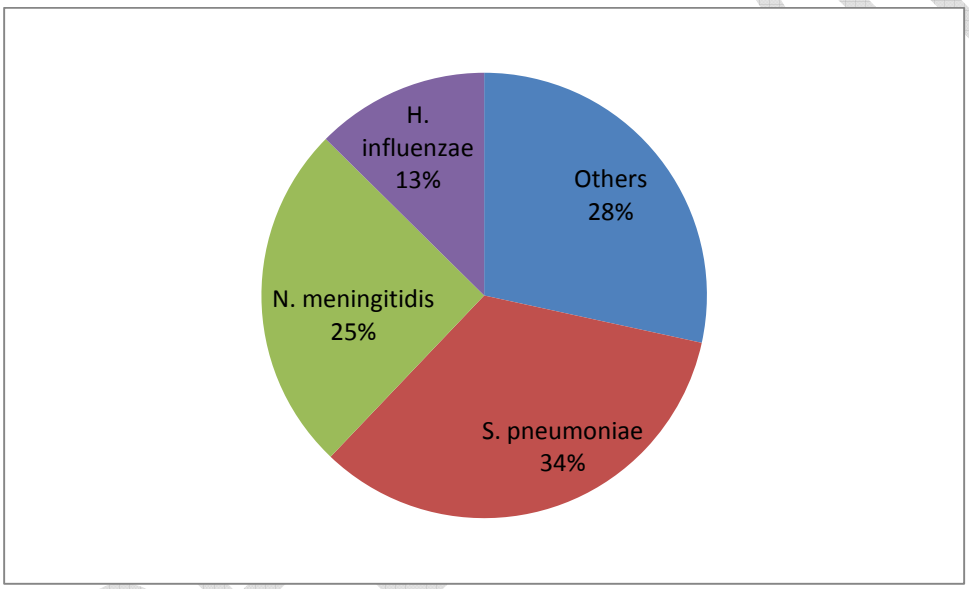

Fig:1 Organisms isolated from CSF cultures of patients of bacterial meningitis in SPHMMC

Clinical feature of bacterial meningitis:

The most common symptom was fever. High grade fever (>38^{o}C) was recorded in 84 cases (88.4%). The second most common sign was neck stiffness which was present in 67 cases (70.5 %). Headache and nausea or vomiting was present in 40 and 32 cases, respectively. Altered mental state such as un-consciousness, behavior change or inability to speak was observed in more than half of the patients. Almost 36% of the cases were reported to have had one or more incidence of seizures before

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presenting to the hospital. Respiratory symptoms such as cough, wheezing or effort breathing were present in less than a quarter of the patients.

Table 3: Clinical symptoms at presentation in patients of bacterial meningitis at St.Paul Hospital Millenium Medical College during Sep 2012 to Dec 2016.

Sign and symptoms	Frequency	Percentage (%)
Fever >38^{0}C	84	88.4
Neck stiffness	67	70.5
Headache	40	42.1
Nausea and Vomiting	32	33.7
Altered mental state	55	57.9
Seizures	34	35.8
Respiratory symptoms	21	22.1
Shock	5	5.3

Outcome of bacterial meningitis:

The clinical files of 95 cases of bacterial meningitis to find out the outcome of the treatment. Final treatment outcomes were recorded in 84 cases. The most common outcome of the treatment was complete recovery which was observed in 55 (65.5 %). Death was the second most common outcome with 17(20.2 %) cases recorded as fatal cases. Neurological or other sequelae were present in 9(10.7 %) cases at the time of discharge from the hospital.

In the 11 cases the medical records from the clinical files were insufficient to reveal the final outcome of the treatment.

Adverse outcomes of bacterial meningitis: Death

During the study period 17 deaths were recorded due to bacterial meningitis, thus giving a case fatality rate (CFR) of 20.2 %. These fatal cases were then further analyzed by breakup into the various age groups. Most of the fatal cases were in infants. When age specific CFRs were studied, infants had the

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highest CFR of 33.3%. A gender-wise breakdown of the fatal cases showed that more deaths were recorded in males then females.

Table 4: Fatal cases of bacterial meningitis at St.Paul Hospital Millenium Medical College during September 2009 - December 2011

AGE GROUP	CASES WITH KNOWN OUTCOMES (N)	DEATHS IN EACH AGE GROUP (D)	CASE FATALITY RATE (CFR) NO. OF DEATHS X 100 / NO. OF CASES
Infant (0-12 months)	15	5	33.3 %
1-->4 years	13	1	7.7 %
5-->9 years	11	3	27.3%
10-->14 years	10	3	30.0%
15-->18 years	35	8	22.8%
Total	**84**	**17**	**23.5%**

Adverse outcomes of bacterial meningitis: Sequelae

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Complications of bacterial meningitis were recorded at the time of hospital discharge in 9 cases (10.7%). The most common sequelae were neurological complications such as paralysis or weakness of the limbs (5 cases); facial palsy (3 cases), muscle wasting (2 cases), deafness or hearing impairment (1 case) and acute psychosis (1 case).

Discussion and Conclusion

The aim of the study was to explore the various demographical, epidemiological and clinical aspects of the bacterial meningitis in SPHMMC. The results are based on 95 cases from a 5-year period (2007 to 2011). These 95 cases include only those cases that had been confirmed by laboratory identification of the causative organism.

The data on 95 laboratory confirmed cases of bacterial meningitis showed marked male predominance (male to female ratio of 2.06:1). Throughout the various age groups the trend of male predominance tends to persist. Various large scale studies conducted worldwide show a higher incidence in males. A study on the characteristics of bacterial meningitis was conducted in four major tertiary care hospitals in Bangladesh during 2003 and 2004. The study showed that out of 1841 cases, 1307 were males, giving a male to female ratio of 2.5:1. Similarly, studies from SMHMMC have also shown a higher incidence in males. A 5-year retrospective study conducted in Gondar University Hospital during 1998 to 2003 identified 151 children with bacterial meningitis. This study also reported a higher incidence in males with a male to female ratio of 2:1. During the meningococcal epidemic in Gondar in 2001-2002, a total of 1619 probable cases of meningococcal meningitis were reported. Out of these 1619 cases, 960 were males (male to female ratio of 1.5:1). The comparison between Gondar study and our study shows a much lower number of patients of bacterial meningitis in the former study. The reason for this number of cases is due to the exclusion of probable cases which were not laboratory confirmed. The current study focuses on the etiology and has only included the laboratory confirmed cases which were confirmed either by CSF culture or Gram staining. What has caused this high male to female ratio at both of the study sites may be linked to various factors. As seen in the literature and from results of the studies mentioned above, the organisms of bacterial meningitis show susceptibility patterns indicating a higher affinity for males. This may also highlight the bias or the preference that may be given by the family to the male children over the female children.

Bacterial meningitis is generally a disease of childhood. In this study the most commonly affected age group was found to be the infants. Within the various age groups, a higher incidence in infants has

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frequently been reported in literature. A 10-year study conducted in United States in California during 1998 to 2007 showed the highest incidence of bacterial meningitis in infants less than 2 months of age. For the year 2006-2007 the incidence was 80.7 cases per 100,000 populations. Children greater than 2 months and less than 2 years of age showed the second higher incidence (6.9 cases per 100,000 population) during the same year. A large scale retrospective study in Niger showed that in the year 1995-96 the incidence of bacterial meningitis was highest in infants less than one year of age (638 cases per 100,000 population), this was followed by children between 1-4 years of age (490 cases per 100,000 population). Older children between 10-14 years and young adults also showed a higher incidence (each having 476 cases per 100,000 populations). In contrast to these studies, a study in North Gondar during 2001-2002 showed the highest incidence in young adults between 15-30 years of age (52% of cases). Generally, these results point out at1 peaks of age that have high susceptibility for bacterial meningitis i.e. small children. This also parallels with the findings in this current study.

Certain agents of bacterial meningitis are known to have higher affinity for some age groups, particularly *H. influenzae,* which commonly effects infants. The results of this study show a similar trend in which *H. influenzae* was more prevalent in the infancy and younger children (all 9 culture confirmed cases were less than 14 years). Little variation in the various age groups was observed for *N. meningitidis* and *S. pneumoniae*, both of which showed only a slightly higher incidence in small children between 1-4 years of age. This trend in the different age groups for these common organisms has frequently been reported in literature. A study was conducted in Lazio, Italy during the period 2001–2005 to study these variations in age groups. A slight variation in various age groups was reported for *N. meningitidis* and *S. pneumoniae. S. pneumoniae* had a higher incidence at both extremities of age whereas *N. meningitidis* was more prevalent in smaller children less than 4 years. Marked variation was only observed for *H. influenzae* which had a considerably higher incidence in smaller children less than 4 years Similar results were observed in a study on the laboratory based surveillance of bacterial meningitis in Sudan during the year 2004-2005. The study showed that out of a total of 24 culture or PCR confirmed cases of *H. influenzae*, 21 (87.5%) had occurred in children less than 5 years of age [(11)].

The agents causing bacterial meningitis may vary considerably depending upon the geographical and climatic conditions, socio-economic status and importantly the immunization schemes in the host community [(16)]. Culture results reveal the prevalence of various organisms that cause bacterial meningitis. Almost 35% of the cultures were identified as *S. pneumoniae,* followed by *N. meningitidis* and *H. influenzae* which are isolated from 26% and 13% of the cases, respectively. The predominance

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of these three agents of bacterial meningitis has widely been reported in literature. A large scale WHO study conducted in various countries of meningitis belt including Ethiopia has documented similar patterns with *S. pneumoniae* being the most common organism. It was identified in 26% of the cases. *S. pyogenes* (20%) and *E. coli* (18%) were the other common organisms [(9)]. A laboratory based study on the surveillance of bacterial meningitis in Egypt during 1998-2004 depicted a high *S. pneumoniae* prevalence (42%) followed by Hib (20%) and *N. meningitidis* (16%) [(14)].The etiology of bacterial meningitis may vary with the age of the study group and other characteristics of the population. A 5-year study on children up to the age of 14 years in Gondar during 1998-2003 reported *N. meningitidis* as the leading cause of bacterial meningitis (27.8% of the cases). *S. pneumoniae* and *H. influenzae* were present in 7.1% and 5.6% of the cases [(10)].

It is evident from the literature on bacterial meningitis in the meningitis belt countries that in the lack of availability of laboratory facilities the clinical signs and symptoms play a significant role in the diagnosis of bacterial meningitis. The classic triad of symptoms i.e. fever, headache and neck stiffness are characteristic of bacterial meningitis [(10)]. These were the most common signs and symptoms that were recorded in the clinical record files of the patients in SPHMMC. Fever was present in 88.4% of the cases and 70.5% of the patients had neck stiffness. Headache was the presenting complaint in almost 42% of the cases. A very similar study conducted on a 5-year retrospective clinical data in East England during 2005-2010 [(17)] showed the highest prevalence of fever and headache (82% each), followed by altered mental state (59%), vomiting (51%), neck or back rigidity (33%). The results follow almost a similar trend as observed in the current study. However, in the East England study, 10 out of 39 cases (26%) had purpuric rash, in contrast to only one documented cases of petechial rash in the current study. The darker skin color may offer some hindrance in spotting petechial rash and this may be a contributing factor to the lower incidence of the rash at our study sites. As it has already been mentioned in the literature, that the most common serogroup of *N. meningitidis* in Ethiopia is serogroup A;(15) a serogroup which is not usually associated with petechial rash. As the rash is a manifestation of severe meningococcal sepsis and a tertiary care hospital may often be located very far so some of these serious patients may even expire before reaching the hospital. All these reason may explain the reduced incidence of petechial rash observed in this study.

Data on the clinical outcomes of treatment show a fatality rate (CFR) of 20.2%. When compared with different studies conducted around the world the CFR may be highly variable. In the developed world the CFR may be considerably lower than the CFR observed in this study. In a study conducted in the United States during 2003-2007, a CFR of 6.9 was observed in pediatric patients whereas a CFR of

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16.4 was recorded in adult patients [34]. But earlier studies from Ethiopia have reported a fatality rate of 22-28% [114]. But even the CFR reported in various studies in Ethiopia varies. The exact estimation of the fatality rates due to bacterial meningitis may be somewhat difficult as not all the cases present in the hospitals. These rates represent data from a tertiary care hospital with relatively better facilities. In isolated smaller healthcare units with minimal facilities the fatality rates may actually be much higher.

As in the case of CFR, the rate of sequelae may also be much lower in tertiary care hospitals. This may be the reason for a considerably lower rate of sequelae (10.7%) that was observed in this study as compared to the estimated rates that have been mentioned in the literature (up to 50%) [8]. A systematic review of 37 studies from 21 African countries has documented sequelae rate as high as 37% [7].

Recommendations:

This study has been conducted with an aim to pave way for future studies in similar settings. Following are the recommendation from this study:

1. Similar studies in settings with better laboratory facilities may yield more information on the recent incidence of the causative organisms or the current serotypes. Combining the laboratory results with the clinical outcome will help in better understanding of bacterial meningitis.
2. Many patients of bacterial meningitis may not present at tertiary care hospitals due to vast distances from hospitals and lack of transport facilities. Any study that has its focus laid primarily on the primary healthcare centers in the peripheries will provide valuable information on a large portion of cases that are easily missed when studies are conducted only in the tertiary care hospitals.
3. During the course of study many patients with co-existent infectious diseases were found. The association of bacterial meningitis with other infectious diseases such as Human Immunodeficiency Virus (HIV) infection or in immunocompromised patients may need further exploration.
5. Standardization of the data entry procedures for hospitals' clinical and laboratory records at the study sites along with a more unified collection and storage of records will certainly prove beneficial for the follow up patients, the hospital staff and even the future researchers working on disease prevention in these settings.

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Appendix I: **Retrospective data collection form:**

RETROSPECTIVE DATA COLLECTION FORM

PATIENT DATA		
Age _____	sex_____	Region/city_____
Date of admission_____	Date of discharge____	
Duration of symptoms before admission (day/s) _____	Duration of hospital stay (day/s)_____	
CLINICAL SYMPTOMS AT THE TIME OF ADMISSION		
Fever ☐	Vomiting ☐	Neck stiffness ☐
Irritability ☐	Convulsion ☐	Bulged fontanel ☐
Disturbance of consciousness ☐	Petechiae ☐	Brudinznk's and kerning's sign ☐
Grunting ☐	Headache ☐	Paralysis (specify)_____
Anorexia ☐		
Others (specify)_____		

LABORATORY FINDINGS

TEST	**DONE**	**RESULT**
CSF GRAM STAINING	☐	PISITIVE ☐ NEGATIVE ☐

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CSF CULTURE:	☐	*N. meningitidis* ☐ *H. influenzae* ☐ *S. pneumoniae* ☐ Others …….
CSF CELL COUNT PROTEINS AND GLUCOSE LEVEL	☐	CSF CELL COUNT: _____ /mm3 PROTEINS CONC: _____ g/liter GLUCOSE CONC: _____ g/liter
OTHER LABORATORY FINDINGS:		
Any types of treatment received during hospital admission		Antibiotic ☐ Others (specify)…… Dose _____ Route of administration _____ Duration of taking _____
Course of the disease		Uncomplicated(discharge improved) ☐ Unimproved, discharged against medical advice ☐ Gross neurological sequalae ☐ Death ☐
Neurological sequelae		Behavioral problems, emotional irritability ☐ Convulsion (seizure) ☐ Localized defects ☐ sub-dural effusion ☐

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	cerebral edema (coma) ☐ development Hydrocephalus ☐ Others (specified)…….

Name of Data collector _____

Signature _____

Date _____

Acronyms and abbreviation

BBB…. Blood Brain Barrier

CAF----- Chloramphenicol

CNS -----Central Nervous System

CSF -----Cerebrospinal Fluid

E.C ----- Ethiopian Calendar

Hib**……**Haemophilus influenzae type b

LP-------Lumbar puncture

LRTI ---Lower Respiratory Tract Infection

PCR…..polymerase chain reaction

SPHMMC…St. Paul's Hospital Millennium Medical College

URTI --Upper Respiratory Tract Infection

WHO….World health organization

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