

Clinical Predictors, Antibioqram, and the Relationship Between Abnormal Leucocytes and Positive Cerebrospinal Bacterial Isolates in Children seen at a Tertiary Facility in Nigeria.

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Abstract

Background:

Acute bacterial meningitis (ABM) remains a significant public health concern in resource-limited settings like Nigeria. It is a frequent neurologic emergency among children and often presents at under-resourced medical centers. This study aimed to identify the clinical predictors of ABM, evaluate the antibiogram of bacterial isolates, and assess the relationship, if any, between subjects' white blood cell counts and positive cerebrospinal fluid (CSF) cultures in children suspected of ABM.

Methods:

This prospective study involved 100 post-neonatal children presenting with suspected ABM at the Children's Emergency Room of Federal Medical Centre, Umuahia, from January 2016 to December 2020. Data were collected through a structured proforma, capturing clinical features, CSF analysis, and hematologic findings. The data were analyzed using SPSS version 23, employing descriptive statistics, regression analysis, Wald testing, and ROC analysis.

Results:

Fever, altered consciousness, neck stiffness, convulsion, vomiting, high-pitched cry and bulging anterior fontanelle, were significant predictors of ABM. Antibiotic susceptibility testing revealed that aminoglycosides, fluoroquinolones, macrolides, amoxicillin, cephalosporins, and carbapenems were effective against common bacterial isolates in 68%, 37%, 35%, 37%, and 23% of cases, respectively. No significant relationship was observed between abnormal leucocyte counts and positive bacterial CSF cultures.

Conclusion

Fever, altered consciousness, neck stiffness, convulsion, vomiting, high-pitched cry and bulging fontanelle were reliable clinical indicators of ABM. Fluoroquinolones and aminoglycosides demonstrated the highest sensitivity in the antibiogram. The weak association between abnormal leucocyte counts and positive CSF cultures, highlights the importance of early empirical treatment, particularly when lumbar puncture is delayed.

Introduction

Acute bacterial meningitis (ABM) continues to pose a significant health burden, particularly in resource-limited regions such as Nigeria, where limited access to healthcare, poor sanitation, and low vaccination

rates contribute to its high burden. If not diagnosed and treated promptly, ABM can result in severe neurological complications and permanent cognitive impairments.

The diagnosis of ABM typically relies on clinical suspicion, cerebrospinal fluid (CSF) analysis, and microbiological confirmation. However, in many settings, particularly in developing countries, parental refusal of lumbar punctures (LP) often delays diagnosis. In such cases, alternative diagnostic predictors—such as clinical features and abnormal white blood cell (WBC) counts—become essential for guiding early intervention.

In 2013, Kulik et al. emphasized the importance of using validated clinical prediction rules (CPR) for diagnosing bacterial meningitis, following a systematic review of 11 studies involving 6,675 children. The authors highlighted culture isolates as the gold standard for confirming bacterial meningitis, stressing the need for consistent hospitalization, appropriate parenteral treatments, and prospective validation of clinical features to ensure reproducibility across different healthcare settings.

Weber et al. suggested a more practical approach, advocating for the simplification of clinical features to help primary healthcare workers identify children who require urgent referral. They identified lethargy, neck stiffness, refusal of feeds, and bulging fontanelle as important clinical signs that should prompt immediate referral to tertiary care centers.

A study by Walsh-Kelly et al. compared the clinical features of bacterial and aseptic meningitis, noting that nuchal rigidity was present in only 27% of children aged 0 to 6 months with bacterial meningitis, compared to 95% in children over 19 months of age. Furthermore, among children aged 12 months and older, 72% of those with bacterial meningitis exhibited nuchal rigidity, compared to just 17% with aseptic meningitis. Meningeal signs were observed in 95% of children older than 19 months, compared to only 3% in those under 6 months. This indicates that meningeal signs are highly predictive of bacterial meningitis in children older than 18 months and should guide clinicians in managing acutely ill children in emergency settings.

However, for younger children, the absence of well-defined meningeal signs due to ongoing brain maturation necessitates a higher index of suspicion. In such cases, additional clinical predictors are crucial for timely diagnosis, as these children may not display typical signs of meningitis.

This study aims to identify the clinical predictors of ABM in post-neonatal children, analyze the antibiogram of common bacterial isolates, and assess the relationship between leucocyte counts and positive CSF bacterial cultures. The findings will offer valuable insights for clinicians working in resource-constrained settings, especially when CSF analysis is delayed or unavailable.

Methodology

Study Design and Setting

This was a prospective survey conducted on post-neonatal children presenting with clinical suspicion of acute bacterial meningitis (ABM) at the Emergency Room of the Federal Medical Centre (FMC) Umuahia, between January 2016 and December 2020.

Umuahia is the capital of Abia State, a semi-urban city inhabited primarily by civil servants, business owners, traders, and students. The Federal Medical Centre serves as the major tertiary healthcare facility for the city and surrounding regions, including neighboring cities and states across Southeastern Nigeria. The facility provides healthcare services to a diverse population, addressing both routine and complex medical cases.

A total of 100 post-neonatal children participated in this study. The parents of each child were thoroughly informed about the study, including the potential risks and benefits, and their consent was obtained. Data were collected using a structured proforma designed in line with the study objectives. For each participant, a complete blood count, and lumbar puncture were performed, and the cerebrospinal fluid (CSF) samples obtained were sent for microbiological analysis to confirm the presence of acute bacterial meningitis.

Inclusion Criteria:

Children aged 2 months to 17 years with symptoms such as fever, reduced appetite, lethargy, convulsion, or impaired consciousness, and whose parents provided informed consent for participation, were included.

Exclusion Criteria:

Neonates, children younger than 2 months, and those whose parents refused lumbar puncture were excluded.

Recruitment and Data Collection

Participants were recruited using a consecutive non-probability sampling technique. The sample size was determined using Taro Yamane's formula for sample size calculation:

$$n = N / 1 + N(e)^2$$

Where:

- **n** = required sample size
- **N** = population size
- **e** = margin of error
- **1** = constant

Given that the estimated population of post-neonatal children seen in the emergency room from 2016 to 2020 was **1,000**, and using a **margin of error (e) of 0.05** (equivalent to a **95% confidence interval**), the calculated sample size was:

$$n = 1000/1 + 1000(0.05)^2 = 286$$

However, due to recruitment challenges, a range of 10–50% of the calculated sample size was considered. As a result, 80 participants were targeted for this study. The sample size was further approximated to 100 post-neonatal children, who were included in the final study population.

Data Collection:

For each participant, data on sociodemographic characteristics, vaccination history, clinical features, and laboratory results—including complete blood count (CBC), BACTEC blood culture, cerebrospinal fluid (CSF) cell count, protein, glucose, Gram stain, and culture and sensitivity tests—were meticulously recorded using a structured proforma designed for the study.

A thorough physical examination was conducted for all subjects, and pre-procedural counseling was provided to caregivers. Written informed consent was obtained before CSF samples were collected under strict aseptic conditions.

Participants were initially treated with empirical antibiotics, pending the results of culture and sensitivity tests to guide more specific antimicrobial therapy.

Ethical Considerations:

Ethical approval was obtained from the Health Research Ethics Committee (HREC) of the Federal Medical Centre, Umuahia, Abia State, Nigeria..

Informed consent was secured from all participants' parents or guardians before study commencement.\

The study followed the Helsinki declaration guidelines that ensure the protection of vulnerable participants in any research. There was beneficence (Timely treatment of life threatening CNS infections), Non-maleficence (Ensuring that there was no harm to participants) and respect for autonomy by proxy for participants' parents.

Data Analysis

Data were analyzed using SPSS version 23. Descriptive statistics were used to estimate the frequency of abnormal WBC counts, and antibiogram susceptibility patterns. Bivariate logistic regression and ROC analysis were performed to identify clinical predictors of ABM. The level of agreement between abnormal leucocyte counts and positive CSF cultures was evaluated using Kappa statistics.

Results

Among the 100 children enrolled, 51 were male, and 49 were female. Bacterial cultures yielded 75 positive isolates, with 12 cases showing multiple bacterial growth.

Table 1, shows the relative frequencies of participants' clinical features.

There was no significant relationship (Wald: 0.11) between abnormal WBC counts and positive CSF cultures (Table 2).

Table 3 showed the antibiotic susceptibility test findings with fluoroquinolones, aminoglycosides, and cephalosporin having the highest sensitivity against the bacterial isolates.

Additionally, a moderate agreeableness (Kappa value: 0.66) was seen between abnormal leucocytes and positive cultures (Table 4).

Table 1
Relative Frequencies of Clinical features of children with suspected meningitis

Clinical features	Frequency (n)	Percentage (%)
Fever	94	89.5
Convulsion	82	78.1
Vomiting	39	37.1
Altered Consciousness	26	24.8
Irritability	16	15.2
Neck Stiffness	14	13.3
High Pitched Cry	9	8.6
Refusal of feeds	7	6.7
Lethargy	7	6.7
Meningeal Signs	7	5.7
Headache	6	1.9
Bulging AF	5	4.8\
Back Pain	2	1.9

AF =Anterior Fontanel

Wald Test in Table 2, showed clinical features that were significantly associated with ABM in study participants. Fever, altered consciousness, neck stiffness, convulsion, vomiting, high pitched cry and

bulging anterior fontanelle were strongly predictive of ABM.

Table 2
Predictors of ABM in Post Neonatal Children.

Clinical Features	B	S.E.	Wald	dif	Signi
WBC	.018	.054	.110	1	.741
Fever	-16.751	13523.086	.000	1	.999
Age	1.059	.649	2.659	1	.103
Low GCS	– .189	.106	3.157	1	.076
Neck stiffness	19.789	15934.445	.000	1	.999
Convulsion	-19.086	9162.478	.000	1	.998
Headache	18.611	15938.222	.000	1	.999
Temperature Instability	.901	1.664	.293	1	.588
Vomiting	-1.755	.798	4.839	1	.028
Irritability	– .162	1.136	.020	1	.887
High pitched cry	21.895	10865.769	.000	1	.998
Bulging and Tense AF	19.586	16107.551	.000	1	.999
Prostration	18.340	61872.937	.000	1	1.000
Hypotension	-18.958	44196.519	.000	1	1.000
Constant	35.946	16334.774	.000	1	.998

Figure a (ROC), demonstrates the relationship between the ideal (positive csf cultures) meningitis confirmation and observed clinical syndromes in subjects.

The 3rd generation cephalosporins like ceftriaxone, fluoroquinolones (Ciprofloxacin), macrolides, aminoglycosides (Genticin), penicillins (Amoxiclav) and carbapenems (Imipenem), were highly susceptible to isolated pathogens. Table 3, shows other susceptible antimicrobial patterns.

Table 3
Antibiogram rates of common isolates

Antibiogram of common isolates	Susceptibility frequency
Gentamycin	59 (79%)
Ciprofloxacin	51(68%)
Ceftriaxone	28(37%)
Erythromycin	28(37%)
Imipenem	26(35%)
Amoxiclav	17(23%)
Ceftriaxone/Sulbactam	12(16%)
Chloramphenicol	11(15%)
Ampicillin	9(12%)
Cefuroxime/Clavulanic	8(11%)

The level of agreeableness between abnormal leucocytes and positive csf cultures is shown in Table 4.

Table 4
Level of agreement between WBCC and Positive CSF isolates.

Measure of agreement (kappa)	Value	Asymp. Std. Error ^a	Approx T ^b	Approx signif
	0.660	0.83	6.610	.0000
No of valid cases	100			

1. a. Assumes the Null hypothesis.
2. b. Doesn't assume the Null hypothesis.

Discussion

The predictors of acute bacterial meningitis (ABM) identified in this study partially align with those reported by Weyori et al. in Northern Ghana (2023), which highlighted neck stiffness, convulsions, altered consciousness, and abdominal pain as key predictors. However, this study found additional features, including fever, vomiting, high-pitched cry and bulging anterior fontanelle, to have higher odds of association with ABM.

The differences may be attributed to the varying age groups studied. While the Ghana study included patients of all ages, this study focused exclusively on post-neonatal children, most of whom were young. Specific signs of meningeal irritation, such as neck stiffness, are less pronounced in younger children, potentially explaining the differences in predictive characteristics.

The present study utilized a prospective design, ensuring comprehensive and proactive evaluation of clinical features during admission, in contrast to retrospective approaches, which are often limited by incomplete data. This thorough assessment likely contributed to the identification of more positive culture isolates.

Children with acute central nervous system infections face significant risks of neurological sequelae if untreated or improperly managed. Thus, healthcare personnel in resource-limited settings must initiate empirical antibiotic therapy while awaiting confirmatory cerebrospinal fluid (CSF) results.

The choice of antibiotics for young children has traditionally favored cephalosporins and aminoglycosides, based on susceptibility patterns. However, this study highlights reduced susceptibility to cephalosporin, with fluoroquinolones and aminoglycosides demonstrating greater efficacy.

Given these findings, a polymicrobial de-escalation approach, incorporating the antibiotic groups identified, should be considered when initiating empirical therapy for suspected ABM, particularly in resource-constrained settings like Nigeria.

One significant challenge in managing childhood meningitis in resource-limited settings is obtaining informed consent from parents or caregivers for lumbar puncture to perform cerebrospinal fluid (CSF) analysis. Critically ill patients, who constitute the majority of cases in such settings, may present with absolute contraindications to lumbar puncture, further reducing the likelihood of parental consent. Additionally, relative contraindications, combined with parental anxiety about potential adverse outcomes, often deter consent for the procedure.

It is, therefore, essential to identify alternative diagnostic indicators, such as common clinical features of acute illnesses, that can assist in early clinical suspicion of meningitis in young children. The Wald test applied in this study demonstrated that some prodromal features of acute illness like high pitched cry, altered consciousness, convulsion, fever and vomiting, as well as signs of raised ICP like bulging anterior fontanel, were significant predictors of acute bacterial meningitis (ABM). Regression analysis of these clinical syndromes as demonstrated by this statistic test suggested a high predictiveness of these clinical syndromes. Kappa statistics revealed a moderate agreement between abnormal leucocyte counts and positive CSF bacterial culture results, although there was no significant difference between leucocyte counts and positive pathogenic yield in participants' CSF cultures.

Based on these findings, children with suspected ABM and clinical syndrome of fever, altered consciousness, neck stiffness, convulsion, vomiting, high pitched cry and bulging anterior fontanel, should be promptly treated with carefully selected antimicrobial combinations, even in the absence of CSF analysis results. This is particularly critical when parental consent for lumbar puncture is denied, a common occurrence in resource-poor settings due to ignorance, poverty, religious beliefs, socio-cultural factors, and other barriers.

In summary, the predictors of ABM in young children may differ from those in older children and adults. This study found that

fever, altered consciousness, neck stiffness and convulsion among other prodromes, were strongly correlated with positive CSF culture isolates in children with clinical suspicion of ABM.

Conclusion

Fever, altered consciousness, neck stiffness, convulsion, vomiting, high pitched cry and bulging anterior fontanelle were significant predictors of ABM. Antibiotics such as fluoroquinolones, aminoglycosides, amoxicillin, cephalosporins, macrolides and carbapenems showed good susceptibility against common isolates. Abnormal leucocyte counts may not be noted in young children and should not determine clinical decision of early empirical antibiogram of acutely ill children with clinical prodromes suggestive of ABM.

Recommendation

Children presenting with fever, altered consciousness, neck stiffness, vomiting, or high pitched cry should be managed for possible ABM while awaiting CSF analysis results, especially in cases where parental consent for lumbar puncture cannot be obtained.

Limitation of the Study

As a hospital-based study, the findings may not be fully representative of the entire paediatric population in the study environment.

Declarations

Declaration of Interest:

Manuscript authors have no conflicting interest to declare.

Declaration of data availability

Article authors hereby declare that all the data, codes and unique materials and documentation will be made publicly available in line with journal's terms and conditions for publication.

Use of AI

This manuscript was written by the authors but grammatically proof-read with the help of artificial intelligence.

Clinical Trial Number

Not applicable in this study

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Author Contribution

Dr Ihuoma Ukpabi conceptualised the study and assigned roles to the authors. She also supervised the study until its completion. Dr. Nwala corresponded with all the authors, wrote the first draft of the manuscript and effected all the corrections by proof-readers. Dr. Chidomere Ifeyinwa critiqued the manuscript and served as the medical editor for the manuscript. Dr. Okafor proofread the article and provided the needed guidance for the scientific flow of the article. Dr. Oluchi Izuka provided the clinical and scientific correlation of the findings and offered guidance where necessary. Dr Ogbonna re-ran the statistical analysis and guidance for the findings. Dr. Iche Kalu, a medical microbiologist, advised on sample collection and swift transport to the laboratory for analysis, and helped with the interpretation of findings. Dr. Jerry Ugolee contributed to the discussion of the findings and referencing of the manuscript.

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Informed consent was obtained from the parents and guardians of study participants, Mr Samuel Ijaye, a statistician, ran the initial analysis for the study and guided the authors on how to apply the findings. Professor Ngozika Ojinnaka supervised the study and gave her professional guidance to the authors.

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Figures

a. The positive actual state is 1.00000.

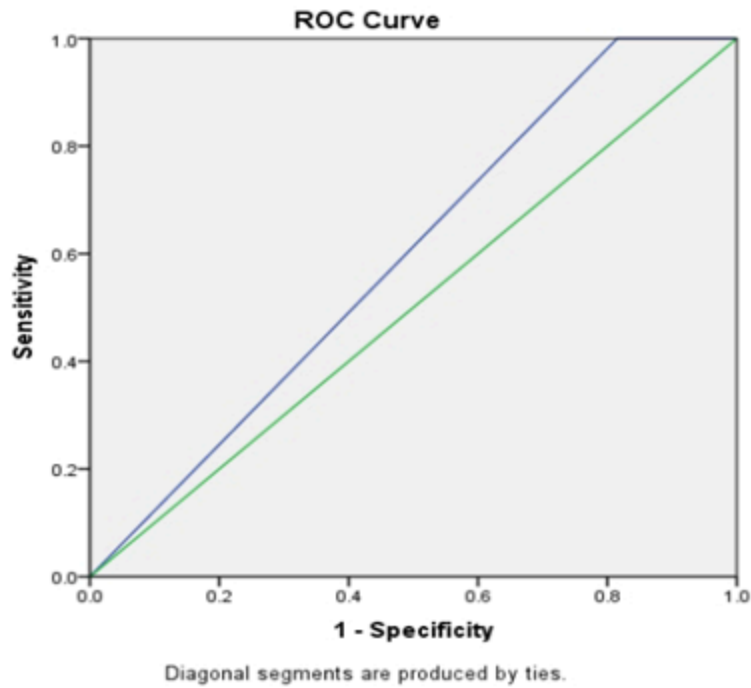


Figure 1

(ROC), demonstrates the relationship between the ideal (positive csf cultures) meningitis confirmation and observed clinical syndromes in subjects.