# BACTERIAL MENINGITIS IN PREGNANCY, NEONATE AND ADOLESCENCE: A REPORT OF FIVE CASES

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**Abstract**
**Background:** Bacterial meningitis is an infection of the meninges, the thin covering of the brain and spinal cord.
**Objective:** This case study identifies the aetiology and the antimicrobial susceptibility of bacterial agents in suspected samples of acute meningitis.
**Methods:** The bacterial agents were detected by culture, Bactec 9050, Directgen and Gram Techniques from five patients of Makoda and Tudun Wada Primary Health care (PHC) facilities as well as Hasiya Bayero Paediatric Hospital (HBPH) that were presented to Microbiology Laboratory unit of Aminu Kano Teaching Hospital (AKTH) – a tertiary hospital located within the meningitis belt of Nigeria. Among the five cases, three were pregnant women all in their second trimesters marked patients 1, 2 and 3 according to the increasing pattern of their ages, an adolescent marked patient 4 and a neonate marked patient 5.
**Results:** The CSF sample of the respective patients was assayed for pus cell, protein, and RBC. The Directgen detected *Haemophillus influenzae* from patients 1 and same organism was isolated from patient 2. *Streptococcus pneumoniae* isolated from patient 3 and *Neisseria meningitidis* from patients 4 and 5 respectively. Antimicrobial susceptibility testing reveals sensitivity to penicillin and gentamicin by *H. influenzae*, *S. pneumoniae* and *N. meningitidis*. *N. Meningitidis* and *S. pneumoniae* were sensitive to ceftriazone, ciprofloxacin and ofloxacin. All the three organisms displayed intermediate sensitivity to chloramphenicol, erythromycin and tetracycline according to Clinical and Laboratory Standards Institute (CLSI) breakpoints.
**Conclusion:** This study demonstrates the relevance of these agents as potential pathogens in the predisposed patients. The antimicrobial sensitivity depicted high sensitivity to the various classes of antibiotics.
**Keywords:** Meninges, Trimesters, *Streptococcus pneumoniae,* Antimicrobial susceptibility, Makoda

## Introduction

Community – acquired bacterial meningitis is a serious and life threatening disease where *S. pneumoniae* and *N. meningitidis* are the leading causes (Durand *et al.,* 1993) with annual incidence of 4 – 6 cases per 100,000 adults with approximately 135,000 deaths worldwide each year (Van de Beek *et al.,* 2006). Although, *H. influenzae*, *S. pneumoniae* and *N. meningitidis*, are the most common pathogens and continued to account for the majority of cases, *Listeria monocytogenes* and *Streptococcus agalactiae* were also incriminated (Schlech *et al.,* 1981). Adults with bacterial meningitis typically present with symptoms of meningeal irritation and brain parenchyma inflammation, whereas only a minority presents with classical clinical triad of fever, altered mental status and neck stiffness (Van de Beek *et al.,* 2006).

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Bacterial meningitis in neonates often presents with non–specific signs and symptoms. Common causative microorganisms of neonatal meningitis during the first week of life are *S. agalactiae, Escherichia coli* and *L. monocytogenes.* Late neonatal onset occurs between first week and three months of age by wide varieties of species (Malbon *et al.*, 2006).

Bacterial meningitis during pregnancy is an uncommon disease, with substantial mortality for both mother and child. During pregnancy, immunosuppressive cytokines are produced by the placenta and foetus to avoid immunological attack by the mother (Adriani *et al.*, 2011). An exception is infection by *L. monocytogenes* which seems to have a predilection for pregnant women and may result in pregnancy loss (Silver, 1998).

**Cases Report and Methodology**

In May, 2015, five samples (one blood and four CSF) were received at Microbiology unit of Aminu Kano Teaching Hospital Kano, Nigeria, from Primary Health care of Tudun Wada and Makoda LGAs as well as Hasiya Bayero Paediatric Hospital, for the laboratory diagnosis of the causative agents of meningitis. Of these patients, 3 were pregnant women, a neonate and an adolescent. All their demographic data consisting of gender, age, and community setting (whether urban or rural) were documented. The immunization history of all the patients revealed that none of them had taken any vaccine regimen against meningitis. The age range of the pregnant women was between 17 – 22 years, while males, the neonate and the adolescent were 7 weeks and 15 years respectively.

**Macroscopy**

The CSF samples were visually examined for the presence of turbidity, with/without clots and blood as markers of meningeal abnormalities

**Direct Demonstration**

The csf samples were examined microscopically for pus cells, rbc and also analysed for protein

**Gram Stain**

Gram stain was carried out using the technique described by Cheesbrough (2004).

**BACTEC$^{TM}$ 9050 Blood Culture System**

The samples received were subjected to the Bactec machine for the rapid detection of the suspected microorganisms. Positive samples were flagged by the machine. In the CSF samples, fastidious organism supplement (FOS) was added to the Bactec bottles to enhance detection of the agents.

**DIRECTGEN$^{TM}$ Meningitis Combo Test**

The CSF samples and serum obtained from the blood sample were further subjected to Directigen Test which is a latex agglutination test for the direct qualitative detection of antigens to *H. influenzae* type b, *S. pneumoniae, N. Meningitidis* group. Visible agglutination occurs when specific antigens in the sample react with antibody – coated latex beads (Fasola and Ferrieri, 1992). The *S. pneumoniae* was tested sensitive with optochin disk and confirmed with bile solubility test.

**Culture and Identification**

The samples were cultured on both Blood and Chocolate Agar to enhance detection and identification. Both plates were incubated at 35 – 37°C for 48 hours in a $CO_2$ enriched atmosphere according to Bohr *et al.* (1983). The neonate sample was also cultured on MacConkey agar and incubated aerobically. In patient number 3, following detection of Gram positive diplococci, optochin disc was added to the blood agar to assist in the identification of *S. Pneumoniae;* since it was sensitive, confirmatory test (bile salt solubility) was ensued.

**Antimicrobial Susceptibility Testing**

The antibiotic sensitivity testing conducted was according to Kirby – Bauer technique (Forbes *et al.*, 2007). Isolates were tested and interpreted using CSLI guidelines (CLSI, 2007). *H. Influenzae* type b isolated from patient number 2 was susceptible to penicillin, ampicillin, gentamicin and chloramphenicol with good diameter of zone of inhibition (Table 2).

*S. pneumoniae* isolated from the sample number 3 was found to be sensitive to ceftriazone, penicillin, ciprofloxacin, and erythromycin while the resistance was recorded in ampicillin, cefuroxime, cotrimoxazole, and oxacillin. Antibiotic susceptibility tested against *N. meningitidis* in patient 4, depicted high sensitivity in the following order to ciprofloxacin, and chloramphenicol. The less sensitivity was shown in ceftriazone, cotrimoxazole and gentamicin. The sensitivity testing against *N. Meningitidis* in patient number 5 also revealed high sensitivity to ofloxacin, ceftriazone and penicillin. Intermediate sensitivity was shown in chloramphenicol and tetracycline. No resistance against any antibiotic tested was observed in this patient (Table 2).

**Results**

Although the data on the prevalence of bacterial meningitis in Nigeria is very scarce, but its presence has been established in different states of the country with varied rates ranging from low to the alarming status. Kano State of Nigeria, located within meningitis belt in sub – Saharan Africa, where seasonal meningococcal epidemics occur during dry season i.e. December–June each year. The prevalence in one of the study conducted in Kano reveals 3.3% (n = 50/1500) (Nwadioha *et al.,* 2010). The demographic profile of the patients in this case study was given in table 1.

The WBC (pus cells) counts of the samples examined, revealed that patients (1 – 3) have higher values, although not so high to cause turbidity formation alone, but coupled with raised protein levels, all the samples appeared turbid. Also the count in patient number 4 was numerous (Table 1). In all the four CSF samples examined, the protein levels of the samples were far beyond normal (normal range: 0.15 – 0.40 g/L), particularly in patient 4 (adolescent) were protein level was 2.8 g/L leading to high turbidity with clots possibly due to the increase in the fibrinogen level. The bacteria detected was *H. influenzae* from patients 1 and it was also isolated from patient 2, *S. pneumoniae* from patients 3 and *N. meningitidis* from patients 4 and 5 respectively (Table 1).

**Table 1:** Clinical characteristics and laboratory findings for five patients with bacterial meningitis

| **Characteristics** | **Patient 1** | **Patient 2** | **Patient 3** | **Patient 4** | **Patient 5** |
|---|---|---|---|---|---|
| Age (Year) | 17 | 18 | 22 | 15 | 7 weeks |
| Gender | F | F | F | M | M |
| Gestational Age(weeks) | 28 | 33 | 18 | N/A | N/A |
| Predisposing factor | Pregnancy | Pregnancy | Pregnancy | Otitis media | Neonate (low immunity) |
| Symptoms on admission | | | | | |
| Neck stiffness | Yes | Yes | Yes | Yes | Yes |
| Fever | Yes | Yes | Yes | Yes | Yes |
| Temp (ºC) | 38.5 | 38.6 | 38.2 | 38.9 | 38.3 |
| CSF/Blood Analysis | | | | | |
| Appearance | Turbid | Slightly Turbid | Turbid | Turbid with clots | Blood |
| Leucocytes× $10^6$/L | 11 – 15 | 10 – 13 | 12 – 16 | Numerous | N/A |
| Protein (g/L) | 1.8 | 1.2 | 1.5 | 2.8 | N/A |
| RBC (mMol/L) | 2 – 3 | 3 – 5 | 5 – 8 | 3 – 5 | N/A |
| Gram stain | G – ve coccobacilli | G – ve coccobacilli | G + ve diplococci | Intracellular G – ve diplococcic | G – vecocci and diplococci |
| Directigen | *H. influenzae* type b | *H. influenzae* type b | *S. pneumoniae* | *N. meningitidis* (W 135) | *N. meningitidis* (W 135) |
| Bactec 9050 | Negative | Positive | Positive | Positive | Positive |
| Culture | No growth | *H. influenzae* type b | *S. pneumoniae* | *N. meningitidis* (W 135) | *N. meningitidis* (W 135) |
| Initial Antibiotic therapy | Gentamicin | No | No | No | No |

**Table 2:** Antibiotic Sensitivity Pattern of the Bacterial Isolates

| BACTERIAL ISOLATES | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Patient 2** ***H. influenzae* type b** | | | **Patient 3** ***S. pneumoniae*** | | | **Patient 4** ***N. meningitidis*** | | | **Patient 5** ***N. meningitidis*** | | |
| **An** | **Sensitivity Pattern (mm)** | **Res** | **An** | **Sensitivity Pattern (mm)** | **Res** | **An** | **Sensitivity Pattern (mm)** | **Res** | **An** | **Sensitivity Pattern (mm)** | **Res** |
| P | 26 | COT | E | 23 | AMP | TE | 36 | P | OFX | 36 | Nil |
| AMP | 36 | ---- | COX | 26 | ---- | COT | 26 | E | E | 27 | Nil |
| E | 24 | ---- | P | 26 | TE | CN | 24 | AMC | OX | 20 | Nil |
| CN | 26 | ---- | CIP | 28 | AMC | CHL | 28 | ---- | TE | 27 | Nil |
| CHL | 28 | ---- | CN | 20 | OX | CRO | 29 | ---- | CHL | 29 | Nil |
| ---- | ---- | ---- | CRO | 32 | CEP | CIP | 40 | ---- | P | 33 | Nil |
| ---- | ---- | ---- | ---- | ---- | CXM | ---- | ---- | ---- | CRO | 36 | Nil |
| ---- | ---- | ---- | ---- | ---- | COT | ---- | ---- | ---- | ---- | ---- | ---- |

**Key:** *P= Penicillin, AMP= Ampicillin, E= Erythromycin, CN= Gentamicin, CHL= Chloramphenicol, COT= Cotrimoxazole, CIP= Ciprofloxacin, AMC= Amoxicillin, TE= Tetracycline, OX= Oxacillin, CEP= Cephalaxin, CXM= Cefuroxim, OFX= Ofloxacin, CRO= Ceftriazone. and COX= Cloxacillin. The patterns of zone of inhibitions indicated above were interpreted using CSLI guidelines, An = Antibiotic, Res = Resistance*

*Note: Erythromycin, Tetracycline and Cotrimoxazole although reported here, they are not to be prescribed clinically. Ofloxacin also contraindicated in neonates and children less than 12 years.*

## Discussion

In this study, four samples yielded positive and a sample of the patient number one yielded negative for Directgen, culture and Bactec, both culture and Directgen indicated *N. meningitidis* (W 135) as the incriminating agent. This agrees with the findings of Kwang, (2010) which recorded predominance of *H. influenzae*, *N. meningitidis*, and *S. pneumoniae* in neonates and young infants. Lack of availability of the meningococcal vaccine in the remote areas of the risk populations possibly fueled the spread of the infection. Although the culture from patient number 1 sample did not yield any growth and hence no sensitivity test was conducted, but *H. Influenzae* type b was detected using Directgen. This may be due to the pre – presentation antibiotic used prior to diagnosis as indicated in her form (Table 1).

The adolescent patient with purulent otitis media was found to harbour *N. meningitidis* (W 135). This is in conformity with the findings of Onipede *et al.* (2002) in which the studies also incriminated *N. meningitidis, H. influenzae*, and *S. Pneumoniae* in older children and possibly with otitis media fueled by overcrowding and absence of vaccination Onipede *et al.* (2002).

Bacterial meningitis during pregnancy is an uncommon disease with substantial mortality for both mother and child (Matthijs *et al.*, 2010). In this study, three cases of community acquired bacterial meningitis were reported and diagnosed. The results indicated *H. Influenzae* type b in the two patients, while *S. pneumoniae* from patients 3 and *N. meningitidis* from patients 4 and 5 respectively. The previous study suggested pregnancy to be a predisposing condition for pneumococcal meningitis (Matthijs *et al.*, 2010).

*H. influenzae* type b isolated from patient number 2 was susceptible to penicillin, ampicillin, erythromycin, gentamicin and chloramphenicol with good diameter of zone of inhibition (Table 2). *S. pneumoniae* isolated from the sample number 3 was found to be sensitive to ceftriazone, penicillin, ciprofloxacin, and erythromycin. This corroborates with the findings of Nwadioha *et al.* (2010) which put ceftriazone, ciprofloxacin and cefotaxime as effective anti – bacterial agents against meningitis causative organisms while the resistance was recorded in ampicillin, tetracycline, cefuroxime, cotrimoxazole, and oxacillin. The problem of antibiotic resistance by some of the meningeal isolates to ampicillin, penicillin, and chloramphenicol was possibly due to misuse of the antibiotics as according to the findings of Akuhwa *et al.* (2010). Antibiotic susceptibility tested against *N. meningitidis* in patient 4, depicted high sensitivity in the following order to ciprofloxacin, and chloramphenicol. The less sensitivity was shown in ceftriazone, cotrimoxazole and gentamicin. The sensitivity testing against *N. Meningitidis* in patient number 5 also revealed high sensitivity to ofloxacin, ceftriazone and penicillin. Intermediate sensitivity was shown in chloramphenicol. No resistance against any antibiotic tested was observed in this patient (Table 2).

## Limitations

One of the drawbacks of this study is the *ab initio* prescription of the antibiotics to the patient number one prior to the submission of her sample for analysis which led to CSF culture negative result. Another limitation of this study, involves the loss of fastidious bacterial agents of interest due to the delay in the submission of the samples as well as non-availability of the suitable transport media from the PHC facilities to the processing hospital in the metropolis.

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