CD11b, E-Selectin and PCR versus Conventional Blood Culture for Diagnosis of Neonatal Sepsis

Yasmine Mohamed Nabiel Mohamed Kamel, Msc.a, Magda Mohamed El Nagdy, MD.a
Samia Abdel-Aziz Hawas, MD.a, Medhat Abdel-Maseih El Dakar, MD.a and
Basma Osama Shouman, MD.b Mansoura, Egypt.
Department of Medical Microbiology and Immunologya and Department of Pediatrics b, Faculty of Medicine, Mansoura University, Egypt

ABSTRACT

Introduction: Early onset bacterial sepsis is a feared complication of the newborn. A large proportion of infants admitted to the neonatal intensive care unit (NICU) for suspected sepsis receive treatment with potent systemic antibiotics while a diagnostic workup is in progress. The gold standard for detecting bacterial sepsis is blood culture. However, the sensitivity of blood culture is suspected to be low. Therefore, the diagnosis of sepsis is often based on the development of clinical signs, in combination with laboratory tests. Immunological assays of CD11b expression on peripheral blood neutrophil & serum E-selectin and molecular assays for the detection of bacterial DNA in the blood represent possible new diagnostic tools for early and rapid diagnosis of neonatal sepsis. Aim: This study aimed at comparing the valuability of bacteriological diagnosis of neonatal sepsis by blood culture technique and indirect methods of diagnosis.

Methods: Bacteriological diagnosis of neonatal sepsis by blood culture technique and comparing it to indirect methods of diagnosis by assaying of neutrophil CD11b expression level by flowcytometry, estimation of elevated concentrations of serum E-selectin by enzyme linked immunosorbant assay and detection of bacterial DNA in blood samples by broad range PCR.

Results: The infected group represented 60%. Klebsiella pneumoniae were the commonest isolated organisms in culture positive cases. CD11b expression assay by flowcytometry in infected and non infected cases showed a sensitivity of 77.8%, specificity of 100%, a PPV of 100% and a NPV of 75.1%. Serum E-selectin assay by ELISA in infected and non infected cases showed a sensitivity of 57.8%, specificity of 83.3%, a PPV of 83.8% and a NPV of 85%. PCR results had 88.5% sensitivity, 89.5% specificity, a PPV of 92% and a NPV of 85%. Conclusion: There is a need for CD11b expression assay, serum E-selectin level estimation and PCR as methods to quickly point out the infants with sepsis so such methods can be used as a supplement to traditional blood culture in diagnosis of neonatal sepsis and provide better diagnostic values as regarding rapidity of obtaining results and higher sensitivities and specificities, besides combination of multiple methods may provide more ease and accuracy for diagnosis.

Key words: Neonatal sepsis, CD11b, E-selectin, PCR

INTRODUCTION

Infection is still an important cause of neonatal morbidity and mortality (ranging from 15 to 50%) despite development of broad spectrum antibiotics and clinical advances in life support therapy due to prematurity, maternal genital colonization, transplacental spread and invasive procedures (1). Initial diagnosis is based upon clinical suspicion accompanied by nonspecific clinical signs making diagnosis difficult because the infant’s signs and symptoms may mimic other medical conditions (2).

Blood culturing is considered to be the gold standard for diagnosing neonatal bacterial sepsis(3). However, even blood culturing techniques can have low sensitivities(4). The reasons for this include intermittent seeding of low numbers of bacteria within the blood stream and the extremely small blood volumes obtained from infants for culturing (5).

The most common etiologies of neonatal sepsis include gram positive organisms (as Viridans streptococci, group B Streptococcus, Coagulase-negative and Coagulase-positive Staphylococcus, Enterococcus spp., and Listeria monocytogenes), gram negative organisms (such as Citrobacter, = Klebsiella, Pseudomonas, Enterobacter, and Serratia), and fungal organisms mostly Candida albicans (6).

C-reactive protein (CRP) is specific, but less sensitive in the early stages of neonatal sepsis(7). However, the neonatal immune response includes increased production of other inflammatory mediators, and assessing them may improve diagnostic accuracy; as tumour necrosis factor (TNF), Interleukin-1, 6 and 8 (8) that enhance the shedding of adhesion
molecules from cell membranes\(^9\). Elevated concentrations of soluble adhesion molecules (ICAM-1 and E-selectin) have been observed during sepsis among adults and in neonates and it has been suggested as a sensitive parameter of neonatal infection\(^10\).

Neutrophil cluster of differentiation 11b (CD11b), a neutrophil surface antigen that is normally expressed at a very low concentration on the surface of non-activated neutrophils\(^11\). CD11b increases on the neutrophil surface within 5 minutes of exposure to bacteria or endotoxin showing that it has high sensitivity and specificity in diagnosis of neonatal sepsis\(^12\).

Detection of bacterial DNA in blood samples of neonates is suggested to represent a rapid and sensitive supplement to blood culture in diagnosing bacterial sepsis in neonates. In particular, broad range PCR analysis, which relies on the fact that the bacteria specific 16SrRNA gene is highly conserved in all bacterial genomes, so it is a useful method for identification of bacteria in clinical samples\(^13,14\).

**PATIENTS & METHODS**

**Patients**

This prospective study was carried out in neonatal intensive care unit, Children's Hospital, Mansoura University. It included 75 neonates who showed evidence of acute clinical deterioration or had a risk factor for infection and 13 full term healthy neonates with no evidence or risk factor for infection included as control. A written informed consent was obtained from the parents of studied cases. Full history taking, clinical examination and routine laboratory investigations were carried out for each studied case.

**Study design**

1- **Blood culture**: one ml of blood was collected under complete aseptic precautions to be immediately inoculated into blood culture bottles followed by subculture on different media. The developed colonies were picked up and characterized in systemic manner including colonial morphology, gram stained films, biochemical reactions and antibiotic susceptibility testing.

2- **CD11b expression assay by flowcytometry (DakoCytomation)**: a half ml of blood was collected on EDTA and level of mean fluorescence intensity of CD11b expression on peripheral blood neutrophils was detected using purified monoclonal mouse antibody conjugated with R-phycoerythrin.

3- **E-selectin immunooassay by ELISA (Raybiotech)**: one ml of blood was collected under complete aseptic precautions for E-selectin immunoassay by ELISA. Blood samples were centrifuged at 1000 rpm for 15 minutes, and the separated serum was stored at -20 °C until assayed\(^15\). The mean absorbance for each set of standards, controls and samples, was calculated.

4- **Broad range PCR**: a half ml of blood was collected on EDTA under complete aseptic precautions for DNA extraction by QIAtamp DNA Mini Kit (blood protocol) followed by PCR amplification for 16SrRNA gene (Sigma Company). Primer used (16S ribosomal RNA gene-540 bp) with a sequence from 5’ to 3’: AGA GTT TGA TCA TGG CTC AG- ACC GCG ACT GCT GCT GGC AC\(^16\). Using (Norwall, CT, USA) thermal cycler. Initial denaturation step at 94 °C for 3 minutes, then up to 35 PCR cycles were performed, each consisting of three steps: denaturing step (30 seconds at 94 °C), annealing step (30 seconds at 55 °C) and primer extension step (60 seconds at 72 °C) followed by a final extension step at 72 °C for 5 minutes.

5- **Statistical analysis**: Qualitative data were presented in the form of numbers and percentage while quantitative data were presented in the form of means ± standard deviation. Statistical Package of Social Science (SPSS) software version 17 was used for data analysis and MedCalc v12 statistical program to obtain receiving operating characteristics (ROC) curve. Tests were considered significant when P value < 0.05.

**RESULTS**

Neonates included in this study were classified on basis of provided data including their clinical presentation, routine laboratory and radiological investigations (sepsis work up) in addition to response to therapy into two groups: Infected group that showed clear evidence of infection and non infected one that showed transient or specific non infective cause for clinical deterioration, no radiological evidence of infection and administration of antibiotics did not result in clinical improvement.
The infected group represented 60% (45 cases) and were sub-classified as culture positive infected ones; (26 cases) and culture negative; (19 cases), based on blood culture results. The culture negative infected subgroup included infants in whom there was either laboratory or radiological evidence of infection or those who responded significantly to administration of antibiotics. Gram negative organisms were isolated from 20 cases (76.9%), whereas gram positive ones were isolated from the remaining 6 cases (23.1%) of the culture positive infected group. *Klebsiella pneumoniae* were the commonest isolated organisms as detected in 46.2% of culture positive infected cases with a significant P value ($<0.0001 \ast$), followed by *Pseudomonas aeruginosa* and *E. coli* (in 11.5% each), then *Staphylococcus aureus*, *Group B streptococci* and *Proteus mirabilis* (in 7.7% each) and finally *MRSA* and *Enterococci* which were isolated from 3.8% of cases each.

Gram positive isolates were most sensitive to vancomycin and impenem (100%) but none was sensitive to penicillin. Gram negative isolates were most sensitive to impenem (100%) followed by amikacin (90%) then third generation cephalosporins (85%), gentamicin (80%) and cefuroxime (40%), whereas piperacillin (15%) recoded the least sensitivity.

Prematurity and foreign devices applications were statistically significant risk factors for acquisition of neonatal sepsis in 42.2% and 68.9% infected cases respectively.

Measured levels of mean fluorescence intensity of CD11b on neutrophils of peripheral blood were higher in infected group than non infected one in which they were higher when compared with the control group. The results were statistically significant (P value $<0.0001 \ast$). Also measured levels in culture positive cases were higher than culture negative ones and the results were statistically significant (P value $<0.0001 \ast$).

Measured levels of serum E-selectin were higher in infected group than non infected one in which they were higher when compared with the control group. The results were statistically significant (P value $<0.0001 \ast$) and also culture positive cases were higher than culture negative ones and the results were also statistically significant (P value 0.0008\ast).

Table (1): Types of organisms isolated from culture positive infected cases.

<table>
<thead>
<tr>
<th>Types of isolated organism (Total 26 cases/ 100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram positive organisms (Total 6/23.1%)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
</tr>
<tr>
<td>MRSA</td>
</tr>
<tr>
<td><em>Enterococci</em></td>
</tr>
<tr>
<td><em>Group B streptococci</em></td>
</tr>
</tbody>
</table>

Table (2): Results of CD11b expression assay on peripheral blood neutrophils by flowcytometry and serum E-selectin levels by ELISA in studied cases.

<table>
<thead>
<tr>
<th>Cases</th>
<th>Readings of CD11b on peripheral blood neutrophils</th>
<th>Readings of serum E-selectin levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean</td>
</tr>
<tr>
<td>Infected case</td>
<td>6.00-17.76</td>
<td>11.64</td>
</tr>
<tr>
<td>Non infected cases</td>
<td>5.56-9.34</td>
<td>7.55</td>
</tr>
<tr>
<td>Control</td>
<td>3.51-6.01</td>
<td>5.27</td>
</tr>
<tr>
<td>One way ANOVA</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table (3): Results of CD11b expression assay on peripheral blood neutrophils by flowcytometry and serum E-selectin levels by ELISA in relation to blood culture results.

<table>
<thead>
<tr>
<th>Cases categorized according to blood culture results</th>
<th>Readings of CD11b on peripheral blood neutrophils</th>
<th>Readings of serum E-selectin levels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Range</td>
<td>Mean</td>
</tr>
<tr>
<td>Culture positive</td>
<td>9.50-17.76</td>
<td>13.78 +/- 2.38</td>
</tr>
<tr>
<td>Culture negative</td>
<td>6.01-12.11</td>
<td>8.71 +/-1.88</td>
</tr>
<tr>
<td>Independent samples t test</td>
<td>P value &lt;0.0001*</td>
<td></td>
</tr>
</tbody>
</table>
This figure shows the ROC curve analysis of serum E-selectin assay by ELISA in infected and non-infected cases classified according to the neonatal sepsis work up including blood culture results. Serum E-selectin assay results showed a sensitivity of 57.8%, specificity of 83.3%, a PPV of 83.8% and a NPV of 56.8% (considering the cutoff point equals 121 IU/ml).

PCR results when compared to results of blood cultures in infected cases had 88.5% sensitivity, 89.5% specificity, a positive predictive value of 92% and a negative predictive value of 85%.

**Table (4): Comparison of sensitivities and specificities of CD11b expression assay by flowcytometry, Serum E-selectin by ELISA and PCR used for diagnosis of neonatal sepsis.**

<table>
<thead>
<tr>
<th>Diagnostic parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD11b expression assay on peripheral blood neutrophils by flowcytometry</td>
<td>77.8%</td>
<td>100%</td>
</tr>
<tr>
<td>Serum E-selectin assay by ELISA</td>
<td>57.8%</td>
<td>83.3%</td>
</tr>
<tr>
<td>PCR</td>
<td>88.5%</td>
<td>89.5%</td>
</tr>
</tbody>
</table>

PCR recorded the highest sensitivity for diagnosis of neonatal sepsis whereas CD11b expression assay on peripheral blood neutrophils by flowcytometry recorded the highest specificity followed by PCR. Serum E-selectin assay by ELISA recorded the least sensitivity and specificity.

**DISCUSSION**

Out of the 75 studied cases, 45 cases (60%) were infected, whereas 30 cases proved to be non infected (40%). This lies in parallel with Reier-Nilsen et al. (17) who studied the incidence of occurrence of neonatal sepsis, he carried out his study over 48 infants with suspected sepsis admitted to the NICU and he found that 65% of studied cases were infected while 35% were non infected but was in contrast to what estimated by Kayange et al. (18) who said that the infected group represented only 38.9% of studied cases and this may be due to better application of preventive and early therapeutic maneuvers leading to decrease in infection incidence.

The infected group was classified into culture positive and culture negative infected ones, based on the identification of positive microbiological results from blood cultures. Culture positive cases represented 57.8% whereas the remaining 42.2% were culture negative, this agrees with Meremikwu et al. (19), Macharashvili et al. (20) and Al-Shamahy et al. (21) who stated that 50.8%, 63% and 57% of studied cases were culture positive respectively whereas 49.2%, 37% and 43% were culture negative respectively but was against Musoke and Revathi (22) and Kohli-Kochhart et al. (23) who mentioned that only 16.7% and 23% of cases respectively had positive blood culture results.

The percentage of infected cases with negative culture may be a result of the low level of bacteraemia which is common in pediatric patients; difficulty in obtaining sufficiently large amounts of blood for culture from neonates besides the causative agents may be fastidious bacterial organisms requiring specific culturing techniques or may be due to viral or fungal infections.

The most common isolated organisms from culture positive cases were gram negative organisms in 20 cases (76.9%) whereas gram positive organisms were detected in the remaining 6 culture positive ones (23.1%), this was accepted when compared with Macharashvili et al. (20) who stated that gram negative organisms were isolated from 78% of culture positive cases and gram positive isolates were obtained from 22% and to Balkhy et al. (24) & Bhat et al. (25) who stated that gram negative organisms were more commonly isolated from culture positive infected cases.

On the other hand, Downey et al. (26) stated that gram positive organisms were detected in 45 to 77% of culture positive cases and gram negative organisms were isolated from 19 to 36% of cases only and Al-Taiair et al. (27) who reported that group B streptococci were the commonest causative agents of neonatal sepsis. It was also opposite to Meremikwu et al. (19) & Shim et al. (28) who said that gram positive organisms were isolated from about 50% and 43.6% of culture positive cases respectively. Similarly, Russell (29) & Cole et al. (30) reported that gram positive organisms were commoner
and more important in causing neonatal blood stream infections.

*Staphylococcus aureus* and group B *streptococci* were the commonest gram positive isolates (7.7%) each, in addition to one *MRSA* isolate (3.85%) and one *Enterococcus* isolate (3.85%) and this lies in parallel with Macharashvili et al. (19) that estimated an incidence of 7.2% for *Staphylococcus aureus*, 5% for group B *streptococci* and 4.8% for *MRSA*.

But was in contrast to Mugalu et al. (31) who said that *S. aureus* was the commonest isolate from 62.7% of cases followed by *E. coli* (in 15.5%) and Wu et al. (32) who reported that coagulase negative *staphylococci* were the commonest isolates (in 58.9%) followed by *E. coli* and *Klebsiella spp.* (2.9% each). It was also opposite to what reported by Lukacs and Schrag (33) who stated that gram positive organisms were commoner causative agents.

The isolated gram negative organisms included *Klebsiella pneumoniae* as the commonest isolate (12 isolates, 46.2%), besides 3 *Pseudomonas aeruginosa* isolates (11.5%), 3 *E. coli* isolates (11.5%) and 2 *Proteus mirabilis* isolates (7.7%), this lies in agreement with Macharashvili et al. (20), Muugulug and Bat-Erdene (34), Zakariya et al. (35) and Al-Shamaly et al. (36) who stated that *Klebsiella spp.* were the commonest gram negative isolates and also to Trotman et al. (37) that found that *Klebsiella pneumoniae* were isolated from 44% of culture positive cases.

These data were also consistent with other reviews of neonatal sepsis in developing countries where gram negative infections were more frequently isolated, especially *Klebsiella spp.* as Zaidi et al. (38) demonstrated that 60% of neonatal sepsis cases were caused by gram-negative organisms with *Klebsiella pneumoniae* accounting for 23%, *Pseudomonas* 7%, other gram-negatives 14% but this was contradictory to Edgar et al. (39) that estimated a much more lower incidence for coliform isolates (14.6%). These results were explained by the fact that the prevalence of microbial agents differs from one geographic area to another and types of normal flora.

All gram positive isolates were resistant to penicillin G but fortunately, all were sensitive to imipenem and vancomycin, (100%) each, which agreed with Iregbu et al. (40) and Darmstadt et al. (41). All gram negative isolates were sensitive to imipenem (100%) whereas a variable sensitivity patterns to piperacillin (15%) and cefuroxime (40%) but luckily a better sensitivity incidence was recorded for gentamycin (80%), cefotaxime (85%) and amikacin (90%) and this lies in consistency with the results of antibiotic sensitivity testing declared by Kohli-Kochhart et al. (23) which were 38.5% for cefuroxime, 72.4% for gentamycin and 96.1% for amikacin.

A different sensitivity pattern was recorded by Meremikwu et al. (42) as follows; where the sensitivity to third generation cephalosporin was 83.2% and to second generation was 76.5%. The increased incidence of antibiotic resistance may be attributed to the misuse of antibiotics in this era in addition to lack of microbial susceptibility data, patients are treated empirically with broad spectrum antibiotics.

Risk factors that played an important role in increasing incidence of neonatal sepsis were using medical devices; central venous catheterization (in 68.9% cases) and this was accepted when compared with Downey et al. (26) who stated that central venous catheterization was reported as a risk factor in 67% of cases and was also consistent with Butler-O’Hara et al. (42) that considered central venous catheterization an important risk factor for neonatal blood stream infection especially with prolonged duration of use.

Nineteen infected cases (42.2%) gave a history of prematurity this agrees with Trotman et al. (37) & Kuhna et al. (43) who reported an incidence of 34% and 33.4% respectively but was in contrast to Aleman et al. (44) who reported a higher incidence up to 69%.

A significant elevation of CD11b expression level on peripheral blood neutrophils was detected in the infected group, compared with the non infected and control and also was significantly elevated in culture positive cases than culture negative ones. This is explained by the fact that CD11b is a functional molecule that is involved in many of the potent inflammatory mechanisms of neutrophils (45). On activation, the expression of CD11b that is constitutively expressed at low levels on resting neutrophils, is enhanced especially in bacterial infections producing the highest expression levels (46).

These findings lies in parallel with Lai et al. (47), Adib et al. (12) and Genel et al. (47) that declared similar results but disagrees with Cui et al. (48) who stated that the expression of CD11b in neonatal sepsis was presented with a down-regulation. This can be explained by the fact that the readings are affected by the severity of infection and the time of estimation of CD11b level as it is considered an early marker of infection and decreases with time (49), besides CD11b levels in Cui et al. (48) research were studied in different category of neonates.
Estimation of CD11b expression level on peripheral blood neutrophils by flow cytometry had a sensitivity of 77.8%, specificity of 100%, a positive predictive value of 100% and a negative predictive value of 75.1%. This lies in concurrence with Adib et al. who stated that sensitivity and specificity of CD11b expression assay were 75% and 100% respectively but disagrees with Cui et al. that reported a higher value for sensitivity 86.3%. This may be explained by difference in accuracy of performance of used devices and different methods of categorization of studied cases.

In this study a highly significant elevation of serum E-selectin was detected in the infected group, compared with the non infected and in non infected compared with control. Also a statistical significance in elevation was recorded in culture positive cases when compared to culture negative ones.

These findings lie in parallel with Zaki and El Sayed & Edgar et al. who stated that higher elevation of serum E-selectin was detected in the infected group, compared with the non infected group suggesting a role for early diagnosis of neonatal infection within few hours. These findings co applies with the fact that the shedding of E-selectin molecules is considered a component of the immune system and inflammation/infection-induced immune response that develops early in gestation when the endothelium was intensely activated in bacterial infections especially in gram-negative infections due to interaction of bacterial endotoxin with a membrane-specific endotoxin receptors leading to endothelial injury.

On the other hand readings recorded a low sensitivity of 57.8%, a moderate specificity of 83.3%, PPV of 83.9% and NPV of 56.8%. This follows what Edgar et al. & Zaki and El Sayed recorded as they mentioned close values of 54.8%, 59% for sensitivity and 82.3%, 87% for specificity respectively but a little bit different PPV and NPV of 85%, 79% and 66.6%, 73.8% respectively but disagrees with Reinhart et al. who reported a sensitivity of 79% and a specificity of 61%. The low levels of sensitivity may be explained by low performance of used ELISA reader besides various researchers found that better diagnostic results can be obtained by combining E-selectin results with other markers' serum levels as suggested by Kingsmore et al.

On using blood culture results as reference gold standard for calculating sensitivity and specificity of PCR, it had a sensitivity of 88.5%, specificity of 89.5%, a positive predictive value of 92% and a negative predictive value of 85%. This lies in concurrence with Elwan and Zarouk who stated that sensitivity, specificity, positive and negative predictive values of PCR were 92.3%, 88.2%, 90%, and 91% respectively. But it disagrees with Reier-Nilsen et al. that reported lower values as he said that PCR revealed a 66.7% sensitivity, 87.5% specificity and 75% negative predictive values but this may be explained by lower number of tested cases in Reier-Nilsen et al. study leading to a very low percentage of blood culture positive cases.

It also lies in contrast with Yadav et al. who mentioned higher values for sensitivity up to 100%, specificity of 95.6% and negative predictive value of 100% and to Wu et al. who also reported higher values as he stated that PCR proved to have sensitivity of 100% and specificity of 97.17% as the PCR used was gram stain specific probe based real time PCR which is different from what used in our study and proved to be more accurate and reflecting that methodological improvements are required in order for DNA detection to replace or supplement traditional blood culture in diagnosis of bacterial sepsis.

The valuability and efficiency of the 16S rRNA PCR approach differs depending on the microorganisms involved, the expected bacterial load and the presence of bacterial DNA other than that from the pathogen implied in the infectious disease.

Estimating CD11b expression level on peripheral blood neutrophils, serum E-selectin measures and bacterial DNA by PCR proved to be superior for blood culture in diagnosis of neonatal sepsis and starting empirical antibiotic therapy as regarding rapidity of obtaining results besides higher sensitivities and specificities.

On comparing recorded values of the sensitivity and specificity of used diagnostic techniques, variable values were detected as PCR recorded the highest sensitivity for diagnosis of neonatal sepsis whereas CD11b expression assay by flow cytometry recorded the highest specificity followed by PCR while serum E-selectin assay by ELISA recorded the least sensitivity and specificity, besides the lack of fixed standardized cut off values for CD11b expression levels on peripheral blood neutrophils and serum E-selectin among different laboratories suggests that a combination of different markers estimation may ease neonatal sepsis diagnosis and provide better diagnostic values.
CONCLUSION

Diagnosis of neonatal sepsis had benefited from adding other methods to conventional identification by blood culturing as serological detection of elevated levels of CD11b expression on peripheral blood neutrophils & serum E-selectin and molecular identification by PCR especially in ruling out culture negative cases. They proved to be superior to blood culture in diagnosis and starting empirical antibiotic therapy, besides, a combination of different markers estimation may ease neonatal sepsis diagnosis and provide better diagnostic values as regarding rapidity of obtaining results and higher sensitivities and specificities.

REFERENCES

18. Kayange N., Kamugisha E., Mwizamholya D. L., Jeremiah S., and


38. Zaidi A. K., Huskins W. C., Thaver D., Bhutta Z. A., Abbas Z., and Goldmann...


Pediatrics, Armed Forces Medical College, Pune, Maharashtra-411 040, India.


The title of the article is translated to: "The advantage of the newborn's blood culture in the diagnosis of the meningitis of the newborn in the fast technique." The author further explains that the blood culture is a quick and efficient method for diagnosing meningitis in newborns. The article also discusses the importance of early diagnosis and the role of diagnostic tools in improving outcomes for newborns with meningitis.