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EARLY WARNING INDICATORS AND LABORATORY SIGNATURES OF MULTI-DRUG-RESISTANT SEPSIS IN CHILDREN

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Abstract

Background:

Multidrug-resistant (MDR) sepsis is a big cause of morbidity and mortality among children, it also really challenges healthcare systems worldwide. The rising prevalence of antimicrobial resistance, along with those delays in diagnosis, can seriously worsen the clinical picture. If we can spot sepsis early using lab biomarkers that are easy to access, then it might help clinicians act fast and manage patients better. In practice, blood and inflammation related indices, such as C-reactive protein (CRP), total leukocyte count (TLC), and platelet count, are often taken as early clues of infection. This work was designed to look at the lab signatures and antimicrobial sensitivity profiles that are linked with MDR sepsis in pediatric patients.

Methods:

We carried out a descriptive cross-sectional study at the Department of Pathology, Pakistan Institute of Medical Sciences (PIMS) Islamabad. In total , 183 children aged 1 month to 12 years with suspected sepsis were included. After obtaining informed consent, demographic details as well as clinical information were gathered with a structured proforma. Venous blood samples were then collected for hematological assessment (TLC and platelet count), CRP testing, and blood culture. The bacteria or other organisms grown from culture were identified, and antimicrobial susceptibility was evaluated using standard microbiological methods. We processed the data with IBM SPSS Statistics version 23, and we used a p-value of <0.05 as the threshold for statistical significance.

Results:

Out of the 183 participants, about 51% were male and 49% were female. Blood cultures were negative/no growth in 66% of the cases, so the remaining ones were culture-positive. In those culture-positive samples, Salmonella species came up most often as the isolated pathogen (14%), then it was Klebsiella pneumoniae (6%) ,and Pseudomonas aeruginosa (5%). When we looked at

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mean TLC, platelet count, and CRP levels, they seemed pretty similar for male versus female patients, with no meaningful difference ($p > 0.05$). Most patients also showed high TLC and elevated CRP, suggesting ongoing systemic inflammation and infection, even if the numbers are not identical across groups. On antimicrobial susceptibility testing, there was substantial resistance to many of the antibiotics that are commonly prescribed. Imipenem showed the best activity overall against Gram-negative isolates, while Linezolid performed very well for Gram-positive organisms including methicillin-resistant Staphylococcus aureus (MRSA).

Conclusion:

Overall, the results underline the rising burden of MDR pathogens in pediatric sepsis, and they also reinforce why CRP and TLC still matter as earlier laboratory clues, especially when these are used together with blood culture findings. Strengthening antimicrobial stewardship programs plus supporting culture-guided antimicrobial therapy will be important, because that can help improve treatment results and reduce the continuing emergence of antimicrobial resistance in pediatric populations.

INTRODUCTION

Sepsis is a serious and life-threatening condition that occurs when the body's immune system reacts excessively to an infection. Instead of only fighting the infection, the immune response begins damaging the body's own tissues and organs. If sepsis is not identified and treated quickly, it can progress to septic shock, multiple organ failure, and death.[1]

Septic shock defined as a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. It is actually a syndrome of physiological, pathological and biochemical abnormalities induced by infection ,and it is a major health concern .It is not only associated with bacterial and fungal infections but also other infections such as viral , tropical and protozoal diseases.[2]

Pediatric sepsis is a fetal and potentially serious condition resulting extreme response to infections. It can spread rapidly and lead to severe complications if not treated promptly. It is not just an infection, its body's overwhelmed response that results to organ failure and dysfunction in children.[3]

Newborns, especially those who are born early or have a low birth weight, are more vulnerable because their immune systems are not fully developed and they face a higher risk of infections picked up in the hospital. In neonatal intensive care units (NICUs), late-onset sepsis caused by multidrug-resistant (MDR) organisms is especially common.[4]

The capability of bacteria to oppose or to become tolerant to several structurally and functionally distinct drugs simultaneously is known as **multidrug resistance.**"multidrug-resistant organisms (MDROs) are labeled as such because of their in-vitro resistance to more than one antimicrobial agent" [5]

Multi-Drug-resistant sepsis in children is a rising, lethal characterized by severe infections caused by bacteria which is resistant to many antibiotics. Driven by overuse of antibiotics and hospital acquired infections resulting higher mortality, prolonged hospital stays and limited treatment options. Infections with multi-drug resistant (MDR) bacteria are difficult to treat because they have developed resistant against multiple antibiotics. [6]

Although, it's a serious emergency condition and particularly concerning because in children's and neonates have developing immune system that make them to more susceptible to severe infections. A significant challenge in managing sepsis today is the

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emergence of multi-drug resistant (MDR) pathogens.[7]

A single laboratory result cannot be used to diagnose children with multidrug-resistant sepsis. Rather, a "laboratory signature" is created by simultaneously monitoring hematological and inflammatory indicators. This signal is particularly noticeable in MDR cases, where bacteria are frequently more virulent or persistent as a result of antibiotic resistance. [8]

C-reactive protein (CRP), total leukocyte count (TLC), and platelet count are key inflammatory and hematological bio-markers that support early diagnosis and assessment of sepsis in children. CRP is an acute-phase protein produced by the liver in response to pro-inflammatory cytokines, including interleukin-6 (IL-6). Its levels rise quickly during bacterial infection, indicating systemic inflammation and serving as a sensitive early marker.[9]

Total leukocyte count (TLC) represents the body's immune response; in sepsis, it may show leucocytosis due to increased white blood cell production or leukopenia in severe cases and also helps in assessing both the presence and progression of infection.[10]

Platelet count reflects the hematological and coagulation disturbances associated with sepsis. Inflammatory cytokines and endothelial injury lead to platelet activation and consumption, often resulting in thrombocytopenia, which is strongly associated with disease severity and risk of organ dysfunction. Monitoring these three together allows for a multidimensional view of the patient's status tracks the intensity of the infection, TLC tracks the immune capacity, and Platelets track the systemic collateral damage. CRP is a highly sensitive acute-phase protein that serves as an early warning signal. [11]

Blood culture is considered the gold standard for diagnosing sepsis because it directly detects and identifies the causative microorganism present in the bloodstream. It helps determine the exact bacterial pathogen responsible for infection and also provides antimicrobial susceptibility testing,which is essential for selecting appropriate antibiotic therapy, especially in multidrug-resistant (MDR) infections.Non-specific symptoms and limitations of conventional diagnostic methods for children sepsis mandate fast and reliable method to diagnose disease for point of care application.Bio-markers such as C-reactive protein(CRP),Total leucocyte count(TLC) are useful to diagnose pediatric sepsis.[12]

Globally, sepsis is one of the leading causes of illness and death among children, especially those under five years of age. Approximately 20 million cases of pediatric sepsis occur each year, causing nearly three million deaths. Most of these deaths occur in low and middle-income countries where health-care resources are limited.[13]

Acknowledging both the complex nature and wide spread burden of sepsis, the World health organization (WHO) and World Health Assembly declared sepsis as a global health priority through the adoption of a resolution to improve diagnosis, prevention and management of sepsis.[14]

According to recent global estimates, approximately 49 million cases of sepsis occur annually, resulting in about 11 million deaths, representing nearly 20% of all global deaths. Children, particularly those under five years of age, constitute a significant proportion of this burden. Multidrug-resistant (MDR) pathogens are increasingly implicated in pediatric sepsis. [15]

Pakistan carries a particularly high burden of neonatal and pediatric sepsis. Factors such as poverty, incomplete vaccination coverage, poor sanitation, and widespread malnutrition increase the risk among children. In tertiary care hospitals in Pakistan, Gram-negative bacteria such as Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa are the most common causes of infection. .[16]

In Pakistan, many tertiary care hospitals have reported emerging rates of MDR levels reaching up to 38% in recent years driven by overuse of broad-spectrum antibiotics in neonatal settings. In low-income countries, treating infections with MDR can be more challenging due to unavailability of effective medicines. [17]

Major challenge in Pakistan is the lack of rapid and reliable tools to detect MDR sepsis in

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children. Many international guidelines rely on advanced laboratory tests and predictive models that are often not available in local hospitals. This can delay diagnosis and treatment, leading to worse outcomes and further antibiotic resistance. [18]

Moreover, there is significant research gap due to insufficient region-specific data that is related to local microbial landscape and resistant trends, particularly in pediatric settings. The variability in laboratory findings and clinical presentations further complicates the foundation of standardized diagnostic criteria. Additionally, limited access to advance diagnostic tools and bio-markers hinders early identification and appropriate management.

The majority of current research concentrates on single markers, such as CRP which frequently exhibit moderate diagnostic accuracy and are unable to distinguish between MDR and sensitive bacterial strains on their own. [19]

The study of early warning indicators and laboratory signatures of multidrug-resistant (MDR) sepsis in children is critically important for several reasons.Early identification of MDR sepsis enables timely and appropriate treatment, which is essential for reducing morbidity and mortality in pediatric patients. Recognizing early warning signs and specific lab markers guides clinicians to initiate targeted therapies sooner, improving survival rates and minimizing complications.[20]

Additionally, by assisting in the selection of the most effective medicines, knowledge of lab signatures linked to MDR pathogens promotes antibiotic stewardship by lowering the usage of broad-spectrum drugs and preventing the emergence of additional resistance. By reducing hospital stays and the need for critical care, early detection also optimizes health-care resources and lowers total costs. Controlling MDR sepsis in children helps stop the spread of resistant diseases in communities and hospital settings since this group is particularly vulnerable. [21]

Furthermore, the insights gained from this study can inform clinical guidelines, infection control policies, and future research aimed at combating antimicrobial resistance in pediatric sepsis. Overall, this research is vital for enhancing clinical management, improving patient outcomes, and addressing the global challenge of antimicrobial resistance in children with sepsis. [22]

MATERIALS AND METHODS

1. Study Design and Settings

1.1 Type of study:

A cross-sectional study was conducted to assess early warning indicators and laboratory signatures of multi-drug-resistant sepsis in children.

1.2 Location of research:

The study was conducted at pathology department of tertiary care hospital, Pakistan institute of medical sciences (PIMS) Islamabad providing specialized diagnostic and pediatric facilities.

1.3 Duration of research:

After approval from **Ethical Committee**, the study was conducted from December 2025 to May 2026.

2. Sample Size Calculation

In this study, the sample size was calculated using the **WHO calculator.**

Taking the confidence level **95%(Z=1.96)** and expected proportion (p) as **0.219.**A margin of error 0.06 was chosen. Using these parameters, the estimated sample size was **183 pediatric** patients.

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3. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
● Children aged upto12 years were included ● Pediatric patients with a clinical diagnosis of sepsis who were subjected to blood culture and relevant laboratory investigations ● Patients whose parents or guardians provided informed consent	• Patients who received antibiotic therapy prior to sample collection that may significantly alter culture results

4. Study Participants

All pediatric patients who fulfilled the inclusion criteria were participated in the study after obtaining informed consent from their parents or legal guardians. Patients were enrolled from various departments, including the Neonatal Intensive Care Unit (NICU), pediatric wards, and other inpatients units of Pakistan Institute of Medical Sciences (PIMS), Islamabad. Each enrolled patient was assigned a unique identification number to ensure proper documentation, registry management and confidentiality. The patients were then systematically registered, and their relevant demographic and clinical information was documented using a structured data collection form. This included variables such as age, gender, name, presenting complaints, clinical signs and symptoms (e.g., fever, lethargy, poor feeding), and provisional diagnosis made by the attending physician. A total of 183 patient records were collected in this study.

Furthermore, complete and detailed medical history was acquired, which includes history of antibiotic use, hospitalization, and underlying medical conditions. Information related to unit of admission and duration of stay in hospital was also documented to provide a complete clinical profile of each participant.

Data Collection Procedure

Data collection was carried out using a structured and standardized proforma, ensuring uniformity across all participants.

Clinical Assessment

Upon admission, each patient underwent a detailed clinical evaluation. Vital signs such as temperature, heart rate, and respiratory rate were recorded systematically. Additionally, clinicians assessed early warning indicators, including, changes in mental status, Poor feeding in infants and Signs of respiratory distress Circulatory abnormalities.

Laboratory Integration

Laboratory data were extracted from the hospital's information system. Blood samples were collected in yellow-top serum vials from enrolled patients to measure CRP levels. Additional blood samples were collected in EDTA tubes to measure the total leukocyte count and platelet count by using Hematology analyzer (Mindray).

Microbiological Tracking

Each patient's blood cultures were followed from the point of sample collection until the final laboratory reports were issued. This process includes monitoring the incubation process of blood culture samples, Recording the time to culture positive, Identifying the isolated microorganisms and documenting the antimicrobial susceptibility profiles.

5. Laboratory Procedures

5.1. Blood Culture Collection and Inoculation

Blood culture samples were collected under strict aseptic conditions to avoid contamination. After proper patient identification, a suitable venipuncture site was selected and disinfected using 70% alcohol and allowed to dry completely.

A sterile syringe was used to collect an appropriate volume of blood, approximately 1-3 ml in pediatric patients. The sample was

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immediately inoculated into sterile blood culture bottles after disinfecting the bottle septum, maintaining the recommended blood-to-broth ratio.

The inoculated bottles were properly labeled and promptly transported to the microbiology laboratory. Samples were incubated at 37℃ and monitored for microbial growth. Culture bottles were placed in the Versa Trek, an automatic blood culture instrument, to detect Positive cultures.

5.2. Culture Media:

Blood cultures were inoculated in culture bottles such as pediatric aerobic bottles (yellow or pink cap) that support the growth of microorganisms with nutrients and supplements. Then bottles were placed into Versa TREK an automated blood culture instrument and incubate for 5 days at 37℃.

5.3 Identification of pathogens

Once the culture was found to be positive, the we inoculate it into agar such as MacConkey agar, Blood agar, and Chocolate agar. These media are for selective growth and identification of organisms. Then after 24 hours we were read the plates and identify the organisms that are grown on agar plates.

5.4 Biochemical Testing

Identification was confirmed through following tests such as Catalase and Coagulase test and Oxidase test. These tests are useful for identifying species of bacteria.

5.5 Antimicrobial Susceptibility Testing (AST)

All tests were performed under **Kirby-Bauer Disc Diffusion method,** as per the Clinical Laboratory Standards Institute (CLSI)

5.6 Interpretation

Zone of inhibition was measured and written as sensitive, intermediate and resistant.

6. Statistical Analysis:

Data were analyzed using IBM SPSS Statistics version 23. Descriptive statistics, including means, standard deviations, frequencies, and percentages, were calculated to summarize demographic variables such as age, gender and clinical characteristics. The Chi-square test was employed to examine associations between categorical variables, specifically the types of pathogens isolated and their multidrug resistance status, as well as to analyse antibiotic susceptibility patterns across different organisms. For continuous laboratory parameters, including C-reactive protein (CRP) levels, total leukocyte count (TLC), and platelet count, independent samples t-tests were conducted to compare values between multidrug-resistant (MDR) and non-MDR sepsis groups. Statistical significance was determined at a p-value threshold of less than 0.05, with all tests performed as two-tailed to account for differences in either direction

RESULTS

In this study, 183 patients were enrolled. Out of which, male participants were 94 (51%) and female participants were 89 (49%), indicating an almost equal representation of both genders.

The study participants ages ranged from 1 month to 12 years old, The mean age was 2.55 ±2.76 in male participants while that of female participants was 2.48±2.88.For hematological parameters, the mean Total leukocyte count was 13.25±11.52 in male participants and 13.74±10.20 in female participants with p-value(p=0.780) while the mean of platelet counts were 214.8±134.8 in male participants and 210.5±133.6 in females with p-value (p= 0.838). The mean CRP level of 47.69±69.00 in male subjects and 46.09±85.43 in female subjects with p-value (p= 0.903). The detailed baseline characteristics are presented in table 01.

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Table 01: Characteristics of the participants

Parameters	Male	Female	Total	P-Value
Gender, n (%)	93(50.8)	90(49.2)	183(100)	--
Age, mean±SD	2.55±2.76	2.48±2.88	2.52 ±2.81	0.876
TLC, mean±SD	13.25±11.521	13.74±10.205	13.5 ±10.8	0.780
Platelet Count , mean±SD	214.8±134.8	210.5±133.6	212±133.8	0.838
CRP, mean±SD	47.69±69.000	46.09±85.430	46.8±77.4	0.903

n; number, SD; Standard Deviation

Microorganisms isolated from the samples are shown in Figure 02. The majority of samples, 66%, yielded no growth (NG). The most common isolate among culture-positive samples was *Salmonella species* (14%), followed by *Klebsiella pneumoniae* (6%), *Pseudomonas aeruginosa* (5%), and *Enterobacter species* (3%), *Acinobacter species* (2%).

The remaining isolates were much less frequent, comprising only 1% each. They are listed as *Streptococcus species*, *Staphylococcus aureus*, *Methicillin-resistant Staphylococcus aureus*, *Escherichia coli*, *Enterococcus species*.

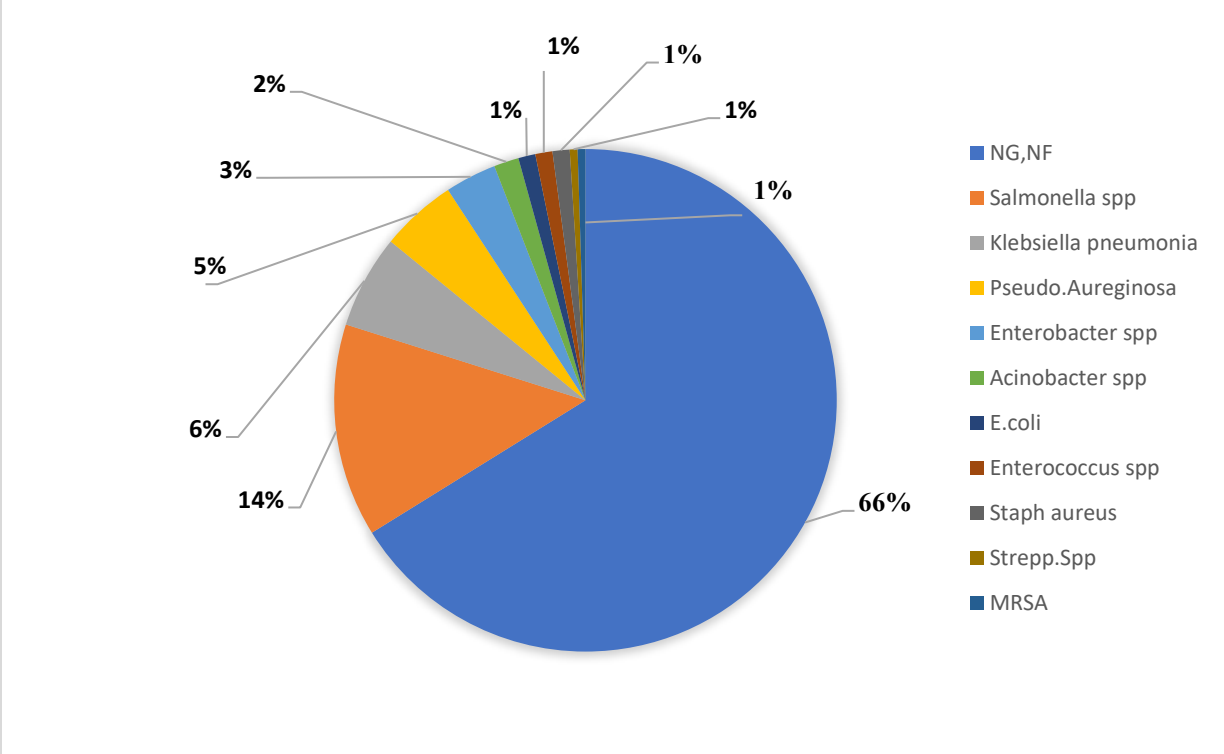

Figure 02: Percentage distribution of organisms isolated in clinical samples

The susceptibility profiles of the Gram-negative isolates were noted, including *Salmonella species*, *Pseudomonas aeruginosa*, and *Escherichia. Coli*. With up to 22 isolates evaluated in specific antibiotic panels, *Salmonella Spp.* was the most commonly isolated Gram-negative bacteria with upto 26(14%) of isolates. The most effective drugs for *Salmonella spp.* were azithromycin and

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imipenem which produced sensitivity rates of 95.45% and 95.23%, with p-values (P<0.001 and P=0.002). Azithromycin and imipenem had the greatest overall sensitivity rates among all Gram-negative isolates, at 80.76% and 70.21%, respectively. On the other hand, *Acinobacter Spp.* shown 100% resistance to almost all examined antibiotics, including Levofloxacin and Imipenem. Ciprofloxacin, which had an overall resistance rate of 95.45%, and Amoxicillin, which had an 84.21% resistance rate, both showed high levels of resistance. *Pseudomonas aerug.* shown 100% resistance to amoxicillin, however it was still comparatively susceptible to levofloxacin (87.5%) and amikacin (87.5%) as shown in table 02.

Table 02: Antibiotic Susceptibility Pattern of Gram-Negative Bacteria

Antibiotics	Susceptibility	E.coli	Pseudomonas Aerug.	Salmonella Spp.	Klebsiella Spp.	Enterobacter Spp.	Acinobacter Spp.	Total	P-Value
Amikacin	Sensitive	1(50)	7(87.5)		4(57.14)	2(40)	0(0)	14(58.3)	0.211
	Resistant	1(50)	1(12.5)		3(42.85)	3(60)	2(100)	10(41.66)	
	Total	2(100)	8(100)	--	7(100)	5(100)	2(100)	24(100)	
Imipenem	Sensitive	1(50)	6(85.71)	20(95.23)	4(40)	2(50)	0(0)	33(70.21)	0.002
	Resistant	1(50)	1(14.28)	1(4.76)	6(60)	2(50)	3(100)	14(29.78	
	Total	2(100)	7(100)	21(100)	10(100)	4(100)	3(100)	47(100)	
Ceftazidime	Sensitive	1(100)	6(75)		1(50)	1(20)	0(0)	9(47.36)	0.100
	Resistant	0(0)	2(25)		1(50)	4(80)	3(100)	10(52.63)	
	Total	1(100)	8(100)	--	2(100)	5(100)	3(100)	19(100)	
Azithromycin	Sensitive		0(0)	21(95.45)	0(0)	0(0)	0(0)	21(80.76)	<0.001
	Resistant		1(100)	1(4.545)	1(100)	1(100)	1(100)	5(19.23)	
	Total	--	1(100)	22(100)	1(100)	1(100)	1(100)	26(100)	
Levofloxacin	Sensitive	0(0)	7(87.5)		3(30)	2(40)	0(0)	12(42.85)	0.077
	Resistant	2(100)	1(12.5)		7(70)	3(60)	3(100)	16(57.14)	
	Total	2(100)	8(100)	--	10(100)	5(100)	3(100)	28(100)	
cefeprazone	Sensitive	1(100)	4(80)		3(50)	3(60)	0(0)	11(57.89)	0.367
	Resistant	0(0)	1(20)		3(50)	2(40)	2(100)	8(42.10)	
	Total	1(100)	5(100)	--	6(100)	5(100)	2(100)		

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Antibiotics	Susceptibility	E.coli	Pseudomonas Aerug.	Salmonella Spp.	Klebsiella Spp.	Enterobacter Spp.	Acinobacter Spp.	Total	P-Value
								19(100)	
Ceftrixone	Sensitive Resistant Total	1(100) 0(0) 1(100)	0(0) 3(100) 3(100)	6(31.57) 13(68.42) 19(100)	1(14.28) 6(85.71) 7(100)	1(20) 4(80) 5(100)	0(0) 2(100) 2(100)	9(24.32) 28(75.67) 37(100)	0.478
Tazobactam	Sensitive Resistant Total	1(50) 1(50) 2(100)	6(75) 2(25) 8(100)	--	3(37.5) 5(62.5) 8(100)	3(100) 0(0) 3(100)	0(0) 3(100) 3(100)	13(54.16) 11(45.83) 24(100)	0.119
Ciprofloxacin	Sensitive Resistant Total	--	0(0) 0(0) 0(0)	1(5) 19(95) 20(100)	0(0) 1(100) 1(100)	--	0(0) 1(100) 1(100)	1(4.54) 21(95.45) 22(100)	0.010
Cefixime	Sensitive Resistant Total	0(0) 1(100) 1(100)	1(50) 1(50) 2(100)	8(36.36) 14(63.63) 22(100)	0(0) 1(100) 1(100)	--	--	9(34.615) 17(65.38) 26(100)	0.580
Sulfamethoxazole	Sensitive Resistant Total	0(0) 1(100) 1(100)	--	12(52.17) 11(47.82) 23(100)	1(50) 1(50) 2(100)	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	13(46.42) 15(53.57) 28(100)	0.496
Colistin	Sensitive Resistant Total	--	2(66.66) 1(33.33) 3(100)	--	1(100) 0(0) 1(100)	0(0) 1(100) 1(100)	0(0) 2(100) 2(100)	3(42.85) 4(57.14) 7(100)	0.255
Amoxicillin	Sensitive Resistant Total	1(50) 1(50) 2(100)	0(0) 4(100) 4(100)	1(20) 4(80) 5(100)	1(16.66) 5(83.33) 6(100)	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	3(15.78) 16(84.21) 19(100)	0.276

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Gram-positive isolates, such as *Enterococcus species(spp)*, *Streptococcus species(spp)*, *Staphylococcus aureus(staph aureus)*, and *Methicillin-resistant staphylococcus aureus(MRSA)*, showed clear differences in resistance to various antibiotic classes based on their susceptibility patterns. The most commonly isolated Gram-positive bacteria were **Staph Aureus** and **Enterococcus species**, both of which showed up in several tests using a sample size of two. With a 100% sensitivity rate for all evaluated Gram-positive species, **linezolid** was shown to be the most appropriate successful medication for *Staph aureus* and *Enterococcus spp.* common isolates. With an overall sensitivity rate of 100% and 83.3% sensitivity for *MRSA* and *Staph Aureus*, vancomycin also shown great effectiveness; however, one isolate of *Enterococcus Spp.* displayed resistance. Imipenem, Ciprofloxacin, and Penicillin, on the other hand, showed 100% resistance in all isolates evaluated. The data for azithromycin, which was 100% efficient against *Strep Spp.* but 100% resistant by *Staph Aureus*, was noteworthy for its statistical significance (P<0.001) as shown in table 03

Table 03: Antibiotic Susceptibility Pattern of Gram-Positive Bacteria

Antibiotic	Susceptibility	Enterococcus Spp.	Strep Spp.	Staph Aureus	MRSA	Total	P-Value
imipenem	Sensitive Resistant Total	‒‒	‒‒	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	0(0) 2(100) 2(100)	0.002
Levofloxacin	Sensitive Resistant Total	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	‒‒	0(0) 3(100) 3(100)	0.077
Ceftriaxone	Sensitive Resistant Total	‒‒	1(100) 0(0) 1(100	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	0(0) 2(100) 2(100)	0.320
Tazobactam	Sensitive Resistant Total	‒‒	1(100) 0(0) 1(100)	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	0(0) 2(100) 2(100)	0.130
Ciprofloxacin	Sensitive Resistant Total	0(0) 1(100) 1(100)	‒‒	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	0(0) 2(100) 2(100)	0.010
Sulfmethoxazole	Sensitive Resistant Total	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	0(0) 2(100) 2(100)	0(0) 1(100) 1(100)	0(0) 5(100) 5(100)	0.496
Linezolid	Sensitive Resistant Total	2(100) 0(0) 2(100)	1(100) 0(0) 1(100)	2(100) 0(0) 2(100)	1(100) 0(0) 1(100)	6(100) 0(0) 6(100)	0.441
Azithromycin	Sensitive Resistant Total	‒‒	1(100) 0(0) 1(100)	0(0) 1(100) 1(100)	‒‒	1(50) 1(50) 2(100)	<0.001

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Antibiotic	Susceptibility	Enterococcus Spp.	Strep Spp.	Staph Aureus	MRSA	Total	P-Value
Vancomycin	Sensitive Resistant Total	1(50) 1(50) 2(100)	1(100) 0(0) 1(100)	2(100) 0(0) 2(100)	1(100) 0(0) 1(100)	5(83.3) 1(16.6) 6(100)	0.572
Erythromycin	Sensitive Resistant Total	0(0) 2(100) 2(100)	1(100) 0(0) 1(100)	0(0) 2(100) 2(100)	--	1(20) 4(80) 5(100)	0.112
Clindamycin	Sensitive Resistant Total	1(50) 1(50) 2(100)	0(0) 1(100) 1(100)	0(0) 2(100) 2(100)	1(100) 0(0) 1(100)	2(33.33) 4(66.66) 6(100)	0.345
Amoxicillin	Sensitive Resistant Total	1(100) 0(0) 1(100)	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	--	1(33.33) 2(66.66) 3(100)	0.276
Penicillin	Sensitive Resistant Total	0(0) 2(100) 2(100)	0(0) 1(100) 1(100)	0(0) 1(100) 1(100)	--	0(0) 4(100) 4(100)	0.199
Fosfomycin	Sensitive Resistant Total	1(100) 0(0) 1(100)	--	1(50) 1(50) 2(100)	--	2(66.66) 1(33.33) 3(100)	0.513

DISCUSSION

Pediatric sepsis continues to be a major worldwide health concern, especially in underdeveloped nations where the high prevalence of infectious illnesses is exacerbated by unsanitary environments and the fecal-oral mode of transmission. It is a potentially fatal illness when the immune system overreacts to an infection, necessitating quick detection using inflammatory and hematological markers. Here, total leukocyte count (TLC) and C-reactive protein (CRP) form the foundation of a "laboratory signature" for early identification.

C-reactive protein (CRP), an acute-phase protein, produced by liver in reaction to inflammatory cytokines during tissue damage and infection. It is frequently employed as a bio-marker for bacterial infection and systemic inflammation. In the present study ,elevated CRP values were seen, which indicate an active systemic inflammatory response in suspected sepsis patients . Standage and Wong (2011) published similar results, identifying CRP as a valuable bio-marker in pediatric sepsis It has been demonstrated that using TLC and CRP together increases the diagnostic sensitivity of early sepsis identification [23] Furthermore, despite its lack of specificity in differentiating between bacterial and non-bacterial causes, Pierrakos and Vincent (2010) pointed out that CRP is still one of the most commonly utilized inflammatory indicators in sepsis assessment.[24] These results validate CRP's function as an early warning sign of sepsis, especially in situations with limited resources when prompt clinical decision-making is required.

The host immunological response to infection is reflected in the total leukocyte count (TLC), where leucocytosis results from cytokine-mediated bone marrow activation. The mean TLC in this research was slightly higher, suggesting that the suspected sepsis patients had greater leukocyte counts. Similar results have been shown in study on pediatric sepsis, where TLC was utilized as a supporting diagnostic marker and was considerably higher in culture proven sepsis patients when combined with other bio-markers.[25]. These results imply that TLC is

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not a stand-alone diagnostic test, but rather a helpful early warning signal.

Blood culture remains the gold standard for determining the causal organisms in sepsis, although sample time, low bacterial load, and previous antibiotic administration all affect its sensitivity. The majority of the samples in this investigation showed no evidence of any bacterial growth. Prior antibiotic usage was found to be a significant contributing factor in other research that indicated similar high culture-negative rates[26] This reveals a serious diagnostic gap in pediatric sepsis, especially when it comes to early clinical treatment. In situations when culture data are not available, our results highlight the significance of early inflammatory indicators like CRP and TLC in supporting clinical diagnosis.

Salmonella species are Gram-negative enteric pathogens that are frequently linked to bloodstream infections, gastroenteritis, and typhoid fever, especially in areas with poor sanitation and contaminated water supplies. The most prevalent Gram-negative bacterium in the current study was *Salmonella species*. Feasey et al. (2012) observed similar results, emphasizing the prevalence of invasive non-typhoidal Salmonella infections in low- and middle-income nations[27] In endemic areas, these diseases continue to be a significant contributor to pediatric bloodstream infections. The study's high prevalence of *Salmonella spp.* is indicative of persistent environmental and sanitation-related transmission factors.

Pseudomonas aeruginosa and Klebsiella pneumoniae are opportunistic Gram-negative bacteria that are typically linked to multidrug resistance and hospital-acquired illnesses. Their existence in this study suggests sources of infection linked to health-care, which is in line with results published in the global sepsis literature[28].These organisms are therapeutically relevant in pediatric critical care settings because of their known capacity to develop resistance mechanisms.

Staphylococcus aureus is the main Gram-positive bacterium that causes Pneumonia, sepsis, and bloodstream infections Due to its multidrug resistance, *methicillin-resistant Staphylococcus aureus (MRSA)* is a major global problem.*Staph. aureus*, including *MRSA* strains, was recovered from Gram-positive organisms in the present study. According to Tong et al. (2015), *S. aureus* is one of the main causes of invasive bacterial infections globally, with rising resistance patterns in clinical settings.[29]These findings are consistent with previous research. The persistent problem of resistant Gram-positive pathogens in pediatric sepsis is highlighted by this.The results of this investigation indicated that Gram-negative bacteria were very resistant, especially to ciprofloxacin and ceftriaxone, although imipenem was highly sensitive. Linezolid was more sensitive to Gram-positive bacteria.Similar resistance patterns have been seen around the world, where an increase in multidrug resistance has been attributed to the usage of broad-spectrum antibiotics[30] Additionally, the World Health Organization has identified antibiotic resistance as a significant hazard to world health that calls for immediate stewardship efforts. [31] These results show that the study population contains organisms that are resistant to many drugs. Imipenem and linezolid's ongoing efficacy indicates their significance as last-resort medications; yet, their usage must be strictly controlled to stop the emergence of new resistance.

Overall, the results of this study show that CRP and TLC are helpful early warning signs of pediatric sepsis, especially when blood culture results are delayed or negative. Although culture is still the gold standard for diagnosis, its shortcomings in early detection emphases the need of supplementary inflammatory indicators. Treatment is made more difficult by the existence of multidrug-resistant pathogens, which highlights the importance of early identification, suitable empirical therapy, and antimicrobial stewardship initiatives

CONCLUSION

This study shows that higher C-reactive protein (CRP) and total leukocyte count (TLC) can be useful early lab signs for pediatric sepsis, and they also help with clinical choices especially when the blood culture results are still pending or end up

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being negative. At the same time, the apparent dominance of Salmonella spp. , Klebsiella pneumoniae , and Pseudomonas aeruginosa, plus the resistance seen against several usual antibiotics, points to a bigger and more serious risk: multidrug-resistant organisms are becoming more common in kids. Also, the very high sensitivity of imipenem for Gram-negative isolates and linezolid for Gram-positive ones suggests these agents are still effective options for treatment. Yet, even so, their use really should follow culture and susceptibility testing, so more antimicrobial resistance doesn't keep building up. Overall, these results underline the importance of better antimicrobial stewardship programs, ongoing routine surveillance of local resistance trends, and faster microbiological diagnosis, because that can improve the care and outcomes in pediatric sepsis. More multicenter studies, with bigger sample sizes, are advised to confirm these findings and to set up more standardized lab-based methods for early detection of multidrug-resistant sepsis in children.

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