Microbiological profile of Pediatric sepsis in a tertiary care teaching hospital of Central India

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Abstract:

Background: As per World Health Organization (WHO), sepsis is a leading cause of hospitalization and death in children in developing countries.The rapidly changing bacteriologic profile of childhood sepsis warrants the need for an ongoing review of the etiopathogenesis and drug susceptibility pattern of causative agents.

Objectives: To find out the etiological profile and antibiotic sensitivity pattern of the pathogens causing pediatric sepsis in a tertiary care teaching hospital of Central India.

Materials and Methods: This is a cross-sectional study. 194 clinical samples were collected from inpatients ranging in age from >1 month to 15 years. Isolation and identification of pathogens were done using Standard microbiological techniques. Antimicrobial susceptibility testing was performed by the standard Kirby Bauer disc diffusion method and interpreted as per CLSI guidelines.

Results:Out of the total 87 blood culture isolates majority were Gram Positive cocci (70%); with Staphylococcus aureus (53%) being the most predominant organism. The GPC isolates showed high susceptibility towards Vancomycin, Linezolid, Piperacillin tazobactam, and Tetracyclines. Methicillin resistance was reported in 38% of *Staphylococcus aureus* isolates. 40% of Enterococcus isolates exhibited High-level Aminoglycoside resistance.Enterobacteriaceae isolates exhibited high susceptibility towards Carbapenems, Colistin, Piperacillin tazobactum& Ceftazidime clavulanate. 40% of *E.coli* isolates & 50% of *K.pneumoniae* isolates were found to be Extended-spectrum β lactamase (ESBL) producers.

Non-fermenters exhibited high sensitivity towards Meropenem, Colistin, Piperacillin tazobactam, Amikacin.

Conclusions: The present study has provided much-needed information on the local antimicrobial profile of the prevailing pathogens causing pediatric sepsis which will be helpful in guiding their management.

Keywords: Pediatric sepsis; Septicaemia; Blood culture isolates; Antibiotic sensitivity pattern; Antimicrobial profile; Antibiotic resistance; Multidrug resistance.

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Introduction

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Due to non-homeostatic host response to infection with the evident systemic inflammatory process, the potential lethality is much more than the infection itself, and requires urgent recognition. Prompt diagnosis & appropriate antibiotic therapy are the key determinants of a positive outcomes in most cases(**Singer et al., 2016**).

As per World Health Organization (WHO), sepsis is a leading cause of hospitalization and death in children in developing countries.The mortality& morbidity related to sepsis is largely preventable with appropriate antimicrobial therapy. The emergence of multidrug-resistant strains is a serious problem in the management of sepsis. The rapidly changing bacteriologic profile of childhood sepsis warrants the need for an ongoing review of the etiopathogenesis and drug susceptibility pattern of causative agents **(WHO, 2015; Tiwari et al., 2013; Tariq et al., 2014)**.

WHO has put forth a global antimicrobial resistance (AMR) action plan. Surveillance and research pertaining to AMR are the key components of this action plan(**WHO,2015**).

Most of the infections in intensive care units are nosocomial. The longer is the hospital stay, the greater is the contact exposure of patients and the higher are the chances of contracting infections through the environment, staff, and procedures, which may end up in septicemia(**Kaur et al..2015**).

Sepsis management requires timely detection and identification of the blood-borne pathogens and their antibiotic sensitivity pattern. The rate of bloodstream infections in children ranges between 20-25% in developing countries. Blood culture remains the gold standard for laboratory diagnosis of bloodstream infections (BSIs) in infants and children(**Muhammad et al., 2020; Negussie et al., 2013; Vaghela et al., 2019**).

Sepsis in children is a life-threatening emergency and any undue delay in treatment maybe lethal. Initial signs of sepsis are mild and nonspecific. Therefore, in suspected cases, empirical antibiotic therapy should begin immediately without waiting for the culture and sensitivity reports. Early treatment and appropriate use of antibiotics minimize the risk of severe morbidity and mortality in sepsis **(Rao et al., 2013; Meremikwu et al., 2005; Mohammad et al., 2010)**.

Antimicrobial Surveillance is needed to implement appropriate timely interventions to restrict the spread of multidrug-resistant clones. Appropriate judicious selection and rotation/cycling of antibiotics guided by the knowledge of their local susceptibility profiles is of utmost importance.With the alarming increase in multidrug resistance, rendering many antimicrobial agents ineffective, clinicians need to remain updated with the susceptibility pattern of the circulating pathogens, for selecting the appropriate antimicrobials for empirical therapy(**Meremikwu et al., 2005; Ahirwar et al., 2018; Saraie et al., 2016; Sharma et al., 2018**).

The implementation of an antibiotic policy at the hospital level for the control

and restriction of injudicious antimicrobial use is imperative in managing nosocomial infections **(Dharmapalan et al., 2017)**.

This is the need of the hour to develop therapeutic protocols for tuning antibiotic therapy regimens to minimize the dissemination of antibiotic-resistant pathogens **(Sharma et al., 2018)**.

Surveillance for multidrug-resistant or pan-resistant strains should be conducted regularly on top priority, this being an issue of grave concern due to the lack of antibiotic options available to clinicians for the treatment of these life-threatening infections **(Kumari et al., 2021; Singh et al.,2017)**.

The uncertainty surrounding the clinical approach to the treatment of septicemia can be minimized by periodic epidemiological surveys of etiological agents and their antibiotic sensitivity patterns. Thus a rational protocol for sepsis management based on this knowledge will serve as a useful guide for the clinicians to initiate empirical as well as definitive antibiotic therapy**(Tariq et al., 2014; Negussie et al., 2013; Rao et al., 2013; Mehta et al., 2014; Jyothi et al., 2013;Khan et al., 2021)**.

In this region of North Madhya Pradesh, very few studies have been conducted to explore the microbiological profile of neonatal &pediatric sepsis cases.The present study aims to fill the gap in our knowledge on the current effectiveness of antimicrobials in the management of pediatric sepsis by analyzing the local antibiotic susceptibility profile of pathogens isolated from such cases.

Early identification of the causative pathogen and the start of appropriate treatment can significantly reduce morbidity, hospital stay, and mortality among sepsis cases. So, in the light of the above facts, a cross-sectional study was undertaken at tertiary care teaching hospital of Central India to find out the etiological profile and antibiotic sensitivity pattern of the pathogens causing childhood sepsis.

Materials and Methods

This cross-sectional study was conducted in the Dept. of Microbiology & Dept. of Pediatrics, of a tertiary care teaching hospital fromMay 2019 to October 2020, after obtaining clearance from the institutional ethics committee and the procedures followed were in accordance with the ethical standards of Helsinki declaration of 1975 as revised in 2000. Informed consent was taken from one of the guardians of each study subject.

Samples were collected from children ranging in age from >1 month to 15 years admitted in the wards & intensive care units of Dept. of Pediatrics at Associated District hospital,Datiafollowing all aseptic precautions. The sample collection & processing was a part of the routine diagnostic protocol for Management of Pediatric Sepsis and not exclusively for research purpose. Confidentiality regarding the identity and personal details of study subjects was maintained throughout the study.

Study Design: Cross-sectional Observational Study

Type of sampling: Purposive sampling

Duration: 18months (May 2019- October 2020)

Sample size: 87 blood culture isolates from 194 clinical samples

Inclusion Criteria: Children ranging in age from >1 month to 15 years, who were admitted to Pediatric wards &Pediatric intensive care unit (PICU)of Associated District Hospital Datia with the signs suggestive of sepsis **(Goldstein et al.,2005)**.

Exclusion Criteria: 1) Neonates were not included in this study. 2) Children who were already on antibiotics . 3) Children with fever for a durationof less than 5 days and with a known clinical conditions such as malignancies, tuberculosis, etc.

Before initiation of antibiotic therapy in children suspected of sepsis, blood samples for blood culture (3-5ml), were collected by peripheral venous puncture and inoculated immediately into 20ml.brain heart infusion broth with 0.025% sodium polyanethol sulphonate as an anticoagulant **(Hi-Media Lab. Mumbai).**

The inoculated broth was further incubated for 24 hrs. at 35-37 ^{o}C and then subcultured on Mac Conkey agar and 5% sheep blood agar. Just before subculture a Gram stain of the inoculated broth was performed and the result recorded. A provisional report was issued after the first subculture on 3rd day. A negative result was followed by the second subculture on the 5th day and if still negative then, the final subculture on the 7th day. If no growth was obtained in 3 subcultures sample was finally reported as negative. Any growth obtained was identified by colony characteristics, Gram staining, and standard biochemical tests. Isolation and identification of pathogens were done using Standard microbiological techniques **(ICMR, 2019;Collee and Marr, 2006; Collee et al., 2006; Koneman et al., 2006)**.

Antimicrobial susceptibility testing was performed by the standard Kirby Bauer disc diffusion method and interpreted as per CLSI 2018 guidelines **(ICMR, 2019; CLSI., 2018)**.

Screening for Methicillin-resistant *Staphylococcus aureus*(MRSA) strains using the Cefoxitindisc diffusion method was done and interpreted as per CLSI 2018 guidelines **(CLSI., 2018)**.

Zone size breakpoints of >22 mm were considered sensitive and < 21 was considered resistant. Suspected ESBL (extended-spectrum beta-lactamases) producing strains of *E.coli&Klebsiella pneumoniae*were subjected to a double disk synergy test as per CLSI 2018 guidelines**(CLSI, 2018)**.

High-Level Aminoglycoside resistance (HLAR) was detected in *Enterococcus spp.* isolates using High content Gentamycin disk (120µgm) diffusion method.

Zone of inhibition$\leq$ 6mm indicates High-level resistance and $\geq$ 10mm indicates lack of HLAR. Zone size of 7-9 mm is inconclusive**(CLSI, 2018)**.

Statistical analysis

All data was maintained in Microsoft Office Excel. All statistical analyses were carried out using Excel and appropriate statistical tools were applied wherever required.

Results

A total of 194 blood samples for culture were collected from the study subjects

during the study period yielding 87 bacterial isolates. The samples were collected from children in the age group ranging from >1month to 15 years. The blood culture positivity rate for males was slightly higher than females; the Male : Female positivity ratio was 1.2:1. Most of the sepsis cases were infants and toddlers. The majority of blood culture isolates (84%) were contributed from PICU (**Table.1**).

Table.1. Demographic profile of Sepsis cases

S.No.	Age group	No. of sepsis cases	Percentage
1.	1month - 11months	48	55
2.	1-5years	15	17
3.	6-10y	13	15
4.	>10 y	11	13
Gender			
1.	Male	48	55
2.	Female	39	45
	Total	87	

Out of 194 non-duplicate samples, 87 bacterial isolates were obtained. None of the blood cultures yielded polymicrobial growth. The overall isolation rate for Blood culture isolates was 44%. The majority of the test isolates were Gram Positive cocci (70%); with Staphylococcus aureus (53%) being the most predominant organism.Amongst 26 Gram-Negative isolates,the majority were Enteric coliforms (58%), followed by Non-fermenters. The organism-wise distribution of test isolates hasbeen depicted in **(Fig.1**).

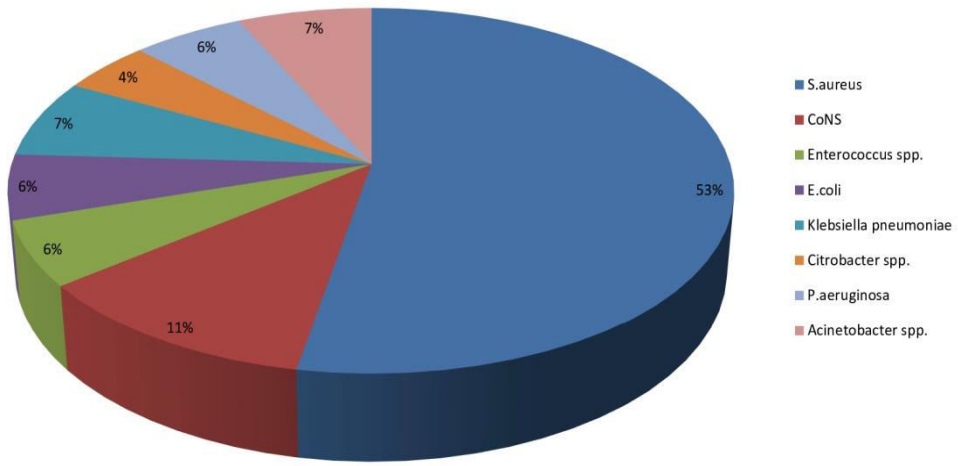

Fig.1: Organism wise distribution of test isolates

As evident from Table.2, S.aureus isolates exhibited remarkable sensitivity towards Vancomycin, Linezolid, Tetracyclin, Doxycyclin, Amikacin,Gentamicin,

Table. 2. Antibiotic susceptibility pattern of GPC isolates

S.No.	Antibiotic	No. of susceptible isolates n(%)		
		S.aureus	***CoNS***	***Enterococcus spp.***
1.	Amoxycillin clavulanate	11 (52)	8(80)	1(20)
2.	Ampicillin sulbactam	13 (62)	7(70)	-
3.	Azithromycin	4 (19)	2(20)	0
4.	Erythromycin	8 (38)	5(50)	0
5.	Clindamycin	14 (67)	7(70)	-
6.	Amikacin	17 (81)	9(90)	-
7.	Gentamicin (10)	16 (76)	5 (50)	-
8.	Gentamicin (High level)	-	-	3 (60)
9.	Ciprofloxacin (5)	11 (52)	7(70)	1(20)
10.	Levofloxacin	14 (67)	8(80)	2(40)
11.	Co-trimoxazole	10 (48)	5(50)	-
12.	Cefoxitin	9 (43)	7 (70)	-
13.	Tetracyclin	18 (86)	7 (70)	4(80)
14.	Doxycyclin	19 (90.5)	6(60)	4(80)
15.	Linezolid	20 (95)	10 (100)	4(80)
16.	Vancomycin	21 (100)	10 (100)	5(100)
16.	Chloramphenicol	-	-	4(80)
18.	Cefotaxime	-	-	-
19.	Ceftriaxone	-	-	-
20.	Meropenem	16 (76)	9 (90)	2(40)
21.	Piperacillin tazobactum	15 (70)	8 (80)	-

Meropenem, Piperacillin tazobactam and low sensitivity towards Azithromycin, Erythromycin & Co-trimoxazole.Coagulase Negative Staphylococcus spp.(CoNS) exhibited high sensitivity towards Vancomycin, Linezolid, Meropenem, Piperacillin tazobactam, Amikacin, Amoxycillin clavulanate, Clindamycin, Levofloxacin, and low sensitivity towards macrolides & Co-trimoxazole.Enterococcus spp. isolates exhibited high sensitivity towards Vancomycin, Linezolid, Tetracyclin, Doxycyclin, Chloramphenicol and very low sensitivity towards Macrolides, Amoxycillin clavulanate, Meropenem & Fluoroquinolones.40% of Enterococcus isolates exhibited High-level Aminoglycoside resistance.

The GPC isolates showed high susceptibility towards Vancomycin, Linezolid, Piperacillin tazobactam, Tetracyclin&Doxycyclin. The gram-positive isolates except Enterococci exhibited modest sensitivity towards Levofloxacin & Meropenem. High resistance was observed towards Macrolides (Azithromycin, Erythromycin), Ciprofloxacin, and Co-trimoxazole.

Amongst GPC isolates 41% (25) were found to be Multidrug-resistant.Methicillin resistance was reported in 38% of *Staphylococcus aureus* isolates (MRSA) and 30% of CoNS isolates (MRCoNS).40% of Enterococcus isolates exhibited High-level Aminoglycoside resistance.

As depicted in (**Table.3**), *E.coli* & *Klebsiella pneumoniae* isolates exhibited remarkable sensitivity towards Carbapenems, Colistin, Piperacillin tazobactam, Levofloxacin, Ceftazidime clavulanate, and Cefotaxime clavulanate.In addition to it, *E.coli* isolates also exhibited high sensitivity towards Tobramycin.

Table. 3: Antibiotic susceptibility pattern of Enterobacteriaceae isolates

S.No.	Antibiotics	No. of susceptible isolates n(%)		
		E.coli (5)	*Klebsiella pneumoniae (6)*	*Citrobacter spp.*(4)
1.	Amikacin	3 (60)	3 (50)	2(50)
2.	Gentamycin	2 (40)	2 (33)	2(50)
3.	Amoxycillin clavulanate	3(60)	2 (33)	-
4.	Ceftazidime	3(60)	3(50)	2(50)
5.	Ceftazidime Clavulanate	4(80)	5(83)	-
6.	Cefotaxime	2(40)	2(33)	3(75)
7.	Cefotaxime Clavulanate	4(80)	4(67)	-
8.	Ceftriaxone	3(60)	2(33)	3(75)
9.	Cotrimoxazole	2(40)	1(17)	0
10.	Ciprofloxacin	3(60)	3(50)	2(50)
11.	Levofloxacin	4(80)	4(67)	3(75)
12.	Tobramycin	4(80)	1(17)	-
13.	Meropenem	5(100)	5(83)	4(100)
14.	Imipenem	5(100)	5(83)	4(100)
15.	Piperacillin tazobactam	4(80)	5(83)	4(100)
16.	Colistin	5(100)	6(100)	4(100)

E.coli isolates displayed very low sensitivity towards Gentamicin, Cefotaxime, and Co-trimoxazole. *Klebsiella pneumoniae* isolates exhibited low susceptibility towards Co-trimoxazole, 3rd Generation Cephalosporins (3GC), and Amoxycillin clavulanate.

*Citrobacter spp.*isolates exhibited high susceptibility towards Carbapenems, Colistin, Piperacillin tazobactam, Levofloxacin & 3GC (**Table.4**).

Multidrug resistance was seen in 46.7% of Enterobacteriaceae isolates.40% of *E.coli* isolates & 50% of *K.pneumoniae* isolates were found to be ESBL producers.

As depicted in (**Table.4**), *Pseudomonas aeruginosa* isolates exhibited high sensitivity towards Meropenem, Colistin, Piperacillin tazobactam, Amikacin.

Acinetobacter spp. exhibited high susceptibility towards Meropenem, Colistin, Piperacillin tazobactam, Tobramycin and very low sensitivity towards Amoxycillin clavulanate, 3rd& 4th generation Cephalosporins and Co-trimoxazole.64% of Non-fermenter isolates were found to be multidrug-resistant.

Table. 4. Antibiotic susceptibility pattern of Non-fermenter isolates

S.No.	Antibiotics	No. of susceptible isolates n (%)	
		P.aeruginosa(5)	***Acinetobacter spp.(6)***
1.	Amikacin (30)	4(80)	4(67)
2.	Gentamicin (10)	3(60)	4(67)
3.	Cefepime (30)	3(60)	2(33)
4.	Ceftazidime (30)	3(60)	1(17)
8.	Ceftriaxone (30)	-	1(17)
11.	Amoxycillin clavulanate	-	2(33)
12.	Piperacillin tazobactum	4(80)	5(80)
13.	Ciprofloxacin (5)	3(60)	3(50)
14.	Cotrimoxazole	-	-
16.	Meropenem	5(100)	5(80)
17.	Aztreonam	3(60)	-
18.	Colistin	5(100)	6(100)
19.	Tobramycin	3(60)	5(80)

Discussion

In our study,the blood culture positivity rate for males was slightly higher than for females. This male preponderance was also reported by other researches **(Kumari et al., 2021; Biswas et al., 2021; Vaghela et al., 2019; Sharma et al., 2018; Kaur et al., 2015; Tiwari et al., 2013)**.

The overall blood culture positivity rate in our study was 44% which is in line with a similar study by Prabhu K et al.**(Prabhu et al., 2010)**.

As against our findings; Biswas et al, Kaur et al and Dharmpalan et al reported blood culture positivity rates around 35%, and other studies reported even lower rates.**(Biswas et al. ,2021; Kaur et al., 2015; Dharmpalan et al., 2017)**.

In our study majority of isolates were Gram-positive cocci and *S.aureus*emerged as the most common isolate followed by *CoNS* as in similar studies by Kaur P et al, Prabhu K et al and Dharmpalan D et

al.(**Kaur et al., 2015; Prabhu et al., 2010; Dharmpalan et al.,2017**).

Although *CoNS* when isolated from blood cultures are often considered as skin contaminants repeated isolation of *CoNS*and its clinical correlation suggests a significant threat. In a number of similar studies, *CoNS* had emerged as a predominant organism and a well-described pathogen amongst Gram-positive isolates even surpassing *S.aureus*.

In the present study Gram-negative isolates were mainly comprised of Enteric coliforms(Enterobacteriaceae isolates) and Non-fermenters, the former being predominant.This finding is in accordance with the similar studies **(Pal et al., 2016; Dharmpalan et al., 2017; Kaur et al., 2015; Sharma et al., 2018; Tiwari et al., 2013;Vaghela et al., 2019)**

In this study,*S.aureus*&*CoNS*isolates exhibited high sensitivity towards Vancomycin, Linezolid, Tetracyclines, Amikacin, Levofloxacin, Meropenem, Amoxycillin clavulanate & Piperacillin tazobactam. Other studies reported similar findings (**Dharmpalan et al., 2017; Kaur et al. ,2015;Prabhu et al., 2010; Sharma et al., 2018; Reddy et al., 2017**).

We reported 38% of *Staphylococcus aureus*isolates as MRSA.A similar trend regarding Methicillin-resistant strains was observed in various studies **(Dharmpalan et al., 2017; Sharma et al., 2018; Rose et al., 2014; Tiwari et al., 2013; Vaghela et al., 2019; Muhammad et al., 2020; Negussie et al., 2013)**.

Studies by the Indian Network for Surveillance of Antimicrobial Resistance (INSAR) group, India reported a 41% prevalence of MRSA(**INSAR, 2013**).A similar study by Kaur P et al reported 61% of *S.aureus* isolates as methicillin-resistant. MRSA is emerging as a notorious pathogen and one of the leading causes of ventilator-associated pneumonia in PICUs(**Kaur, 2015**).

In our study high level of aminoglycoside resistance was reported in 40% of Enterococcus isolates which also exhibited multi-drug resistance.Like our study Choukhachian et al., and Dadfarma et al., also reported a higher prevalence of multi-drug resistance among the HLAR isolates compared to the other isolates(**Choukhachian et al., 2018; Dadfarma et al. ,2018**).

Our study reported Multidrug resistance in 41% of gram-positive isolates like a similar study by **Vaghela et al. (2019)**.

The majority of gram-positive isolates including MRSA & MDR strains exhibited high susceptibility towards Linezolid & Vancomycin. This finding is in accordance with the other similar studies **(Dharmpalan et al., 2017; Sharma et al., 2018; Rao et al., 2013; Rose et al., 2014)**. In addition to it, Sharma et al also reported modest susceptibility towards Tigecyclin& Teicoplanin in MRSA strains **(Sharma et al., 2018)**.

In addition to these reserve drugs, our study has also reported high sensitivity of gram-positive isolates towards Tetracyclin & Doxycyclin. Similar findings were also reported **(Jyothi et al., 2013)**.

Like many similar studies, our study reported high susceptibility of Enterobacteriaceae isolates towards Carbapenems, Colistin, Piperacillin tazobactum&Ceftazidime clavulanate (**Kaur**

et al. ,2015; Vaghela et al. ,2019; Khan et al., 2021; Prabhu et al., 2010).

The increasing resistance of gram-negative isolates towards 3GC, Fluoroquinolones, Co-trimoxazole & Amoxycillin clavulanate which are amongst commonly prescribed drugs in clinical settings is a matter of grave concern. This is also evident in our study as in many other similar studies (**Tariq et al., 2014; Sharma et al., 2018**).

Cephalosporins esp. 3GC are being prescribed empirically as first-line drugs to more than half of the pediatric patients in India. This injudicious and rampant use has led to the emergence of high levels of resistance towards 3GC amongst Gram-negative isolates in pediatric BSI many of which are turning out as ESBL producers (**Muhammad et al., 2020; Vaghela et al., 2019; Rao et al., 2013; Dharmpalan et al., 2017; Kumari et al., 2021; Khan et al., 2021; Prabhu et al., 2010; Ramesh et al., 2012**).

40% of *E.coli* isolates& 50% of *K.pneumoniae* isolates were found to be ESBL producers. Likewise,many similar studies too reported a high prevalence of ESBL producing Enterobacteriaceae isolates (**Tiwari et al., 2013; Tariq et al., 2014; Kaur et al., 2015; Muhammad et al., 2020; Vaghela et al., 2019; Prabhu et al., 2010; Pal et al., 2016**). Muhammad et al reported a very high prevalence of ESBL producers amongst Enterobacteriaceae with all the *K.pneumoniae* and *Enterobacter spp.* isolates exhibiting this trait(**Muhammad et al., 2020**).*Non-fermenters* exhibited high sensitivity towards Meropenem, Colistin, Piperacillin tazobactam, Amikacin but low sensitivity towards Amoxycillin clavulanate, 3rd& 4th generation Cephalosporins, and Co-trimoxazole.This finding is in accordance with the other similar studies (**WHO, 2015;Vaghela et al., 2019; Khan et al., 2021; Biswas et al., 2021; Pal et al. 2016**).

In our study Multidrug resistance was seen in 41% of Gram-positive isolates, 46.7% of Enterobacteriaceae isolates, and 64% of Non-fermenters. Some of the recent studies have reported a very high prevalence of Multidrug resistance amongst Gram-negative isolates(**Muhammad et al., 2020; Negussie et al., 2013; Vaghela et al., 2019**). Kumari et al reported multidrug resistance in all the isolates of *Klebsiella pneumoniae&Acinetobacter spp*.(**Kumari et al., 2021**).

Overall multidrug resistance was seen in 47% of all blood culture isolates in our study which is lower than other similar studies (**Tariq et al., 2014; Kaur et al., 2015; Muhammad et al.,2020; Negussie et al., 2013; Kumari et al., 2021; DeNIS, 2016**).

Emerging multidrug resistance amongst pathogens is making the choice of antibiotics for the management of pediatric sepsis extremely difficult and threatens the return of the pre-antibiotic era in Indian healthcare settings.A relatively slow pace of developing newer antibiotic molecules accompanied by the rapidity in developing drug resistance are major areas of concern(**Kumari et al., 2021; Singh et al., 2017; Mehta et al. ,2014**).

This rapidly increasing multidrug resistance in common pathogens is raising the possibility of cross-transmission of mobile genetic elements able to jump across

genera, including commensals(**Muhammad et al., 2020**; **Pal et al., 2016**).

Sepsis can be fatal if not treated promptly in the early stages. Appropriate and timely interventions to identify and treat sepsis have been shown to reduce this mortality.Blood culture is still one of the most important diagnostic modalities available for the prompt and accurate diagnosis of bloodstream infections in children. In the management of pediatric sepsis, empirical antibiotic therapy must be precisely according to the locally prevalent spectrum of etiological agents and their antibiotic sensitivity pattern.Formulating an appropriate empirical therapy on the basis of the regional & institutional antimicrobial profile of the prevailing pathogens is a prerequisite for the effective management of pediatric sepsis cases(**WHO, 2015; Saraie et al., 2016; Singh et al., 2017; Mehta et al., 2014; Sawhney et al., 2017**).

The increasing prevalence of multidrug resistance, MRSA, HLAR & ESBL is a warning signal and stresses the need for regular monitoring of the etiological and antimicrobial profile of these life-threatening infections affecting the most vulnerable group of our population i.e.children **(Negussie et al., 2013)**.

To combat the menace of increasing Resistance towards commonly used antibiotics few antibiotic utilization strategies relevant to the current scenario are to reintroducing older antibiotics back into practice, combination therapy, antibiotic restriction, antibiotic cycling, and timely de-escalation of the high-end antimicrobials to reduce the antimicrobial(**Kumari et al., 2021**; **Khan et al., 2021**; **Prabhu et al., 2010**; **Sawhney et al., 2017**).

Pediatric septicemia can be prevented to a large extent by strict adherence by healthcare workers to the standard infection control practices, Environmental surveillance, Screening of healthcare providers, and using molecular epidemiology for investigating the clusters of infection with pan-resistant organisms. An antibiotic policy implemented in the hospital to prevent the irrational indiscriminate use of antibiotics thereby following the core principles of antibiotic stewardship would go a long way in helping decrease or prevent the emergence of resistance(**Kaur et al., 2015; Vaghela et al., 2019; Muhammad et al., 2020; Singh et al., 2017; Pal et al., 2016**).

Conclusion

The present study has provided much-needed information on the local antimicrobial profile of the prevailing pathogens causing pediatric sepsis which will help guide their management. Although our antimicrobial resistance results are alarming, the more ominous finding that has implications for policymakers is the risk of mortality attributable to culture-positive sepsis in general.

Regional guidelines for the management of pediatric sepsis can not be framed based on this institutional study which is a small-scale study on a limited study group and can not be generalized to the entire local population.

Exhaustive multicentric prospective studies using a standardized protocol, such as the DeNIS study, are required, which generate huge data on incidence, etiology,

antimicrobial profile, treatment, clinical outcomes, maternal & neonatal risk factors which are essential to give a more in-depth analysis of disease process, especially in relation to the clinical outcome.

But the data from such periodical AMR surveillance at the institutional level gives an overview of the problem, helps in formulating antibiotic policy as a strategy to develop a simple, easy-to-implement antimicrobial stewardship program and serves as a useful guide for the clinicians to initiate empiric antibiotic therapy.

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