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A Diagnostic Stewardship Perspective Of Re-Evaluating The Efficacy And Role Of Cerebrospinal Fluid (CSF) Gram Stain And Culture Testing In The Diagnosis And Clinical Outcome Of Neonatal Meningitis.

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Abstract
Background
Cerebrospinal fluid (CSF) analysis is critical in diagnosing bacterial meningitis, guiding antibiotic therapy. However, the clinical utility of Gram stain and culture results in influencing treatment decisions remains debated, especially in settings where empirical antibiotics are administered early. This study aims to evaluate the impact of CSF Gram stain and culture on clinical decision-making in a tertiary care hospital.
Materials and Methods
A hospital-based retrospective study was conducted over six months (May 2023 to October 2023) in the Department of Microbiology. Eighty-eight CSF samples were analyzed, with Gram staining and culture performed on all samples. Clinical data on patient history, antibiotic treatment before and after CSF Gram stain, and culture results were collected. Inclusion criteria included neonates with CSF collected via lumbar puncture and available antibiotic treatment information. Exclusion criteria included children older than 28 days, CSF collected from an indwelling ventricular drain, and neonates with other predisposing factors.
Results
Out of 88 CSF samples, 49 exhibited abnormal cytochemistry, and 39 had normal cytochemistry. Among the 49 abnormal samples, 5 were Gram stain-positive, and 7 were culture-positive. All 39 samples with normal cytochemistry were negative in both tests. Gram stain findings had no impact on altering empirical antibiotic therapy, with a 0% impact rate. Culture results influenced the choice of antibiotics in only 7.9% of cases, particularly for pathogens like Streptococcus, while no changes were made for Klebsiella pneumoniae and Escherichia coli.
Discussion
The study highlights the limited impact of CSF Gram stain and culture on altering empirical antibiotic therapy in a tertiary care setting. While both diagnostic tools are essential, their role in guiding clinical decisions is minimized when empirical antibiotics are initiated early. These findings underscore the need for refined strategies in using microbiological data to optimize patient management, especially in the context of emerging antibiotic resistance.

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I. Introduction

Application of stewardship practices in microbiological tests effectively can improve laboratory efficiency. A crucial measure of proper test management is its impact on patient care decisions.[1]

Neonatal meningitis, a severe and life-threatening condition, poses significant challenges to clinicians due to its high morbidity and mortality rates. Prompt and accurate diagnosis is critical to initiate appropriate treatment and improve outcomes for affected neonates. Cerebrospinal fluid (CSF) analysis, including gram staining and culture testing, has been the cornerstone of diagnosing bacterial meningitis. However, the utility and efficacy of these traditional diagnostic methods in the context of neonatal meningitis warrant re-evaluation, especially considering advancements in diagnostic technologies and the need for effective diagnostic stewardship. CSF gram staining is a rapid test performed to detect bacteria directly in the CSF. Despite its urgency and perceived impact, the sensitivity of gram staining is often low due to the typically low bacterial burden in neonatal meningitis cases. Studies have shown that the sensitivity of gram staining can vary widely, with some reporting as low as 30% sensitivity in neonatal populations [2]. This low sensitivity raises questions about the test's reliability and impact on clinical decision-making.

CSF culture remains the gold standard for diagnosing bacterial meningitis, providing definitive identification of causative organisms and their antibiotic susceptibilities. However, the turnaround time for culture results is a significant drawback, often taking 24 to 48 hours or longer. During this period, clinicians must rely on empirical therapy based on clinical presentation and preliminary test results, such as CSF gram staining. Empiric treatment is crucial, as delays in appropriate therapy can lead to poor outcomes [3]. However, the impact of CSF culture results on modifying or discontinuing empiric therapy and their role in antibiotic stewardship is less clear.

Diagnostic stewardship aims to optimize the use of diagnostic tests to improve patient outcomes and reduce unnecessary healthcare costs. In the context of neonatal meningitis, this involves critically assessing the value of CSF gram staining and culture testing in guiding treatment decisions. Emerging evidence suggests that gram staining may have a limited role in influencing treatment decisions due to its low sensitivity and often negative results in the presence of normal CSF cytochemistry [4]. Additionally, negative CSF cultures may not significantly alter clinical management, as empiric therapy is typically initiated based on clinical suspicion and continued until bacterial meningitis is ruled out [5]. Furthermore, the impact of CSF test results on antibiotic stewardship is an important consideration. While CSF results rarely prompt the initiation of treatment, they can contribute to the discontinuation of antibiotics in some cases, thereby reducing unnecessary antibiotic use and associated costs [6]. This role in antibiotic stewardship highlights the potential cost-saving benefits of CSF testing, even if the tests themselves are not directly driving treatment decisions.

The limitations of traditional CSF gram staining and culture testing underscore the need for more sensitive and specific diagnostic methods. Nucleic acid amplification tests (NAATs), including multiplex polymerase chain reaction (PCR) panels, offer higher sensitivity and faster turnaround times, enabling more accurate and timely diagnosis of bacterial meningitis [7]. These rapid diagnostic tests can overcome the limitations of culture-based methods, particularly in patients who have received prior antibiotics, which can inhibit bacterial growth in cultures.

In this study, we aim to re-evaluate the efficacy and role of CSF gram staining and culture testing in the diagnosis of neonatal meningitis and their impact on clinical outcomes. By analyzing data from a tertiary care hospital, we seek to understand how these traditional diagnostic methods influence treatment decisions and contribute to antibiotic stewardship. Our findings will inform updated diagnostic protocols that balance the use of conventional tests with modern rapid diagnostic techniques, ultimately improving the management and outcomes of neonatal meningitis.

II. Materials And Methods

Study Design and Setting -This hospital-based retrospective study was conducted over a six-month period from May 2023 to October 2023. The study was performed in the Department of Microbiology at a tertiary care hospital, utilizing cerebrospinal fluid (CSF) samples received during this time frame.

Sample Processing -CSF samples that were collected via lumbar puncture from neonates admitted to the hospital were received. The samples were subjected to gram staining and culture testing in the microbiology laboratory. Simultaneously, cytopathological and biochemical parameters were accessed from patient data and analyzed for each sample.

Inclusion and Exclusion Criteria

Inclusion Criteria:

1)Neonates (aged 0-28 days)
2)CSF samples collected by lumbar puncture (not from indwelling ventricular drains)
3)Availability of detailed antibiotic treatment information before and after CSF collection

Exclusion Criteria:

1)Children older than 28 days
2)CSF samples collected from indwelling ventricular drains

Data Collection

Clinical information was meticulously gathered, including patient history and comprehensive data on antibiotic treatment. The antibiotic treatment data were categorized as follows: Antibiotic treatment administered before CSF collection, Antibiotic treatment modifications following CSF gram stain results and Antibiotic treatment modifications following CSF culture results

Laboratory Analysis- CSF samples were immediately processed for gram staining upon receipt in the laboratory. The results were documented and reported to guide initial clinical decisions. The samples were cultured on appropriate media to isolate and identify causative bacterial pathogens. The culture results, along with antibiotic susceptibility profiles, were reported to the clinical team for further management of the neonates. CSF samples were concurrently analyzed for cytopathological and biochemical parameters, including cell counts,

protein levels, and glucose concentrations. These parameters were used to support the diagnosis of meningitis and to provide additional context for the gram stain and culture results.

Data Analysis -The collected data were compiled and analyzed to evaluate the impact of CSF gram staining and culture testing on clinical decision-making and treatment outcomes. Analyses were performed to determine positivity rates of gram stain and culture and also the overall diagnostic utility of these tests in the context of neonatal meningitis. Additionally, the role of these tests in antibiotic stewardship was assessed by examining changes in antibiotic regimens based on test results.

III. Results-

A total of 88 cerebrospinal fluid (CSF) samples were analyzed in this study. The cytochemical analysis revealed that 49 samples exhibited abnormal cytochemistry, while the remaining 39 samples had normal cytochemistry.Out of the 49 samples with abnormal cytochemistry, 5 were positive on Gram stain during direct microscopic examination. Further culture of these samples showed that 7 were positive, with 2 additional cases being detected that were not identified by Gram stain. Among the 39 CSF samples with normal cytochemistry, none were positive for either Gram stain or culture.

Of the 88 CSF samples, 73 were from patients who had already been started on empiric antibiotic treatment, while the remaining 15 were not yet on empirical therapy. Among the 73 samples from patients on empiric antibiotics, 5 samples were positive on CSF Gram stain, while 68 samples were negative. The clinical decisions were unaffected by the Gram stain results, as the choice of antibiotics was not altered in any of the 5 positive cases.Similarly, among the 68 negative CSF Gram stain results, empiric antibiotics were not discontinued in any cases, indicating a zero percent impact of the Gram stain findings on clinical decision-making.

Out of the 73 samples from patients on empirical antibiotics, 7 were positive on culture, while 66 samples were negative.Among the 7 culture-positive samples, the choice of antibiotics was influenced only in 2 cases, both of which were positive for *Streptococcus* species.In the remaining 5 culture-positive cases, where *Klebsiella pneumoniae* was isolated in 3 cases and *Escherichia coli* in 2 cases, the choice of antibiotics was not influenced. Among the 66 culture-negative samples, antibiotics were discontinued in 5 cases, while the remaining 61 patients continued on antibiotics.

The culture results influenced clinical decisions in a total of 7 cases out of 88 (5 culture-negative and 2 culture-positive cases), resulting in an overall impact rate of 7.9%.

	Gram stain		**Culture growth**	
	Positive	Negative	Positive	Negative
CSF with Abnormal Cytochemistry (n=49)	5	42	7	54
CSF with normal Cytochemistry (n=39)	0	39	0	39

Table-1 : CSF Gram stain and Culture positivity with cytochemical findings.

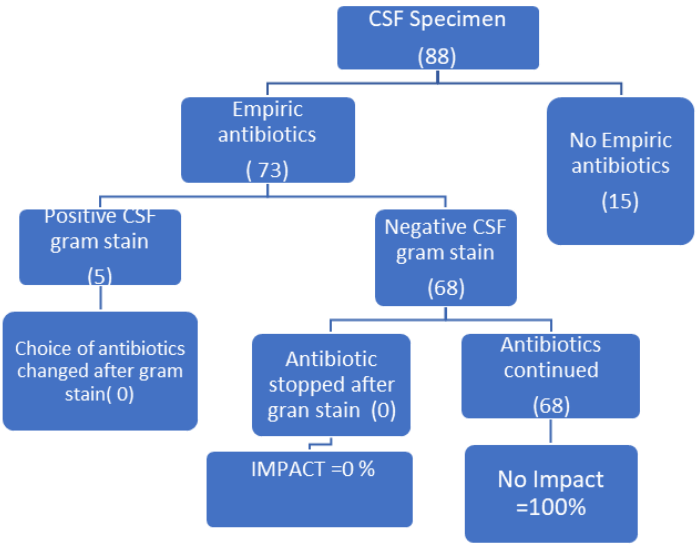

Figure 1- Impact of Gram staining on clinical decision making.

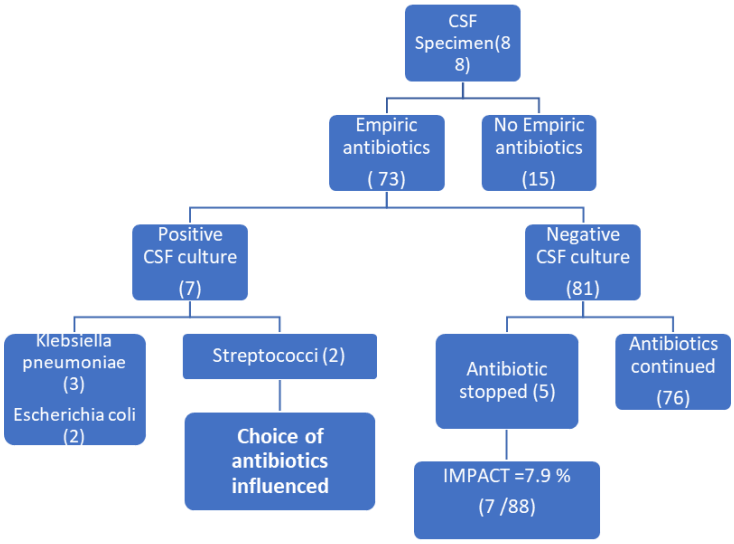

Figure 2- Impact of Gram staining on clinical decision making.

IV. Discussion

The present study focused on the microbiological profile and antibiotic sensitivity patterns of cerebrospinal fluid (CSF) samples, with particular emphasis on the impact of Gram stain and culture results on clinical decision-making in a tertiary care setting. Our findings demonstrate a limited impact of both Gram stain and culture results on altering empirical antibiotic therapy, which is consistent with several other studies in the literature.

Among the 88 CSF samples analyzed, 49 exhibited abnormal cytochemistry, and 39 had normal cytochemistry. Notably, none of the samples with normal cytochemistry yielded positive results in either Gram stain or culture, indicating a low likelihood of bacterial infection in these cases. This observation aligns with the findings of several studies that have reported the limited utility of CSF cytochemistry in predicting bacterial meningitis, especially in cases where the cytochemical parameters are within normal ranges . Our study revealed that CSF Gram stain had no impact on clinical decision-making, as the results did not lead to any change in the choice of antibiotics, even in cases where the Gram stain was positive. This finding is consistent with the study by Visser et al.[8] which reported that the Gram stain had a limited role in influencing the management of patients with suspected bacterial meningitis, particularly in settings where empirical antibiotics had already been initiated .Similar findings were also reported by Struthers et al. [9], who concluded that while Gram stain is a valuable diagnostic tool, its utility in guiding therapy may be diminished in settings where empirical treatment is initiated early, often before microbiological results are available . In our study, the initiation of empirical antibiotics likely overshadowed the influence of Gram stain findings, leading to a zero percent impact on therapeutic decisions.

The impact of CSF culture on clinical decisions in our study was modest, with only 7 out of 88 cases (7.9%) showing a change in antibiotic therapy based on culture results. This aligns with the findings of Tunkel et al. [10], who observed that the introduction of culture results had a limited but significant impact on treatment, particularly in cases where pathogens with specific antibiotic susceptibilities were identified .However, our study also noted that in cases where *Klebsiella pneumoniae* and *Escherichia coli* were isolated, the choice of antibiotics was not altered, possibly due to the broad-spectrum nature of the empirical therapy already in place. This observation is supported by the work of Brouwer et al. [11], who reported that broad-spectrum empirical antibiotics often cover the pathogens identified in CSF cultures, thereby reducing the need for modifications in therapy .

Our findings are in line with several studies that have highlighted the challenges in altering clinical management based on CSF Gram stain and culture results. For instance, a study by Lee et al. [12] found that the delay in obtaining culture results, combined with the initiation of broad-spectrum antibiotics, often reduces the clinical utility of culture findings in acute settings . In contrast, other studies, such as those by Thigpen et al. [13], emphasize the importance of culture results in guiding therapy, particularly in settings where antibiotic resistance is prevalent. In these contexts, culture findings can significantly influence the choice of antibiotics, highlighting the variability in the impact of microbiological results based on the clinical and epidemiological context .

In conclusion, our study underscores the limited impact of CSF Gram stain and culture results on clinical decision-making in a tertiary care setting where empirical antibiotic therapy is commonly initiated before microbiological results are available. While Gram stain remains a valuable diagnostic tool, its influence on altering therapy appears minimal in this context. Similarly, culture results, while important, impacted treatment decisions in only a small percentage of cases.

The role of traditional staining and culture techniques in diagnostic bacteriology is undergoing transformation due to the advent of newer genotypic, proteomic, and automated identification and susceptibility methods. Medical microbiology laboratories are now reassessing the value of these diagnostic approaches, focusing on how test results influence clinical decision-making and patient outcomes. Although the literature has predominantly centered on the diagnostic accuracy of these methods, there is a growing recognition that tests must also demonstrate a tangible impact on patient management and public health to justify their clinical utility. Tests that fail to influence treatment decisions or improve disease control, despite high diagnostic performance, may not represent an efficient use of laboratory resources. This evolution calls for a balanced approach, where the clinical relevance of diagnostic tools is weighed alongside their technical capabilities.These findings also suggest that in settings where empirical therapy is widely used, the role of Gram stain and culture in guiding treatment may be more limited than traditionally thought. Future research should focus on refining the use of these diagnostic tools to optimize their impact on patient management, particularly in the context of emerging antibiotic resistance.