Healthcare-Associated Infections in Neonates

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ABSTRACT

Background: Healthcare-associated infections occur during the process of care in a healthcare facility, and manifest 48 hours after admission. These vary widely in demographic characteristics, clinical and microbiological profile. The threat of antimicrobial resistance is a critical issue in healthcare. **Objective**: To assess the spectrum of different types of healthcare associated infections in neonates. **Materials and Methods**: A cross-sectional, descriptive study conducted from November 2023 to October 2024 at a tertiary care hospital in New Delhi. The study population consisted of neonates admitted in hospital and developing HAIs. Primary data was collected by interviewing the caregivers of neonates and medical records were reviewed to collect secondary information. **Results**: The study found that only three types of HAIs (BSI, VAP and CAUTI) were prevalent in neonates. The major risk factors were low birth weight, pre-term births, delivery by LSCS, multiple births, history of previous hospitalisation and underlying co-morbidities. Clinical presentation varied for each type of infection. The microbial profile showed a high prevalence of gram-negative organisms. Maximum anti-microbial resistance was encountered to penicillins and fluoroquinolones. **Conclusion**: BSI and VAP were the most common types of HAIs, with multiple risk factors, some of which were significantly associated with infection. Significant anti-microbial resistance was found.

INTRODUCTION

Often known as 'nosocomial' or 'hospital-acquired' infections, healthcare-associated infections (HAIs), are those that develop in a patient during the course of care in a hospital or any healthcare facility.(1) These infections are neither present nor incubating at the time of admission; usually being contracted after hospitalisation and typically appearing forty-eight hours after admission to the hospital.(2)

The occurrence of HAIs is the result of the failure of infection control, jeopardising the health of patients and complicating the disease trajectory, especially the critical cases.(1) Despite advancements in healthcare and public health, unfortunately, infections persist to plague the hospitalised patients, sometimes also affecting the hospital workers. HAIs represent one of the most commonly encountered adverse events during healthcare delivery, being a cause for considerable morbidity and mortality and, thus, a significant burden to health systems across the globe.

Globally, HAIs are unacceptable health events that tremendously impact the entire health system, from the patients to their caregivers to the healthcare facility itself. No health system in any country, no matter how sophisticated, can claim to be entirely ridden of these infections. As per the WHO Global Report on Infection Prevention and Control (2022), the odds of acquiring HAIs ranges from seven in HICs to fifteen in LMICs, for every hundred patients admitted in acute care hospitals. For patients admitted in intensive care units, up to 30% of them can be affected, with a much higher incidence (two to twenty times) in LMICs compared to HICs. This is particularly true for neonates, who are at a higher risk of acquiring it.(3)

The HAIs can be classified into broadly four categories based on the cause of infection:(4) Central Line-Associated Bloodstream Infection (CLABSI): when infection enters the body through a central line or peripheral cannula. It is confirmed when a central catheter has been inserted for more than two days and the infection cannot be attributed to any other site; Ventilator-Associated Pneumonia (VAP): when infection occurs in a person on invasive mechanical ventilation, such as endotracheal intubation, often with symptoms of worsening oxygenation; Catheter-associated Urinary Tract Infection (CAUTI): infection that occurs due to urinary catheterization in a patient. It occurs when an indwelling urinary catheter has been inserted and kept in place for more than two days; and Surgical Site Infections (SSI): infections that occur on or near the surgical wound; presenting up to thirty days after the procedure and affecting either the incision or deep tissue at the operation site.

HAIs differ widely in their demographic characteristics as well as clinical features and microbiological profile. Several factors can increase the probability of contracting these infections. While the factors are mostly modifiable and seldom non-modifiable, they can be related to the infectious agent, host and environment.(4) The most important risk factors for include underlying co-morbidities, invasive diagnostic and therapeutic procedures, irrational use of antibiotics, lack of proper healthcare infrastructure and facilities such as isolation units, inappropriate biomedical waste management and contaminated equipment. Transmission of infection occurs due to inadequate hand hygiene practices, making hand hygiene the foremost intervention for prevention.(5)

Depending on the patient's underlying conditions and health profile, the severity of infection and outcomes may vary.(6) The consequences of HAIs can be myriad and often dire, ranging from a prolonged stay in hospital to long-term complications such as disability and even premature mortality. This adds to the suffering for the patients and their caregivers, aggravating the social and psychological repercussions.(3)

A neonate, or new-born infant, is a child under twenty-eight days of age. The first twenty-eight days of life is the most crucial and vulnerable time for survival of newborn.(7) Neonates are at an increased risk of developing HAIs, due to their relatively compromised immunological capacity, thus contributing enormously to neonatal morbidity and mortality.(8) The rate of HAIs is directly proportional to both the degree of prematurity and low birth weight. There can be various risk factors for infections in neonates such as invasive diagnostic and therapeutic procedures, which exacerbate the already immature immune system along with poor barrier functions of the skin and gastrointestinal system. The micro-organisms responsible for infection in neonates may be their indigenous microbiota, present externally on the skin or internally in the nasopharynx or gastrointestinal tract, or might be organisms transmitted from visitors and caregivers.(9)

Late-onset sepsis is the infection acquired after seventy-two hours of life (except those caused by HSV or Group B streptococci). It is typically hospital-acquired, particularly in infants hospitalised from birth itself.(10) Care bundles streamline the practices and enable the reliable implementation of evidence-based solutions for infection control.(11) As infections are usually multifactorial, the approach of 'bundling' whereby care interventions are bundled in form of multiple interventions that operate synergistically, has excellent potential for preventing neonatal infections.(12)

Further adding to the woes is the threat of antimicrobial resistance, with the emergence of microbes resistant to commonly prescribed antibiotics, thus rendering the treatment ineffective. Mortality among patients infected with resistant micro-organisms is at least two to three times higher than among those infected with sensitive micro-organisms.(4) Anti-microbial Stewardship Program (AMSP) is a hospital-based program dedicated to alleviate the menace of AMR by improving antibiotic use. It can help improve the quality of patient care and safety by means of better infection cure rates, reduced treatment failures, and promoting appropriate prescriptions for therapy and prophylaxis. AMSP is imperative to sensitise healthcare workers on the rational and prudent use of anti-microbials.(13)

Aims & Objectives:

i. To assess the spectrum of different types of healthcare-associated infections (BSI, VAP, CAUTI, SSI) in neonates.
ii. To identify the various risk factors associated with the acquisition of these infections.
iii. To describe the clinical presentation and microbiological profile, including antimicrobial resistance patterns, of HAIs in neonates.

MATERIAL & METHODS

Study Type & Study Design: Cross-sectional, descriptive study
Study Duration: November 2023 to October 2024
Study Setting: A tertiary care hospital in New Delhi.
Study Population: Neonates developing HAIs during their hospital stay.
Sample Size Calculation: A convenience sampling method was used to include all neonates

developing HAI during the study period; 85 neonates were considered for the study.

Inclusion Criteria: neonates admitted to the neonatology department for preterm care or non-infectious co-morbidity and developing any of these after 48 hours of admission (as per STGs by Indian Academy of Pediatrics):(14) Bloodstream infections (BSI): Symptoms/signs of sepsis (fever, hypothermia, apnea, tachypnea, sclerema) with positive sepsis screen or positive blood culture; Pneumonia (VAP): Mechanically ventilated for more than 48 hrs with two or more abnormal chest radiographs and symptoms of worsening gas exchange; Urinary tract infection (CA-UTI): Positive urine culture, with or without clinical symptoms, where a urinary catheter was inserted for two or more days.

Exclusion Criteria: Neonates with infections present or incubating at the time of admission, or those whose caregivers did not provide consent.

Strategy for Data Collection: Primary data was collected by interviewing the caregivers of neonates regarding risk factors, disease progression, and symptomatology. Medical records of neonates diagnosed with HAI were reviewed to collect secondary information on the onset and type of infection, treatment provided, drugs prescribed, injections, consumables, and surgical or medical procedures performed.

Working Definition: As per the inclusion criteria, an HAI was defined as an infection occurring 48 hours after admission that was not present or incubating at the time of admission.

Ethical Issues & Informed Consent: Institutional ethics committee approval was obtained. Informed consent was taken from the caregivers of all enrolled neonates. Confidentiality of patient data was maintained throughout the study.

Data Analysis: After proper scrutiny, the collected data was entered into IBM SPSS Version 26 and analysed using descriptive and analytical techniques. As per the objectives of the study, univariate and multivariate tables were generated. The chi-square test was applied to find the association between variables. A p-value of <0.05 was considered statistically significant.

RESULTS

The profile of neonates revealed that males comprised 62.3% of the neonates, while females comprised the rest 37.7%. While 58.8% of neonates were outborn i.e. at some other healthcare facility, the rest 41.2% were born at the hospital under study itself. Out of all the admissions, 40% were due to neonatal asphyxia and neurological conditions, 28.2% due to respiratory disorders, 14.1% due to growth, development and metabolic issues, 11.8% had gastro-intestinal and hematological issues and 5.9% had other miscellaneous conditions. (Table 1)

Out of the four types of HAIs acquired by the neonates, 75.29% had bloodstream infections, 28.23% had ventilator-associated pneumonia and 4.7% had catheter-associated urinary tract infection. None of them had any surgical-site infection. (Figure 1)

For the various signs and symptoms of HAIs, poor feeding was the most prevalent symptom (51.8%) followed by lethargy (50.6%), respiratory distress (44.7%) and fever (42.4%). Symptoms like jaundice, tachycardia, hypothermia, hypotension, hypoglycemia, seizures, and abdominal distension occurred less frequently. (Figure 2)

There were various risk factors associated with HAIs. Term of pregnancy showed a significant association with BSI (p= 0.047) and VAP (p= 0.036). Birth weight showed a significant association with BSI (p= 0.011) and VAP (p= 0.001). Mode of delivery and multiple were not significantly associated with any of the infections. (Table 2)

Table 1: Profile of neonates (n=85)

Characteristic	Number	Percentage (%)
Sex		
Males	53	62.3
Females	32	37.7
Place of Birth		
Outborn	50	58.8
Inborn	35	41.2
Primary Diagnosis		
Neonatal Asphyxia & Neurological Conditions	34	40
Respiratory Disorders	24	28.2
Growth, Development & Metabolic issues	12	14.1
Gastro-intestinal & Hematological issues	10	11.8
Miscellaneous Conditions	5	5.9

Figure 1: Types of HAI (n=85)*
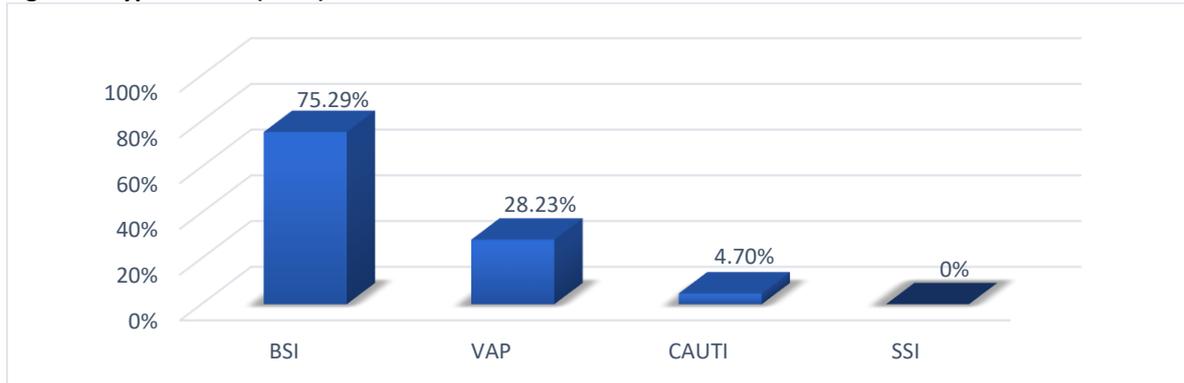
Multiple responses present, hence, sum may not be 85.

Figure 2: Clinical presentation of infection (n=85)*
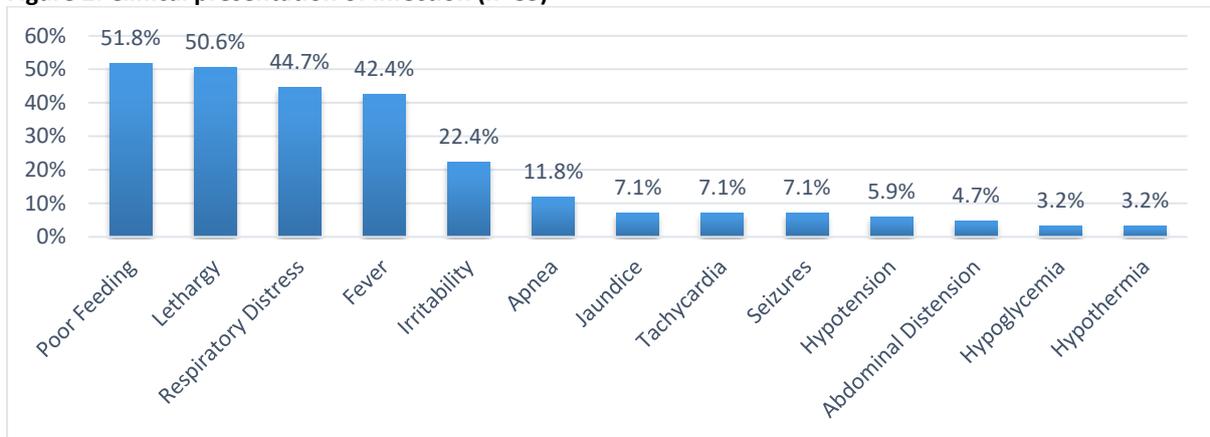
Multiple responses present, hence, sum may not be 100%.

Table 2: Association of HAIs with risk factors (n=85)

Characteristic	BSI (n)	p-value	VAP (n)	p-value	CAUTI (n)	p-value
Term of Pregnancy						
Pre-term	30	0.047*	17	0.036*	3	0.353
Term	34		7		1	
Post-term	0		0		0	
Mode of Delivery						
Vaginal	28	0.066	14	0.305	2	0.981
LSCS	36		10		2	
Multiple Births						
Single birth	55	0.212	22	0.540	3	0.403
Twin births	9		2		1	
Birth Weight						
Less than 1000g	7	0.011*	4	0.001*	0	0.533
1000-1499g	4		8		2	
1500-2499g	21		8		1	
2500g and above	32		4		1	

Significant p-value

For the high-risk factors that put them at risk for acquiring infection, 57.6% had a history of previous hospitalization while 42.4% had no prior hospitalization; 58.8% had one or the other underlying co-morbidities while 41.2% had none; and all 100% of the neonates were given antibiotics in the last 72 hours. Underlying co-morbidities was significantly associated with only VAP (p= 0.052). Previous hospitalizations and antibiotic use were not significantly associated with any of the infections. (Table 3)

Table 3: Association of HAIs with high-risk characteristics (n=85)

Characteristic	BSI (n)	p-value	VAP (n)	p-value	CAUTI (n)	p-value
Previous Hospitalization						
Yes	26	0.576	13	0.169	1	0.474
No	38		11		3	
Underlying Co-morbidities#						
Yes	36	0.403	18	0.052*	3	0.503
No	28		6		1	
Antibiotic Use						
Yes	64		24		4	
No	0		0		0	

Significant p-value   #Underlying co-morbidities: any congenital abnormality, birth defect, birth complication.

The association between the interventions done and the infection acquired was assessed. Invasive MV was significantly associated with BSI (p= 0.001) and VAP (p=0.001); non-invasive MV was significantly associated with BSI (p=0.002) and VAP (p=0.001), urinary catheter use was significantly associated with BSI (p= 0.001) and CAUTI (p=0.001). There was no significant association between central line use & peripheral line use and any of the HAIs. (Table 4)

Table 4: Association of HAIs with interventions done (n=85) #

| Intervention	BSI (n)	p-value	VAP (n)	p-value	CAUTI (n)	p-value
Central Line						
Yes	27	0.475	6	0.078	1	0.533
No	7		28		33	
Peripheral Line						
Yes	64	0.081	23	0.111	4	0.824
No	20		61		80	
Invasive MV						
Yes	13	0.001*	23	0.001*	2	0.567
No	18		8		29	
Non-invasive MV						
Yes	34	0.002*	24	0.001*	2	0.604
No	19		29		51	
Urinary Catheter						
Yes	0	0.001*	1	0.884	4	0.001*
No	4		3		0	

*#Multiple responses present, hence, sum may not be 85.   *Significant p-value*

The microbiological profile of infections was examined using the culture sensitivity reports that depicted the causative micro-organisms. While 77.6% of the infections were due to gram-negative bacteria, 22.4% were caused by gram-positive bacteria and 9.4% by fungi. (Figure 3)

Figure 3: Microbiological profile of HAIs (n=85) *
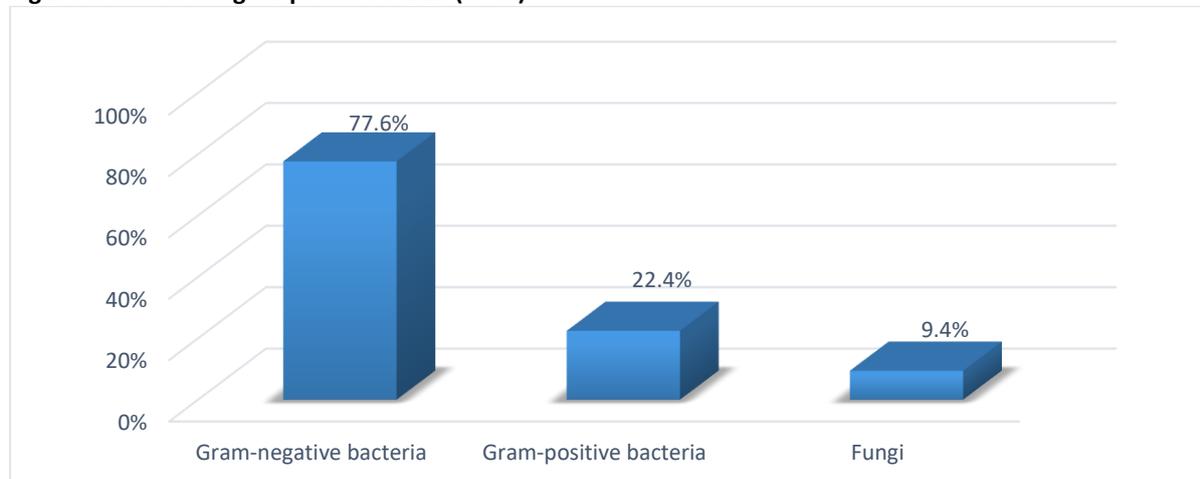
Multiple responses present, hence, sum may not be 100%

Klebsiella was the most common causative organism, accounting for 41.2% of all cases, followed by Staphylococcus in 16.5% cases. Acinetobacter, Pseudomonas, Candida, E. coli and Enterobacter each accounted for between 7.1% and 10.6% of cases. Enterococcus, Citrobacter, Proteus and Providencia were less common, accounting for 1.2% to 5.9% of the cases. (Table 5)

Table 5: Causative micro-organisms for HAIs (n=85) *

Micro-organism	Number	Percent (%)
Klebsiella	35	41.2
Staphylococcus	14	16.5
Acinetobacter	9	10.6
Pseudomonas	8	9.4
Candida	8	9.4
E. coli	7	8.2
Enterobacter	6	7.1
Enterococcus	5	5.9
Citrobacter	2	2.4
Proteus	2	2.4
Providencia	1	1.2

Multiple responses present, hence, sum may not be 100%

Beta-lactams were the most common (96.5%) antibiotics prescribed for the treatment of infections, followed by aminoglycosides and polymyxins (56.5%), other antibiotics like tetracyclines, fluoroquinolones and macrolides (16.5%) and anti-fungals (7.1%). (Figure 4)

Figure 4: Antimicrobials prescribed for HAIs (n=85) *
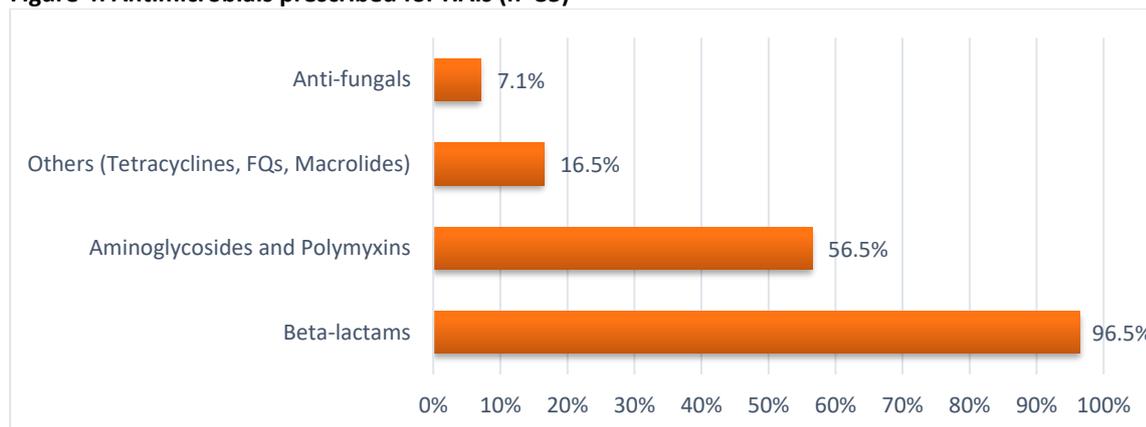
Multiple responses present, hence, sum may not be 100%

Antimicrobial resistance was encountered in many cases, based on the culture sensitivity reports. Klebsiella demonstrated resistance to penicillin (77.5%) and fluoroquinolones (47.5%). Pseudomonas showed resistance to penicillin (12.5%), cephalosporins (32.5%), and aminoglycosides (37.5%). E. coli exhibited resistance to penicillin (12.5%) and fluoroquinolones (47.5%). Acinetobacter showed high resistance to penicillin (12.5%), carbapenems (5%), cephalosporins (32.5%), and aminoglycosides (37.5%). Enterococcus showed resistance to penicillin (12.5%), carbapenems (5%), and aminoglycosides (37.5%). (Table 6)

Table 6: Antimicrobial resistance patterns (n=45[#])*

Anti-microbial	Klebsiella n (%)	Pseudomonas n (%)	E. coli n (%)	Acinetobacter n (%)	Enterococcus n (%)
Penicillin					
Amoxycillin	16 (40%)		4 (10%)	3 (7.5%)	2 (5%)
Ampicillin	15 (37.5%)	1 (2.5%)	4 (10%)	2 (5%)	1 (2.5%)
Carbapenem					
Meropenem	11 (27.5%)			2 (5%)	1 (2.5%)
Imipenem	9 (22.5%)		1 (2.5%)	1 (2.5%)	1 (2.5%)
Cephalosporin					
Cephalexin	6 (15%)		1 (2.5%)		
Ceftazidime	12 (30%)		1 (2.5%)	1 (2.5%)	1 (2.5%)

Cefepime			1 (2.5%)	
Aminoglycoside				
Gentamycin	19 (47.5%)		2 (5%)	2 (5%)
Amikacin				
Fluroquinolone	15 (37.5%)		1 (2.5%)	3 (7.5%)
Ciprofloxacin	13 (32.5%)	2 (5%)	2 (5%)	1 (2.5%)
Polymyxin				
Colistin	22 (55%)	2 (5%)	2 (5%)	2 (5%)
Sulphonamide				
Cotrimoxazole	2 (5%)	1 (2.5%)	1 (2.5%)	1 (2.5%)
Glycopeptide				
Vancomycin				1 (2.5%)
Tetracycline				1 (2.5%)

*Multiple responses present, hence, sum may not be 100%   *#Culture sensitivity reports not available for all*

DISCUSSION

The study reveals that the majority of neonates were males and admitted either due to neonatal asphyxia/ neurological conditions or respiratory disorders. This profile aligns with general neonatal ICU admissions, where respiratory and neurological issues are common. A study done by Tsai et al. (2014) found similar male predominance (61.5%) in NICU admissions and reported respiratory and neurological conditions as primary causes, similar to the findings in this study.(15)

For the risk factors, majority either had low birth weight (less than 2500g) or were pre-term births. There was a significant association of term of pregnancy and birth weight with BSI and VAP. Almost half were delivered by LSCS and majority had a history of previous hospitalisation and underlying co-morbidities. A study by Liu et al. (2019) confirmed a significant association between low birth weight and increased risk of BSI (p=0.009) and found similar rates of pre-term births (54.2%) associated with infections, aligning with the study findings.(16)

Only three types of HAIs were prevalent in neonates, with no SSI reported. Clinical presentation varied for each type of infection, with poor feeding being the most common symptom, followed by lethargy, respiratory distress and fever, suggesting that these are the probable symptoms for suspecting infection in neonates. It also underscores the challenge of detecting HAIs in neonates, as these symptoms are often non-specific, highlighting the need for routine screenings in high-risk cases. A study by Kannan et al. (2022) found similar rates of infections with CLABSI (25–30%), followed by VAP (20–25%), CAUTI (15%) and lastly SSI (11%).(5)

While multiple interventions were done in most of the neonates, invasive MV was significantly associated with BSI and VAP, non-invasive MV with BSI and VAP and urinary catheter use with BSI and CAUTI. A study done by Venmugil et al. (2018) found that vascular site infection is the most common HAI in the PICU, in accordance with the findings in this study.(8)

For the treatment, beta-lactams were the most prescribed drug, with piperacillin-tazobactam being the most prescribed antibiotic followed by meropenem. The microbial profile showed a high prevalence of gram-negative organisms, with Klebsiella species being the most common organism responsible for causing infection. The predominance of gram-negative infections is particularly concerning, as these pathogens are associated with severe outcomes in neonates, especially in the case of Klebsiella, where infections can be severe and difficult to treat. A study done by Salamati et al. (2006) showed the most common pathogenic organisms responsible for HAIs were Enterobacter (27%), Staphylococcus aureus (21%), Klebsiella (18%), E. coli (14%) and Staphylococcus epidermis (9%), similar to the causative organisms found in this study.(17)

There was maximum resistance to penicillin and fluoroquinolone in the antimicrobial patterns. Klebsiella and E. coli had similar resistance patterns and were found to be resistant to penicillin and fluoroquinolone, while Enterococcus exhibited resistance to vancomycin. Pseudomonas and Acinetobacter also had similar resistance patterns, showing resistance to penicillin, cephalosporin, and aminoglycosides. Klebsiella was found to be significantly resistant to carbapenems, while Acinetobacter and Enterococcus were resistant to a smaller extent. A study by Mathur et al. (2022) found that Klebsiella species (24·8%) were the most frequent organisms in bloodstream infections and Candida species (29·4%) in UTIs, similar to the findings in this study.(18)

CONCLUSION

The study delved into the profile of neonates contracting infection during their hospital stay, which shows a male preponderance, with several

risk factors such as low birth weight, pre-term birth, existing co-morbidities etc., some of them being significantly associated with the occurrence of infection. BSI and VAP were the most common types of HAIs found, with varying clinical presentation and association with the interventions being done. There was significant anti-microbial resistance to drugs like penicillin and fluoroquinolones, even last-line antibiotics like vancomycin, with few organisms sharing similar resistance patterns.

HAIs are an unintended consequence of the hospitalisation process. Patients seek to be cured of the illness for which they are admitted, but in the process, end up contracting another infection, which further prolongs the journey to recovery. Inter-sectoral collaboration is the need of the hour, where diverse stakeholders must come together and work towards finding solutions to tackle HAIs.

RECOMMENDATION

The threat of HAIs is a global concern, and best practices must be disseminated to help all nations overcome this burden. Robust surveillance systems should be in place to monitor trends and provide timely interventions. High-quality research is vital to get insights into the current scenarios and suggest possible solutions. Neonates are the most vulnerable group, and their care must be a priority for all healthcare facilities. The existing infrastructure should be ramped up using the latest technology equipment. An adequate workforce must be deployed for neonatal care, and dedicated resources should be allocated to ensure the smooth functioning of NICUs, wards, etc.

AMR is the silent pandemic that continues to plague all nations. There is an urgent need to prevent the emergence of superbugs that render all treatments ineffective and leave us with no remedies. AMSP needs to be implemented to ensure optimal and prudent use of antibiotics, and follow all the necessary steps to curtail the rise of antimicrobial resistance.

LIMITATION OF THE STUDY

First, the findings may not be generalizable to other settings, particularly primary or secondary care facilities in rural areas. Second, the convenience sampling method and relatively small sample size may limit the statistical power and precision of the estimates. Third, culture sensitivity reports were not available for all cases, which may have introduced bias in the patterns reported.

RELEVANCE OF THE STUDY

This study adds to the current knowledge by providing contemporary, real-world data on the spectrum of HAIs in neonates from an Indian tertiary care setting. It confirms the ongoing predominance of gram-negative infections and documents alarming rates of antimicrobial resistance. The findings can serve as a baseline for future multi-centric research and can help clinicians develop a high index of suspicion for HAIs based on specific clinical presentations.

DECLARATION OF GENERATIVE AI AND AI ASSISTED TECHNOLOGIES IN THE WRITING PROCESS
The authors haven't used any generative AI/AI assisted technologies in the writing process.

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