A RETROSPECTIVE STUDY TO DETERMINE CULTURE POSITIVITY, SUSCEPTIBILITY, TREATMENT OUTCOME AND FACTORS ASSOCIATED WITH CULTURE POSITVITY IN CLINICALLY DIAGNOSED BACTERIAL MENINGITIS PEDIATRIC PATIENTS IN JUSH PEDIATRIC WARD FROM JANUARY 2013-JUNE2015.

BY: MOHAMMED BESHIR (MD)

A RESEARCH PAPER SUBMITTED TO JIMMA UNIVERSITY COLLEGE OF HEALTH SCIENCES, SCHOOL OF POSTGRAGUATE AND DEPARTMENT OF PEDIATRICS AND CHILD HEALTH FOR PARTIAL FULFULLIMENT OF CERTIFICATE IN PEDIATRICS AND CHILD HEALTH SPECIALITY

JIMMA,ETHIOPIA

OCTOBER,2015

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ABSTRACT

Background:-Bacterial meningitis remains a common disease worldwide. Although no age group is exempt from acquiring the infection, bacterial meningitis has the highest incidence during the first month of life than during any other subsequent period and it is associated with high morbidity and mortality. The causes of bacterial meningitis in the neonatal period are generally distinct from those in older infants and children and reflect the maternal gastrointestinal and genitourinary flora and the environment to which the infant is exposed. The most frequent causes of bacterial meningitis above neonatal period are *Nessieria meningitides*, *Streptococcus pneumonia*, and *Haemophilus influenza*. Information on the relative frequency of the isolation and antibiotic susceptibility patterns of these pathogens is scarce in Ethiopia, in particular to Jimma University teaching Hospital.

Objective:-The aim of this study is to determine culture positivity, susceptibility, treatment outcome and factors associated with culture positivity in clinically diagnosed pediatric bacterial meningitis patients admitted to JUSH pediatric ward.

Methods and Materials:-A cross sectional study involved about 178 clinically diagnosed Bacterial meningitis patients (≤14 years) was conducted from January, 2013 to June, 2015 at pediatric units of Jimma University Specialized Hospital.

Results:- Among 178 study subjects 108 (57.8%) were males, making the male to female ratio was 1.4. The mean ages of the children were 26.694 months. The highest frequency of clinically diagnosed Bacterial meningitis was observed in patients below the age of one month 122 (65.2%).The highest number of bacteria was isolated from subjects above neonatal ages (>90 days). Out of the 110 CSF cultures samples, cultures were positive in 9 of cases showing an isolation rate of 8.1%.

Conclusion:-The isolation rate of bacterial pathogens from cerebrospinal fluids culture was found to be low. The frequency of multiple drug resistance was high among the bacterial isolates, which mandates culture and susceptibility testing before prescribing any antibiotics whenever possible.

ACKNOWELEDGMENT

I would like to thank Jimma university college of public Health and Medical Sciences School of Graduate Studies, Department of pediatrics and child health for giving opportunity to conduct this research. I am very grateful to Dr.Netsanet Workneh & Mr.Henock Asefa for their valuable comments and assistance in developing this research.

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ABBREVIATIONS

BBB-Blood Brain Barrier

CDC- Center for disease control and prevention

CFRs -Case fatality rates

CNS-Central nervous system

CSF- Cerebrospinal fluid

GBS -Group B streptococcus

G-Gram-reaction

Hib- Haemophilus influenza type B

JUSH-Jimma University Specialized Hospital

LBW-Low birth weight

LP-Lumbar puncture

NICU-Neonatal Intensive care unit

Spp-Species

VLBW-Very Low birth weight

WHO-World health organization

CHAPTER ONE: INTRODUCTION

1.1 BACKGROUND OF THE STUDY

Bacterial meningitis is a life-threatening illness that results from bacterial infection of the meninges and leaves some survivors with significant sequelae. (**1**).Despite advance in vaccines development and chemoprophylaxis, morbidity and mortality rates from the disease remain high. The disease is more common & occurs more frequently in developing countries (**2**).

Meningitis can affect anyone in any age group, from the newborn to the elderly. From its recognition in 1805 until the early 20th century, bacterial meningitis was virtually uniformly fatal. Until recent years, up to 50% of patients who survived the acute infection would be left with permanent sequelae such as mental retardation and hearing loss (**3**).

Invasive meningococcal infection is probably a relatively new disease. The first recorded major outbreak occurred in Geneva in 1805. African epidemics became much more common in the 20th century, starting with a major epidemic sweeping Nigeria and Ghana in 1905–1908 (**4**).

Africa experiences a disproportionately large burden of meningitis due to its young population, epidemics in the meningitis belt and high rates of endemic diseases. In the African "meningitis belt" (a region of savanna that extends from Ethiopia in the east to Senegal in the west), this disease frequently occurs in epidemics during the hot and dry weather (December to March). The meningococcal meningitis pandemic that began in 1996 has resulted so far in approximately 300,000 cases being reported to the World Health Organization (WHO).

The incidence & Case fatality rates (CFRs) associated with pediatric HIb and *Pneumococcal meningitis* were highest in Africa compared in a recent global review. In addition Africa is the only region with cyclic epidemics of meningitis that affect persons of all ages, with attack rates of ranging from 100 to 800 per 100,000 populations. Epidemics of meningitis are mostly associated with meningococcal, but there is some evidence that increases in *Pneumococcal meningitis* cases occur in parallel during, the hot and dry season (**5**).

The etiology of bacterial meningitis is affected mostly by the age of the patient. In neonates, the most common etiologic agents are *group B streptococci (GBS)* and *gram-negative enteric bacilli*. In infants and young children worldwide, *Streptococcus pneumonia, Neisseria meningitides* and *Haemophilus influenzae* type b (Hib) are the most common causes of bacterial meningitis. Among children older than 5 years of age and adolescents, *S. pneumonia* and *N. meningitides* are the predominant causes of bacterial meningitis (**6**).

All three of these organisms are respiratory pathogens. They are spread from person to person by close contact with respiratory secretions. Once acquired, each species can colonize the mucosa of the nasopharynx and oropharynx, which is known as pharyngeal carriage. From there, they may cross the mucosa and enter the blood. Once in the blood, they can reach the meninges, causing meningitis, or other body sites causing other syndromes (**7**).

Meningitis occurs more commonly during the first month of life than during any other subsequent period and it is associated with high morbidity and mortality (8).The neonatal meningitis is an illness characterized as a result of infection and inflammation of the meninges and it typically happens between birth and the first 28 days of life(**9**). During the neonatal period, the illness has special characteristics, the etiology, the clinical symptoms and the mortality appear too different from the observed in older children. The mortality varies based on the treatment, with survival rates of 17% to 29% and with complications rates of 15% to 68 %. Although there have been medical advances of medicines and preventive medicine, the incidence of newborn bacterial meningitis for the last 30 years has been barely affected (**9**)

Manifestations of bacterial meningitis depend on the age of the patient. Most common signs and symptoms include the "classic triad" of fever, headache and neck stiffness. However, these classical symptoms occur in less than half of the cases. Signs of meningeal irritation contribute significantly to the diagnosis of bacterial meningitis, more so in the settings devoid of modern day laboratory facilities.

But these signs may not be present in unconscious patients, very small children or in the immune-compromised patients(**7**).The most common symptoms of neonatal meningitis include; feeding poorly or refusing to feed, irritability, trouble breathing, Bulging fontanelle, diarrhea ,and feeling too warm or too cold (**10**).The incidence and case-fatality rates for bacterial meningitis vary by region, country, pathogen, and age group. Without treatment, the case-fatality rate can be as high as 70 percent, and one in five survivors of bacterial meningitis may be left with permanent sequelae including hearing loss, neurologic disability, or loss of a limb (**11**).

The diagnosis of acute bacterial meningitis confirmed by analysis of the CSF which typically reveals microorganisms on Gram stain and culture, a neutrophilic pleocytosis, elevated protein, and reduced glucose concentrations. The biochemistry and cytology of CSF aspirate is very helpful in the overall diagnosis of bacterial meningitis, initiation of antibiotic therapy and accessing the progress of treatment. The CSF characteristics highly suggestive of bacterial meningitis depends on the age of the patients, include an elevated CSF cell count for age, predominantly neutrophil, increased protein levels for age in the CSF is also an important diagnostic factor and indicates disruption of the blood-brain or the blood-CSF barrier (12).

Appropriate antibiotic therapy is a critical aspect of management. Antibiotic choice is empirical, based on age at onset, likely pathogens, and antibiotic susceptibility patterns. Antibiotics are modified according to culture and antibiotic susceptibility result.CSF culture is dependent on achieving bactericidal antibiotic concentration within the CSF. This will be influenced by the dose of antibiotic that can be administered safely; the penetration of antibiotics into the CSF, and the minimum bactericidal concentration of the infected organisms (13) .Initiation of proper treatment within 6 hours of presentations reduce the mortality rates by more than 8 times (**14**). Delay in initiation of antibiotic therapy is shown to be the single most important risk factor related to the outcome of bacterial meningitis (**15**).Vaccination and antibiotic prophylaxis of susceptible at-risk contacts represents the two available means of reducing the likelihood of bacterial meningitis. Bacterial meningitis is a vaccine preventable disease and vaccines form a cornerstone in its prevention. Various types of vaccines are currently being used to prevent bacterial meningitis. The availability and application of each of these approaches depends on the specific isolating bacteria (**16**).Currently the best means of neonatal *Group B streptococcus* prevention is the use of maternal intra-partum antibiotic prophylaxis to prevent early onset *Group B streptococcus* disease.

1.2) STATEMENT OF PROBLEM

Globally, bacterial meningitis affects approximately 1.2 million people each year and causes almost 170,000 deaths (**17**). In the absence of proper treatment, the mortality rate associated with bacterial meningitis can be as high as 50% (**9**). In recent years, despite improvement in antimicrobial therapy and intensive care support, overall mortality rates related to bacterial meningitis of around **20% to 25%** have been reported by major centers (18). Two-thirds of meningitis deaths in low income countries occur among children under 15years of age (**5**).

Africa children have some of the highest rates of bacterial meningitis in the world. Bacterial meningitis in Africa is associated with high cases fatality and frequent neuropsychological sequelae. Neonatal meningitis remains a serious problem with the high mortality rates of 60%. In no other age group is meningitis more common than in the new born with an incidence of 0.4/1000 live births (**19**). Located on the eastern part of meningitis belt, Ethiopia is one of the countries which are most affected with bacterial meningitis. Both endemic and epidemic forms of meningococcal meningitis have affected Ethiopia for a number of years. For instance outbreaks and epidemics have been reported in 1935 and 1940 and the 1950s, 1964, 1976 1977, 1981 to 1983, and 1988 to 1989. Prior to 1988, the majority of epidemics cases occurred in the north, the northwest, and parts of the central regions of Ethiopia, which lie within the eastern end of the traditional belt of Africa (**20).**

Epidemics were also reported in Ethiopia in the years 2001 to 2003. The numbers of cases in each year from 2000 to 2003 were 855, 6,266, 2,329 and 3,540 respectively and the case fatality rates (CFRs) in the same year were 2.2, 5.0, 5.0 and 4.7 respectively (**21)**.Apart from *N. meningitides* other agents of bacterial meningitis such as *Hib* and *S. pneumonia*are also very common. During the year 1993-1995, a study conducted in a pediatric hospital in Addis Ababa in 1993-1995 showed that almost 5.5% of all hospital admissions were bacterial meningitis.

The emerging resistance among the organisms causing bacterial meningitis is a matter of serious concern. Studies have reported increased resistance to the commonly used antibiotics such as penicillin G and chloramphenicol (22).

Bacterial meningitis accounts for about 6-8% of all the hospital admissions in Ethiopia and the case fatality ratio associated with bacterial meningitis is as high as 22-28% (16).

Up-to-date information on local pathogens and their drug susceptibility patterns is very crucial for the treatment of patients, to decide health priorities, to allocate resources, to monitor the onset of resistance and for planning the effective use of   in the region. However, as far as I am concerned, there are no fully fledged studies conducted in this regard to generate adequate evidence and thereby address the underlying problem particularly in JUSH pediatric ward. This is one of the existing gaps that need to be sorted out and which this study is interested in. The purpose of this study is, therefore, to identify the prevalent bacterial pathogens that cause meningitis and to assess their antibiotic susceptibility patterns in JUSH pediatric ward and forward possible suggestion to solve this problem.

1.3. OBJECTIVES OF THE STUDY

1.3.1. General Objective

To determine culture positivity, susceptibility, treatment outcome and factors associated with culture positivity in clinically diagnosed bacterial meningitis pediatric patients.

1.3.2. Specific Objectives

- To determine the prevalence of culture positive bacterial meningitis
- To determine antibiotic susceptibility among culture positive bacterial meningitis.
- To determine treatment outcome in clinically diagnosed bacterial meningitis.
- To identify associated factors with culture positivity among clinically diagnosed bacterial meningitis.

1.4. SIGNIFICANCE OF THE STUDY

African children have some of the highest rates of bacterial meningitis in the world. This highest rate in Africa is associated with high case fatality and frequent neuropsychological squeal. Many meningitis related studies have been conducted in different countries especially in developed countries but less in developing countries.

As Ethiopia is endemic for bacterial meningitis with cases of bacterial meningitis presenting in the hospitals throughout the year. Therefore, this study is aimed at providing the actual burden of bacterial meningitis, antimicrobial susceptibility pattern and clinical variables among children.

The study outcome in turn helps to design effective diagnostic and treatment options, control and preventive strategies of the bacterial meningitis in that locality. In addition to this the study will also serve as an input for further investigation in this area.

1.5. Operational definitions

Antimicrobial - An agent that kills microorganism or inhibits its growth.

Antibiotics - Chemical products produced by one organism that is destructive to another.

Neonates -A baby from birth to 28 completed days of life.

Clinically diagnosed meningitis - A child with signs and symptoms of meningitis [fever, neck stiffness, mental status changes (irritability, confusion, or lethargy), headache, bulging anterior fontanels, forceful vomiting or seizure].

Laboratory confirmed bacterial meningitis -is defined as bacterial identification in cerebrospinal fluid (CSF) by culture, Gram stain, rapid antigen test, latex agglutination or polymerase chain reaction, or bacterial isolation from blood culture accompanied by CSF abnormalities such as high white blood cell count, low glucose or high protein levels than normal for the patient's age.

Treatment outcome categories

In-hospital sequelae- Any neurological sequelae that occurred after the initiation of treatment and prior to discharge.

Cure without immediate neurological sequelae- Patient recovered after treatment of meningitis without any immediate neurologic sequelae.

Cure with immediate neurological sequelae -Patient recovered after treatment of meningitis with any of neurologic sequelae.

Deaths- define as death that occurred after the initiation of treatment for meningitis & prior to discharge.

Neurologic Sequelae- included hearing loss, vision loss, cognitive delay (including mental retardation and learning disability), speech/language disorder, behavioral problems, motor delay/impairment (including gross motor and fine motor impairment, impaired activities of daily living, hypertonic, and paralysis), seizures, and other neurological sequelae.

CHAPTER TWO: LITERATURE REVIEW

It is well known that the incidence, case-fatality rates & antimicrobial susceptibility pattern for bacterial meningitis vary by region, country, pathogen and age of the patient.

In retrospective study of patients with bacterial meningitis who were admitted to Bangkok Children's Hospital, Thailand during the period Jan, 1980 to Dec, 1990(11 years) , there were 618 patients with 77 cases (12.5%) occurring below the age of one month (neonatal meningitis), and 541 cases (87.5%) between one month to 15 years (childhood meningitis). *Pseudomonas aeroginosa* was the most common pathogenic organism (16.9%) in neonatal meningitis; other causative agents in this age group included *K. pneumoniae* (13.0%) *group B streptococcus* (11.7%), *E.coli* and *Enterobacter* spp (10.4%). In childhood meningitis, *H. influenzae* was the most common causative organism (42.3%), and followed by *S.pneumoniae* (22.2%) and *salmonella* Spp (12.4%). S*almonella* meningitis occurred exclusively in infants, 87% of them were under six months, and 13% of them developed relapsing meningitis. The overall fatalities during 1980-1990 were 45.4% and 17.3% for neonatal meningitis and childhood meningitis, respectively. The fatalities of the two age group decline 1987-1990 to 26.3% and 11.4% respectively (**23**).

In related study done at Ahmedabad Hospital in India from July 2010 to December 2011 included 1470 CSF samples of clinically suspected pyogenic meningitis cases in all age groups. Bacterial pathogens were isolated from 205 samples showing an isolation rate of 13.94%. Gram's stain positivity was 61.95%. Among the isolated organisms, 69.26% were *gram negative bacilli* and 30.74% were gram positive cocci. The most commonly isolated bacteria were *K. pneumoniae* (22.92%) &*S. aureus* in 19.02%.Pyogenic meningitis was more common in pediatric patients than adults. *K. pneumoniae* and *Enterococci spp.* were most common isolated in neonatal age group. Ceftriaxone, cefotaxime, had the most effective antibacterial activity across all the bacterial isolates tested in the study (**24**).The other study in carried out in a tertiary care hospital in India during March 2005 to December 2011 A total of 780 samples of cerebrospinal fluid from clinically suspected cases of meningitis in all age groups were subjected to bacteriological examination. A total of 184 (23.58%) bacteria were isolated and further identified by biochemical tests. *Staphylococcus aureus* was the commonest isolate (30.43%) followed by *Streptococcus pneumonia* (14.67%) &*Escherichia coli* (11.41%).

The most common pathogen isolated in the present study was *Staphylococcus aureus* (n=56, 30.43%) which predominated across all age groups. In this study ,unlike to other pediatric series the usual pathogens of meningitis like *Neisseria meningitides, Haemophilus influenzae* and *Listeria monocytogenes* were isolated in only 3 (1.63%), 1 (0.54%) and 2 (1.08%) cases respectively. Antimicrobial susceptibility testing was done by Kirby Bauer disk diffusion method. Methicillin resistant *Staphylococcus aureus*, high level amino glycoside resistance *Enterococcus* spp.and extended-spectrum-β-lactamases were detected. Antibiogram showed that the amino glycosides had the best spectrum of antimicrobial activity. However, Vancomycin and imipenem showed 100% sensitivity against gram positive and gram negative organisms respectively (25).

The other retrospectively Study done on children (age, 5 months to 10 years) suspected with meningitis, who were admitted in a referral regional children's hospital in Tehran, Iran from August 2009 to February 2011. Laboratory data as well as symptoms and signs on admission, organism identification and antibiotic susceptibility results, physical examination findings, and neurologic features of 31 patients with suspected invasive bacterial infection were evaluated, of which 20 (64.5%) had positive cerebrospinal fluid (CSF) cultures. The mean patient age was 2.39 ± 0.4 years (range, 5 months to 10 years). Among all patients, 22 (71%) were males, and the male to female ratio was 2.4. The highest frequency of bacterial meningitis was observed in children ≤2 years (15/20, 75%). This study showed that the microorganisms most frequently isolated from children were *S. pneumonia* (22.5%), H. *influenzae*(10%), and *N. meningitides* (10%), whereas no bacterial pathogen was identified in 35.5zof presumptive bacterial meningitis cases. Fever was noted in 80% (14/20) of patients. Seizures occurred during the first several days post-admission in 60% (12/20) of the patients. In this study, similar to other pediatric series, the most important causative organisms of bacterial meningitis were *S. pneumonia, N. meningitides*, and *H. influenzae*. In the study, the rates of mortality and sequelae were 10% and 35%, respectively (**26**). Another retrospective study done in Iran, of 7112 suspected cases of meningitis admitted to Tabriz Children Educational-Health Care Center between April 2003 and March 2013, 107 cases with confirmed acute bacterial meningitis were reported based on positive results in culture of cerebrospinal fluid. Patients included 60 males (56.07%) and 47 females (43.93%) Fever, vomiting, and meninges irritation were the most prevalent symptoms of patients. In the study, the results of simultaneous blood culture were also examined.

The most prevalent organism isolated from blood cultures was *H. influenzae* type b (20.65%). While, *S. pneumonia* (34.5%) and *H. Influenzae* type b (23.36%) was the main bacteria isolated from CSF, respectively. In this study, 70.09% of patients were under 2 years, which 89.18% of them had pneumococcal meningitis. According to antimicrobial susceptibility testing, most species were identified to have relatively high resistance against some conventional antibiotics including the third-generation cephalosporin's (**27**).In a retrospective study conducted in Oman from January 2000 to December 2005 on all cases of acute bacterial meningitis among children younger than five years of age there were 344 cases of suspected bacterial meningitis. The most common identified etiologic agent reported in this study was *Haemophilus influenzae* 76 (22%) followed by *Streptococcus pneumoniae* 53 (15%) and *Neisseria meningitide*s 37 (11%). In one hundred seventy four (52%) cases of presumptive bacterial meningitis, the etiologic organism remains unidentified. The peak occurrence of meningitis was in young children younger than one year old. The total male to female ratio was 1.4:1 and the case fatality rate (7deaths) was 2% (**28**).

A retrospective study from a teaching hospital in Ghana on Etiological agents of cerebrospinal meningitis from January 1, 2008 to December 31, 2010 .laboratory records of all(4,955 cerebrospinal fluid samples)patients suspected of bacterial meningitis who underwent lumbar puncture from January 1, 2008 to December 31, 2010 were analyzed. Of these, 163 were confirmed meningitis and 106 were probable meningitis cases. Confirmed meningitis cases were made up of 117 (71.8%) culture positive bacteria, 19 (11.7%) culture positive *Cryptococcus neoformans* and 27(16.6%) Gram-positive bacteria with negative culture. The most prevalent bacteria was *Streptococcus pneumonia* 91 (77.7%), followed by *E.coli* 4 (3.4%), Salmonella species 4 (3.4%), *Neisseria meningitides 3 (2.5%)*, *Pseudomonas species 3(2.5%)* and others. *Pneumococcal* isolates susceptibility to penicillin, chloramphenicol and Ceftriaxone were 98.9%, 83.0% and 100.0% respectively. The majority of those infected with *S. pneumoniae* 53 (58.2%) were below 18 years of age and the highest cases of *Cryptococcus neoformans* 17 (89.4%) occurred among patients between 18 and 50 years. Other Gram negative rods such as *Salmonella species, Pseudomonas species, and E.coli and H. influenza* were more common among children less than 5 years compared to older children and adults. The most prevalent bacteria were *S. pneumoniae* occurring mostly among patients less than 18 years of age. Neonates accounted for 8.7% and children from one month to less than 5 years accounted for 23% (**29**).

There are few studies done in Ethiopia. A retrospective study done on etiology of bacterial meningitis Ethiopia, from 2007 – 2011 in two cities i.e. Gondar and Awassa. The disease incidence was highest in small children and young adults. Infants were the most commonly affected age group at Gondar University Hospital which formed almost 27% of the cases. Young adults between 15-24 years of age were among the most effected age groups at Awassa. Among the various agents of bacterial meningitides, *Streptococcus pneumonia* was the most common organism which was identified in the CSF cultures of 35 patients (35.3%). This was followed by *Neisseria meningitides* from 27 cases (27.3%) and *Haemophilus influenzae* from 9 cases (9.1%). 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 treatment 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 (**33**).

Another study conducted during the year 1993-1995 in a pediatric hospital in Addis Ababa in 1993-1995 showed that almost 5.5% of all hospital admissions were bacterial meningitis. Out of 385 cases diagnosed as bacterial meningitis 74 cases were due to *H. influenzae,* 63 cases were recognized as *M. tuberculosis* and 46 cases were due to *S. pneumonia*. Meningococcal meningitis was very rare and was identified only in 6 cases. However, in 196 cases out of total 385 cases the exact etiology could not be traced. The study also reported incidence of antibiotic resistance in *S. pneumoniae* and *H. influenzae* (**34**).

Hospital data from developing countries suggest that resistance to the WHO-recommended regimen of ampicillin and gentamicin in pathogens causing neonatal infections is common: 71% of isolates of *Klebsiella* spp and 50% of *E coli* are resistant to gentamicin (**32**).A retrospective analysis of 2510 CSF and blood specimens submitted to the bacteriology laboratory of Tikur Anbessa Specialized Hospital for culture in the period between Jan, 2001 and Dec, 2010. The study was done from April, 15- June, 2011. Of 2510 total culture 1321(52.63 %%) were from blood and 1189(47.37%) were from CSF. The causative agent had been isolated (414) showing an isolation rate of (16.49%) of the total 2510 meningitis suspected cases; 358(27.10%) were isolated from blood, while 56(4.71%) have been isolated from CSF culture.

The most common isolated pathogens were *Coagulase-negative-staph* 148(35.75%), *S.aureus*65 (15.70%), *K.pneumoniae*50 (12.08%), *Acinetobacter*45 (10.87%), *E.coli*28 (6.76%). *Coagulase-negative-staphylococcus* was the predominant pathogen accounting for 148(35.75%) of all cases. Whereas *S.aureus* and *K.pneumoniae* accounted for 65(15.70%), 50(12.08%) respectively: More than 50% of the pathogens were isolated from neonates having preterm birth and LBW. Of 75 positive cases that have been properly treated; 66(88%) were given a combination of ampicillin and gentamycin (**30**).Another retrospective study on neonatal meningitis conducted in Addis Ababa University Teaching Hospital, 55 cases was identified over a period of 10 years. The prevalence of meningitis for preterm and term newborns were 3.66 and 0.97 per 1000 live birth, respectively (22/6465 Vs 33/36638; $p<0.01$). The overall prevalence was 1.37 per 1000 live births. 22(40%) babies with meningitis died, more preterm than term (13/22 Vs 9/33; $p<0.05$). known maternal risk factors for neonatal meningitis were observed in 15 (27%) babies. The risk factors were more common in preterm than in term newborns (10/22 Vs 5/33; $p<0.05$). The common causative organisms were *Klebsiella pneumonia*, *E.coli* and *Enterobacter Spp.* which together accounted for 67% of all CSF isolates. These organism were evenly distributed between early and late-onset meningitis, and among term and preterm newborns. Seven of 33(21%) of the surviving newborns developed neurological complications (**31**). The limitations of the studies mentioned in this literature are most studies were carried out during the epidemic periods; less emphasis is laid on non-epidemic periods. The laboratory techniques used in many studies were outdated and did not meet the criteria of “gold standard” which is considered vital for clinical research. Most of the studies were carried out either in a single hospital or a single city. The results from one specific area cannot be generalized over the whole population.

CHAPTER THREE: METHODS AND MATERIALS

3.1. Study Area and Period

The study was conducted in Jimma University Specialized Hospital. Jimma is a town located to the southwest of the country, 335km away the capital city, Adis Ababa. The town is found at 07039’ Latitude $36^{0}50'$ Longitude and at an altitude of 1700-1750m above sea level.JUSH is the only teaching and referral Hospital for an estimated 15,000,000 populations living in southwestern part of Ethiopia. The hospital has 300 beds and provides curative and preventive service for 300-400 patients per day at its outpatient department. The study was conducted in JUSH pediatric ward from January/2013 to June/2015 as this is the specific time the Hospital started to provide CSF culture for confirmation of clinically diagnosed bacterial meningitis.

3.2. Study Design

A retrospective cross-sectional study design was employed.

3.3. Study Population

Target population

All children admitted to JUSH pediatric ward.

Source population

All children admitted to JUSH pediatric ward with clinical diagnosis of bacterial meningitis.

Study population

All children admitted to JUSH pediatric ward with clinical diagnosis of meningitis who fulfill the inclusion and exclusion criteria were used in the study.

3.4. Eligibility criteria

3.4.1. Inclusion criteria

In the study those patients who fulfilled the below mentioned criteria were included;

- Children between 0-15 years of age.
- Children with clinical document containing at least 85% of study variables during the specified period.

Exclusion criteria

- Patients with clinical record having less than 85 % of study variables were excluded.

3.5. Sample size and sampling techniques

The study included all children admitted to pediatric ward with clinical diagnosis of bacterial meningitis during the study period. There were not being any specific sample size and Convenience sampling technique employed as the research time was limited.

3.6. Study variables

3.6.1. Dependent variables

- Culture positive bacterial meningitis

3.6.2. Independent variables

Socio-demographic status,

- Age and sex

Nutritional status

- WFH or WFL

Clinical data

- HIV status,
- Antibiotic use prior to admission,
- Contact with similar illness,
- Duration of illness prior to admission,
- Duration of stay in the hospital for treatment,
- Vaccination history,
- Outcome of treatment,
- Biochemical diagnosis of meningitis,
- Specific bacteria isolates,
- Antimicrobial susceptibility pattern of isolates,
- Whether LP was done or not,

3.7. Data Collection Method and Procedures

3.7.1 Data collection Method

Structured questionnaire was the instrument employed to gather the required patient's information for this study. The questionnaire has three major sections. The first section examined the socio-economic status of patients. The second section includes items that gather information from patients charts about the clinical profile of the patients. The third section included questions regarding laboratory data of admitted patients. All the data was collected from the hospital clinical and laboratory records.

3.7.2 Study Procedures

As a study procedure, children admitted for bacterial meningitis within the specified period were identified from the hospital admission registration data. However, additional cases were identified from JUSH laboratory result log book for which CSF cultures and Gram staining results were conducted and registered. After the identification of cases, all clinical records of eligible patients collected to gather the required information through the structured questionnaire.

3.8. Data Quality Control

To ensure proper data quality, orientation was provided to data collectors on how to go about data collection process. Besides this, supportive supervision and monitoring was done by a principal investigator to assure data completeness, accuracy and clarity. This helped to guaranty the inclusion of all relevant information in the study.

3.9. Data processing and analysis

The data from the filled-in data collection forms were entered into statistical package for social sciences (SPSS) for windows version 20 and analyzed using ~~descriptive methods~~. These analysis techniques included frequency tables, pie charts, and graphs and so on.

Moreover, appropriate interpretations were done to indicate the implications of findings of the study and forward plausible suggestions for the future.

3.10. Ethical considerations

The study has followed appropriate ethical procedures to undertake this research process. First official permission letter was obtained from Jimma University medical science faculty research committee and publication office.

Then by submitting the official permission letter to the relevant hospital staff the necessary data was collected from the clinical records of identified patients.

3.11 Dissemination of results

The final results were disseminated to advisors, pediatric and child health department, Jimma university research committee and to other respective bodies for possible evaluation and scientific publication.

CHAPTER FOUR:RESULT

The study included 178 children clinical and laboratory records of Bacterial meningitis cases admitted to JUSH Pediatric ward from January, 2013 to June, 2015 that fulfill the inclusions criteria.

4.1) Socio demographic and clinical background characteristics of the study subjects

In the study a total of 178 patients were included among them male accounted for 107(60.1%). The mean age of the 178 children was 26.7 months (standard deviation..), and the boy-to-girl ratio was ~~1.5:1.~~

Seventy seven(43.3%), 21(11.8%), 34(11.8%) and 46(25.8%) of patients were between 0-7 days ,8-30 days, 31-90 days and above 90 days of age respectively.

The highest frequency of clinically diagnosed Bacterial meningitis was observed in patients below the age of one month 98(55.1%).

The majority 148(83.1 %) had normal weight for height/length, 3 cases had SAM (severe wasting) and 4 cases had moderate wasting. HIV status is unknown in 79 cases, in 96 of them they are nonreactive, and there is 3 cases HIV positive and one cases of RVI exposed cases. In 132 (74.2%) cases vaccination status unknown, 18(10.1%) fully vaccinated, 16(9%) of them Vaccinated for age and 12(6.7%) unvaccinated. Out of total samples, 28(15.7%) of children have received antibiotics for current illness before specimen was collected.

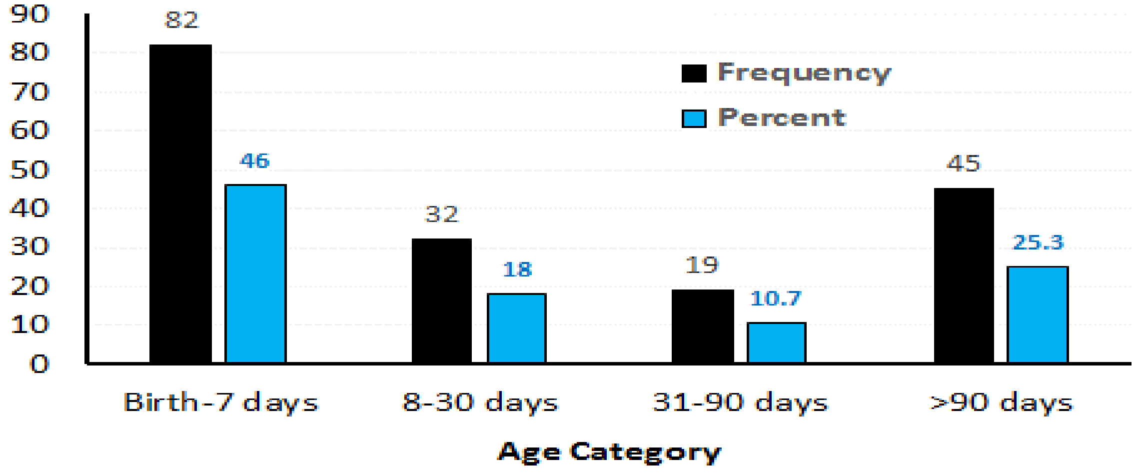

Figure 1: Bar chart showing the age distribution of children with clinically diagnosed bacterial meningitis admitted to JUSH, pediatric ward from January 2013-June 2015.

Table 1: Clinical Data's of children with clinically diagnosed bacterial meningitis admitted to JUSH, pediatric ward from January 2013-June 2015.

Characteristic's		**Frequencies**	**Percentage**
Age categories (in Days)	0-7	77	43.3
	8-30	21	11.8
	31-90	34	19.1
	>90	46	25.8
Sex	Male	107	60.1
	Female	71	39.9
WFH	< 70%	3	1.7
	70% - 79.9%	4	2.2
	80% - 89.9%	22	12.4
	>90%	148	83.1
Vaccination	fully vaccinated	18	10.1
	vaccinated for age	16	9
	unknown status	132	74.2
	Unvaccinated	12	6.7
HIV Status	Negative	96	53.9
	Positive	3	1.7
	Unknown	79	44.4
Prior antibiotic use	Yes	28	15.7
	No	150	84.3
Outcome of treatment	discharged improved	109	61.2
	not documented	15	8.4
	Improved with sequelae	18	10.1
	self-discharged	16	9
	Died	20	11.2

Table 2: Clinical data's with CSF analysis findings of children admitted to JUSH, pediatric ward with clinical diagnosis of bacterial meningitis from January 2013-June 2015.

Characteristic's		**CSF analysis of patient**			
		Culture done & bacteria isolated	Culture done but bacteria not isolated	CSF analyzed but Culture not done	No CSF sample
Age categories of patients (in Days)	0-7	1	41	5	30
	8-30	1	12	3	5
	31-90	0	17	2	14
	>90	7	31	5	4
Sex	Male	6	59	9	33
	Female	3	42	6	20
WFH or WFL	< 70%	1	1	0	1
	70% - 79.9%	1	1	0	2
	80% - 89.9%	0	18	2	2
	90%	7	81	13	48
Vaccination	fully vaccinated	2	12	2	2
	vaccinated for age	0	13	1	2
	unknown status	6	71	10	45
	Unvaccinated	1	5	2	4
HIV	Negative	5	60	8	23
	Positive	0	2	0	1
	Unknown	4	39	7	29
Prior antibiotic use	Yes	4	19	0	5
	No	5	82	15	48

4.2) Prevalence of culture positive meningitis

From 178 patients with clinically diagnosed bacterial meningitis , Culture was done in 110 of the cases, of which 9 had positive cerebrospinal fluid (CSF) cultures, showing an isolation rate of 8.1%.The highest number of bacteria was isolated from children age above 90 days.

Figure 4: showing Prevalence of culture positive bacterial meningitis in children admitted with clinically diagnosed bacterial meningitis to JUSH, pediatric ward from January 2013- June 2015.

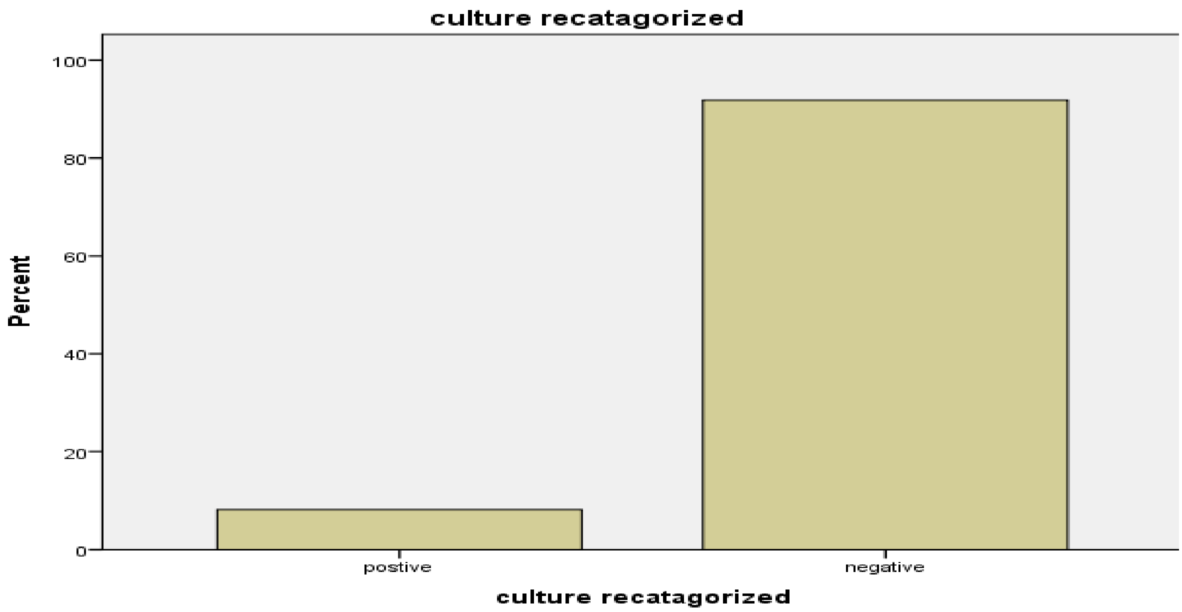

Table 3: Common bacterial isolates from CSF by sex and age distribution, among children clinically diagnosed bacterial meningitis in JUSH, pediatric ward from January 2013-June 2015.

Organism isolated	Number (%)	Male	Female	0-7 days	8-28 days	29-90 days	Above 90 days
S. pneumonia	2	1	1				✓
H. influenzae	2	2					✓
N. meningitides	2	1	1				✓
E. coli	1	1	-	✓			
Group B streptococcus	2		2	✓			

Table 4: Antibiotic susceptibility pattern of bacterial isolates from CSF, among children clinically diagnosed bacterial meningitis admitted to JUSH, Pediatric ward from January 2013-June 2015.

Organism isolated	**No of isolate**	**Age**	**Ceft No (%)**	**Amp No (%)**	**Gen No (%)**	**Pen No (%)**	**Sxt No (%)**	**TTC No (%)**	**CAF No (%)**	**Cip No (%)**
S. pneumonia	2	>90 days	S	R	R	ND	R	ND	R	S
H. influenzae	2	>90 days	I	R	S	ND	ND	ND	R	S
N. meningitides	1	>90 days	ND	ND	ND	ND	ND	ND	ND	ND
E. coli	1	0-7 Days	S	ND	ND	ND	ND	S	ND	S
Group B streptococcus	2	7-90 days	S	S	ND	ND	ND	S	S	S

Key:-Amp=Ampicillin, Pen=Penicillin, Gen=Gentamycin, Sxt=Co-trimoxazole, TTC=Tetracycline, CAF=Chloramphenicol, Cip=Ciprofloxacin, Ceft=Ceftriaxone S=sensitive, I=Intermediate, R=Resistant , ND= not done.

There were .. isolates of … bacteria name with high or intermediate Resistance to CAF … antibiotics.

4.3) Prevalence of chemical meningitis

From the total of 178 patients LP was done for 125 (70.2%) patients. and based on biochemical and cell count diagnosis parameters which included; protein, glucose, WBC count for age and Gram stain of CSF, 72 (40.4%) patients were diagnosed to have meningitis with either fulfill one or more derangement in chemicals analysis or cell count.

Overall, the diagnosis of acute bacterial meningitis was confirmed with CSF culture in 9( ) of cases from 110 culture or in 72 (40.4%) of the cases with either one or more derangement in glucose ,protein or cell count for the patients age.

In 53(29.8%) of the cases CSF analysis not done. Among the listed reason for CSF not done was presence of contraindications in 12 (6.7%), not documented in 36 (20.2%), unavailability of laboratory in 4(2.2%) of cases.

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4.4) Factors associated with prevalence of culture positive meningitis

The study assessed the prevalence of culture positive meningitis, with Sociodemographic and clinical data of patient using linear regression. Sociodemographic factors analyzed as risk factors were age & sex of the patient, with prevalence of culture positive meningitis. Clinical data of patient which were studied for chi-square to identify possible association were nutritional status, HIV status , duration of illness before admission, vaccination status, treatment outcome, duration of treatment and chemical meningitis diagnosis with culture result positivity.

Age of the patient and chemical diagnosis of bacterial meningitis were significantly associated with culture positivity with p- value 0.0335 & 0.0454 respectively. See table 5 below.

Table 5 : Chi-square of risk factors associated with culture positivity of CSF among clinically diagnosed bacterial meningitis pediatric children admitted to JUSH, Pediatric ward from January 2013-June 2015. **(N=110)**.

variable		Culture result					
		Positive	**Negative**	**X^2 value**	**p-value**	**significance**	
Age (continuous variable)		9	101	8.703	0.0335	P<0.05	
Age(in days) categorical	**Early onset (Birth -7)**	1	41				
	Late onset (8-28)	1	12				
	Late Late onset (29-90)	0	17				
	>91(above neonatal age)	7	31				
Sex	**Male**	6	57	0.233	0.63	p>0.05	
	Female	3	42				
WFH /WFL	**< 70%**	1	1	10.92	0.012	P<0.05	
	70% - 79.9%	1	1				
	80% - 89.9%	0	18				
	>90%	8	79				
Vaccination	**fully vaccinated**	2	14	2.433	0.49	p>0.05	
	vaccinated for age	0	13				
	unknown status	7	70				
	Unvaccinated	1	4				
HIV status	**Negative**	5	60	.271	0.873	P>0.05	
	Positive	0	2				
	Unknown	4	39				
Prior antibiotic use	**Yes**	4	19	3.28	0.069	P>0.05	
	No	5	82				
Outcome of the patient in the hospital	**discharged improved**	9	79	0.9803	0.9803	P>0.05	
	not documented	0	3				
	improved with sequelae	0	3				
	self-discharged	1	10				
	Died	0	4				
Duration of treatment	**Needs days category**			.659	0.003	-.009	.014
Duration of illness before admission	**Needs days category**			.729	-0.003	-.020	.014
Chemical diagnosis of meningitis	**yes**	8	55	4.004	0.0454	.p<0.05	
	no	1	46				

4.5) Treatment outcomes of study participants

Various treatment outcomes were recorded. including: - discharged improved109 (61.2%), self discharged 18 (8.99%), death16 (11.24%), improved with sequelae 20(10.11%) and clinical outcome not documented in 15(8.43%) of the case.

Of 178 patients diagnosed with acute bacterial meningitis, 16 (11.24%), died and -- of these deaths were among patients with age --- .The mean length of hospital stay was 11.58 days with SD of 7.065. The Minimum and maximum hospital stay was 1 day and 31 days respectively. The duration of illness prior to admission ranged from less than a day to 20 days with the mean duration of illness prior to admission was 2.63 days with SD of 2.846.

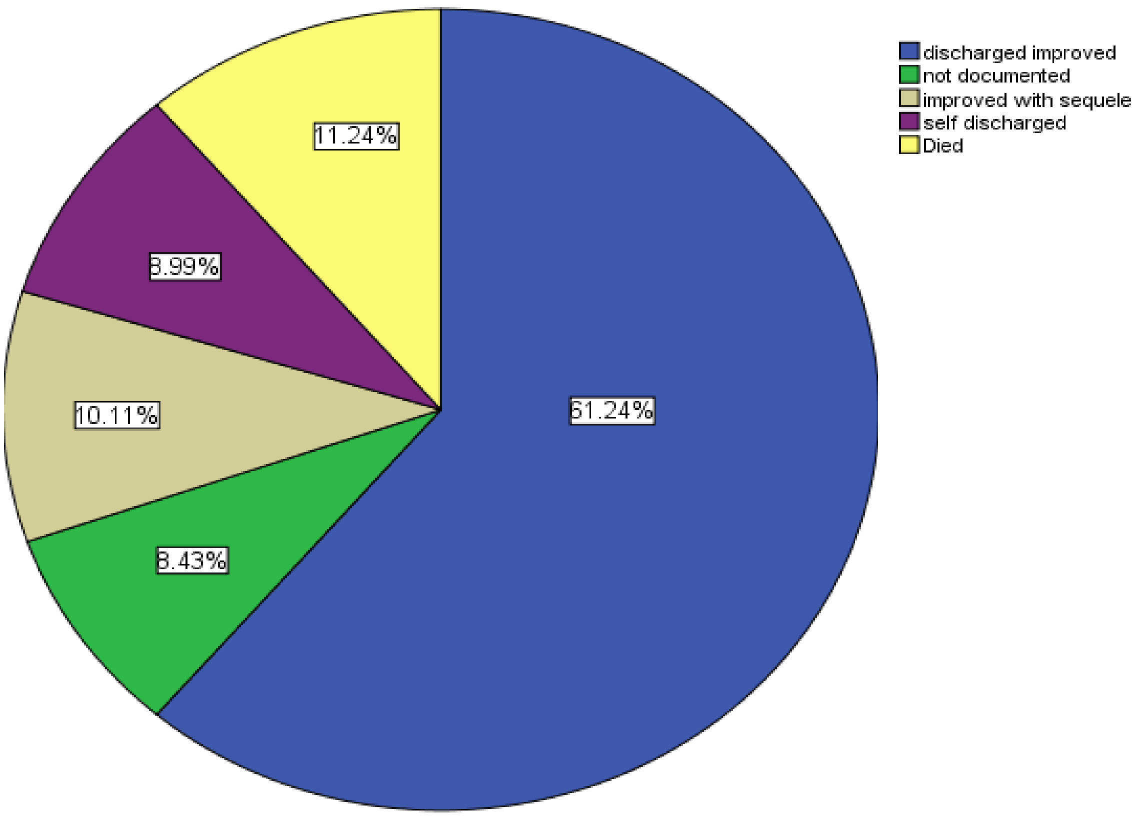

Figure 2: Treatment outcomes of children admitted to JUSH pediatric ward with clinical diagnosis of bacterial meningitis from January 2013-June 2015.

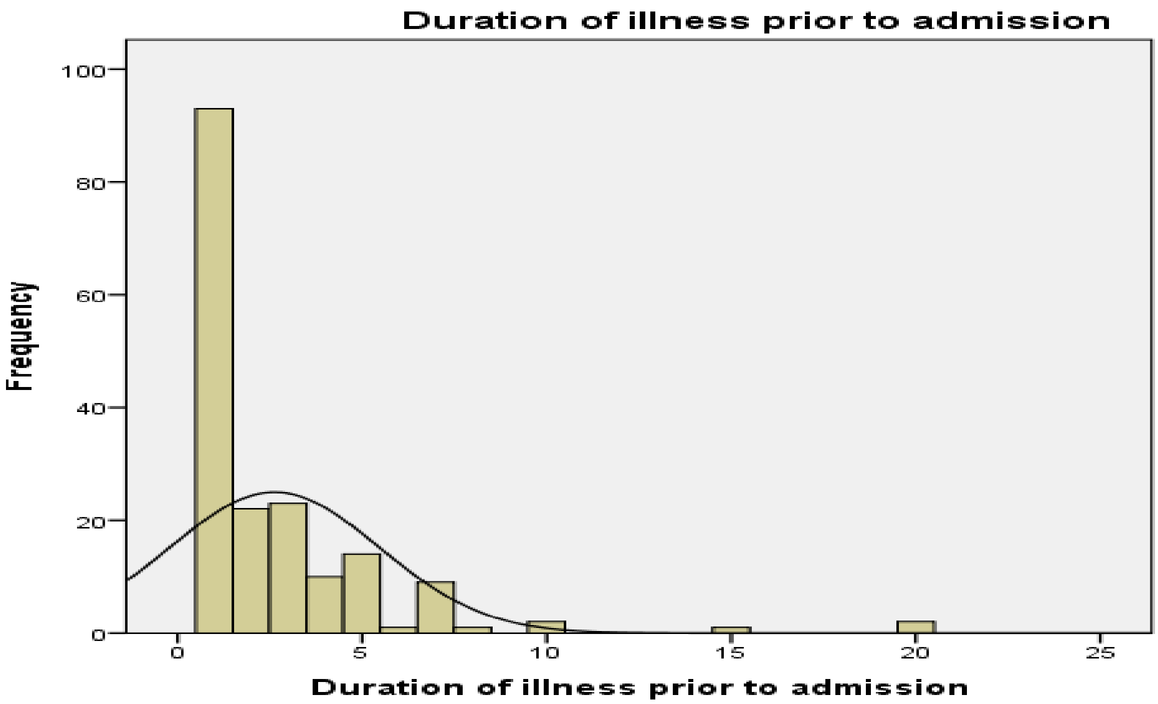

Figure 3: Showing the duration of illness prior to admission in children admitted to JUSH, pediatric ward with clinical diagnosis of bacterial meningitis from January 2013-June 2015.

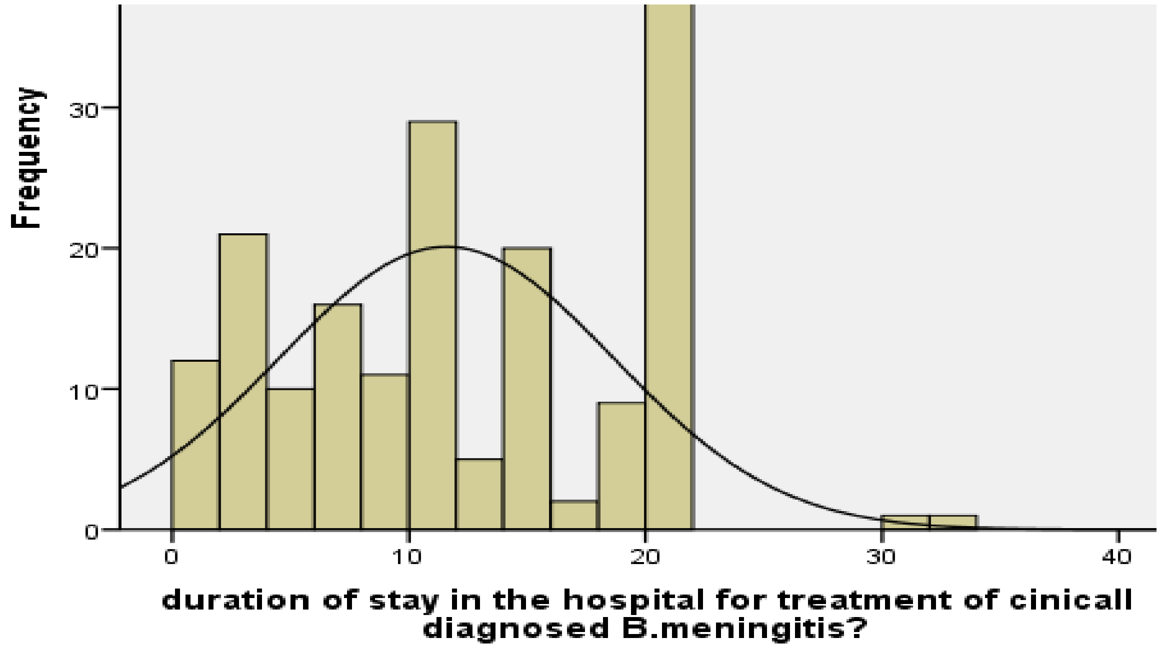

Figure: Showing the duration treatment in the hospital in children admitted to JUSH, pediatric ward with clinical diagnosis of bacterial meningitis from January 2013-June 2015.

CHAPTER FIVE: DISCUSSION

Antimicrobial resistance becomes increasingly a challenge for clinicians who care for infectious diseases worldwide. Bacterial meningitis is one of the most common reasons for inpatient admissions in our hospital which implies antimicrobial susceptibility testing is one of the priority health research topics. In this study the most commonly affected age group was found to be the infants less than 2 months and small children less than 5 years of age. Within the various age groups, a higher incidence in infants has frequently been reported in literature (8).A large scale retrospective study in Niger also 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) which is consistent to this study (35).

The spectrum of bacterial isolates from CSF in general is basically similar to reports from elsewhere. (6,36). *H. influenzae*, *N.meningitis* and *S. pneumonia* were the common pathogens of meningitis in patients above neonatal age. This trend in the different age groups for these common organisms has frequently been reported in literature. Similar results were observed in a study on the laboratory based surveillance of bacterial meningitis in Sudan during the year 2004-2005.

Laboratory investigations of CSF specimens in suspected cases of bacterial meningitis are extremely important for prompt diagnosis and management of patients. Several studies have reported Gram's staining as the most useful single test for identifying bacterial meningitis, as it revealed more positive cases than cultures (24). Some studies have reported a CSF Gram stain sensitivity of 60-90% and a high specificity of >97%, stressing its importance in the rapid and accurate diagnosis of the causative bacteria. In our study Gram's stain positivity was 9 (7.2%) which is low (26).The yield of bacteria on a Gram stain depends on several factors like the number of organism present, prior use of antibiotics, technique used for smear preparation (centrifuged deposit, direct smear etc.), staining techniques and the observer's skill and experience. The isolation rate of organisms from CSF samples was found to be 8.1% in the present study is low in agreement with a previous study conducted in Gondar where an isolation rate of 5.2% was reported (33, 37).Even though all children with clinical features of meningitis have underwent lumbar puncture to rule out bacterial meningitis, the bacterial isolation rate was found to be low. This may be due to the fastidious nature of the organisms or prior exposure to antibiotics or over clinical diagnosis of meningitis.

Several similar studies done in India report culture-negative cases of meningitis or a low CSF culture positivity, ranging from 6-50%.Culture results from Gondar University hospital reveal the prevalence of various organisms that cause bacterial meningitis. Almost 35% of the cultures were identified as *S. pneumonia,* followed by *N. meningitides* and *H. influenzae* which are isolated from 28% and 9% of the cases, respectively (33).

The predominance 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. pneumonia* being the most common organism (38) in agreement with this study. The other similar laboratory based study on the surveillance of bacterial meningitis in Egypt during 1998-2004 depicted a high *S. pneumonia* prevalence (42%) followed by Hib (20%) and *N. meningitides* (16%) (39).

Regarding the clinical outcomes of treatment, from 178cases of bacterial meningitis patients, death was recorded in 16 of cases , thus giving a CFR of (11.24%). Partial recovery with sequelae documented in 20(11.7%). 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 8(4.2%) that was observed in this study as compared to the estimated rates that have been mentioned in the literature (up to 50%). The same sequelae, but to a varying degree, have been reported in various studies. A systematic review of 37 studies from 21 African countries has documented sequelae rate as high as 37% (**5**). The rate was higher with Hib and *S. pneumonia* 44% and 38%, respectively. Therefore, the chances of sequelae may be highly variable depending upon the treatment facilities, age of the patient and also the organism causing infection as mentioned earlier. Early detection and timely treatment is therefore essential for the prevention of these long-lasting sequelae.

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. The other study done in Awassa Referral Hospital show a fatality rate (CFR) of 23.5%.The CFR reported in various studies in Ethiopia varies. In a study on 151 cases of bacterial meningitis in Gondar, 20 patients died, thus giving a CFR of 13.2% (40) similar with these study. The exact estimation of the fatality rates due to bacterial meningitis may be somewhat difficult as not all the cases present in the hospitals.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1. Conclusion

- The isolation rate of bacterial pathogens from CSF cultures was found to be low.
- Identification of the causative agent by Gram staining shows low rate.
- The frequency of multiple drug resistance was high among some bacterial isolates.
- The frequency of single as well as multiple drug resistance was found among isolates.
- Ciprofloxacin had the most effective antibacterial activity across all the bacterial isolates tested in the study.
- Age of the patient and biochemical diagnosis of bacterial meningitis were significantly associated with culture positivity.
- The CFRs in these study was low compared to the major centers report .
- An accurate laboratory confirmations of the etiology in acute bacterial meningitis is essential to provide optimal patient therapy, appropriate case contact management, and reasoned public health actions.
- It could not conclude that the negative parameters are not a rationale for exclusion of diagnosis of bacterial meningitis and it would be hard to justify not treating patients in the first hours of diagnosis with antibiotics or to suggest a nonbacterial etiology. Further studies are needed to reach this

6.1. Limitations of the study:

- All isolates not underwent susceptibility test which affects the study's ability to determine antibiotic susceptibility pattern of the isolate.
- In some of the identified isolates, some of the commonly used antibiotics like, crystalline penicillin, Vancomycin were not tested for susceptibility.
- In majority of the cases, all CSF parameters were not analyzed completely which affect the diagnosis of meningitis.
- In some of the cases laboratory result paper(CSF culture findings) kept in the laboratory log book, the patients card number were not documented which made difficult to retrieve the patients clinical record .

6.2. Recommendations

- Treatment of suspected bacterial infection should always be guided by culture and susceptibility whenever possible.
- An accurate laboratory confirmations of the etiology in acute bacterial meningitis is essential to provide optimal patient therapy, appropriate case contact management, and reasoned public health actions.
- Since antimicrobial resistance is increasing, large scale antimicrobial susceptibility assessment is recommended .
- Ways to to analyze all CSF parameters.
- 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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Annex-II: Questionnaire

Data collection format

Jimma university college of public Health and Medical Sciences School of Graduate Studies, Department of pediatrics and child health. Data collection format prepared to assess etiology of bacterial meningitis among children admitted to pediatric ward in JUSH.

Patient information

I) Socio-demographic characteristics

1) Address: Region---------------, Woreda---------------, Zone----------
2) Age:---------------(hrs/dys/wks/mnths/yrs)
3) Sex: 1) male 2) female

II) Anthropometric Indices and Nutritional Status

1) Weight(kg)---------------
2) Height(cm)----------------
3) MUAC(cm): 1) < 11 2) 10.9-12.493) 12.5-13.494) > 13.5
4) HC(cm)---------------------
5) WFA: 1) normal 2) underweight 3) Marasmic
   4) Kwashiorkor 5) Marasmic-kwashiorkor
6) HFA: 1) Normal 2) Stunted
7) WFH: 1) < 70% 2) 70%-79.9% 3) 80-89.9% 4) > 90%

III) Clinical Background

1) Vaccination status: 1) completed 2) vaccinated for the age
   3) Unknown 4) unvaccinated
2) History of contact with meningitis: 1) yes 2) no
3) Duration of illness prior to admissions…………..(dys/wks/months)
4) Previous history of admission: 1) yes 2) no
5) HIV status: 1) Negative 2) Positive 3) unknown
6) Antibiotic use prior to admission : 1) yes 2) no
7) Previous history of similar illness: 1) yes 2) no
8) Obstetric risk for infection (neonate): 1) yes 2) no

Presenting clinical symptoms

1) Vomiting: 1) Yes 2) No
2) Fever : 1) Yes 2) No
3) Poor appetite: 1)Yes 2) No
4) Loss of consciousness: 1) Yes 2) No
5) Failure to suck breast milk: 1)Yes 2) No
6) Irritability: 1) Yes 2) No
7) Abnormal body movement: 1) Yes 2) No
8) Headache: 1) Yes 2) No
9) Photophobia: 1) Yes 2) No
10) Excessive cry: 1) yes 2) no
11) Neck pain: 1) yes 2) no
12) Others----------------------------

IV) Presenting clinical signs

1) Documented fever: 1) yes 2) no
2) Documented hypothermia: 1) yes 2) no
3) Fast breathing: 1) yes 2) no
4) Any sign of respiratory distress: 1) yes 2) no
5) Neonatal reflex: 1) intact 2) depressed or incomplete
6) Petechiae rash: 1) yes 2) no
7) Neck stiffness: 1) yes 2) no
8) Brudziski sign: 1) yes 2) no
9) Kernig's sign: 1) yes 2) no
10) Fontanelles:1) normal 2) bulged 3) sunken
11) Mental status: 1) alert 2) lethargy 3) stupor/obtunded4) coma
12) Others --------------------

V) Clinical condition summary

1) Clinical Diagnosis:-------------------------------------

 ----
2) Outcome of the patient: 1) discharged improved 2) improved with sequelae 4) self-discharged 5) not documented 3) died
3) Duration of stay in the hospital: -----------------------days

VI) Laboratory and bacteriology profiles

1) Was CSF analysis done? 1) yes 2) no
2) If no to Q1, why? 1) Presence of contraindications 2)Can't afford for CSF analysis 3)Family interest 4)Unavailability of laboratory 5)Not documented 6) Other------------
3) If yes to Q2:

   3.1 protein: -----------

   3.2 glucose: -------------

   3.3 gram stain: -----------------

   3.4 total WBC count: ------------

   3.5 WBC differential count------------------
4) List other laboratory results:--

   ----
5) Was CSF culture done? 1) yes 2) no
6) If yes to Q5, was there bacteria isolate(s)? 1) yes 2) no
7) If yes to Q6, what was the isolate? -----------------------------
8) Write the antibiotics for which the isolate is susceptible to:

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9) Write the antibiotics for which the isolate is resistant:
