

# Pattern of microbial profile and their susceptibility pattern in a tertiary level neonatal intensive care unit, Dubai, UAE: 11 years surveillance study

## Abstract

**Introduction:** Neonatal sepsis is a global burden on the health and wellbeing of the neonates. It mounts too many neonatal mortality and morbidity. However, rational use of antimicrobial therapy and aggressive supportive management has modified the outcome over the past few decades. A good knowledge of locally prevalent microbes and antibiotics sensitivity pattern help in formulating antibiotics regimen.

**Methodology:** This study is a retrospective analysis of prevalent microorganisms isolated from various culture samples collected from neonates aged 0 - 90 days, suspected to have early or late onset neonatal sepsis. All the neonates were admitted to Neonatal intensive care unit (NICU) of Latifa Women and Children Hospital (LWCH) over an 11 year period (from January 2011 till December 2021). Descriptive analyses were used with results presented as proportions. Data were analyzed using Microsoft excel 2016 and online calculators.

**Results:** A total of 4849 microbial culture positive isolates were identified from our NICU. These isolates included samples taken from, blood, cerebrospinal fluid, endotracheal aspirates, throat/nasopharynx, urine, rectal, stool, eyes and superficial cultures. Gram-negative bacteria were isolated in 56.3% (n= 2730). Gram positive bacteria accounted for 43.7% (n=2119) of isolates. Most common isolated bacterial species were *Klebsiella pneumoniae* (15.7%), Coagulase Negative Staphylococcus (CONS) (14.6%), *Stenotrophomonas maltophilia* (11.5%) and *Pseudomonas aeruginosa* (11.1%). Among the multidrug resistant organism (MDRO), Extended spectrum beta lactamase (ESBL) *K. pneumoniae* (n=208, 4.3%) and Methicillin resistant staphylococcus aureus (MRSA) (n=145, 3%) are the predominant strain. Over the study period, there is a significant reduction in both gram positive and gram negative bacterias (n=1055 in 2011 to 226 in 2021).

**Discussion/conclusion:** The need of the hour is implementation of strict infection control measures and rationalized use of broad-spectrum antibiotics and continuous surveillance of emergence of MDROs. Regular tracking of the microbiological prevalence pattern kept us updated regarding prevailing organisms and emergence of MDROs. Our NICU antimicrobial policy modified in accordance with the surveillance data.

**Keywords:** neonates, sepsis, culture, microbiological profile, antibiotics

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## Introduction

Sepsis in the neonatal period till date remains the most dramatic and significant, yet avoidable cause of mortality and morbidity in the NICU (Neonatal intensive care unit). Rational use of antimicrobial therapy and aggressive supportive management has however proved to modify the outcome over the years. It is also observed that, an increasing number of neonates are now dying due to MDRO sepsis.<sup>1</sup>

Inherent handicaps of preterm and critically ill neonates, need of invasive devices, inappropriate use of antimicrobials, poor antimicrobial stewardship policies and ineffective hand hygiene are just few among the risk factors that facilitate transmission of microbes from animate and inanimate surfaces to cause blood stream infection.<sup>2</sup> Many outbreaks due to colonized microbes such as *Serratia*, *Klebsiella* and *Pseudomonas* have been reported in the neonatal units.<sup>2,3</sup> To face this seemingly insurmountable problem, NICUs worldwide needs to follow strict and mandatory infection-control principles.<sup>3</sup>

Outcome of neonatal sepsis depends on the type of microbe, site of infection, onset of sepsis and other risk factors.<sup>4</sup> The type of microbe incriminated for neonatal sepsis differs in different regions and geographical areas and also show significant changes in the same place

over time.<sup>5</sup> This variation in pattern is owing to antibiotic use pattern and life style changes.<sup>5</sup> Evolution of multidrug resistant organisms such as MRSA, ESBL, AMPC & carbapenemase producing microbes have achieved pandemic proportions.<sup>5</sup> Lack of data on local microbial profile and their antimicrobial sensitivity/resistance patterns and thus, reliance on data from different settings in other countries would definitely affect correct decision making in this readily preventable problem.<sup>5</sup>

Neonatal Intensive Care Unit (NICU) at Latifa Women and Children Hospital (LWCH) in Dubai, United Arab Emirates is a tertiary care level unit and is one of the largest referral facilities in the region. The unit admits both inborn and out born neonates. On an average annually > 5000 deliveries are conducted at LWCH and many of them are high risk pregnancy and referred from other hospitals in the region. Our NICU has 64 bed capacities and annual NICU admission exceeds 1000, most of them are preterm babies. Average occupancy rate remains very high all around the year and sometimes exceeds the bed capacity. Invasive and non-invasive ventilation, total parenteral nutrition, standard invasive procedures are provided routinely. Facilities of prevention & control of infection, local and central infection control task force team support the NICU.

Continuous surveillance of microbes and their susceptibility patterns in the NICU has seen an uptrend in the Middle Eastern region and few peer reviewed published articles.<sup>4,6-9</sup> In order to understand the prevalent microorganism and their susceptibility, data should be reviewed periodically to ascertain the choice of antimicrobials use. We therefore, present results of microbial profile and their susceptibility pattern at our Neonatal Intensive Care Unit over the past 11 years.

## Materials and methods

This study is a retrospective analysis of microorganisms isolated from various body fluids such as; blood, CSF, urine and culture taken from respiratory tract, gastrointestinal tract and genitourinary tract etc. from neonates aged 0 - 90 days, suspected to have early or late onset neonatal sepsis who were admitted to NICU of LWCH over a period of 11 years (January 2011 till December 2021). These cultures were taken based on clinical suspicion of sepsis raised by the attending neonatologist. If these were positive, they were temporally correlated with the clinical situation.

Samples were taken in a sterile manner from, blood, cerebrospinal fluid, urine etc. rectal and nasopharyngeal samples, or tracheal aspirates in intubated patients, were collected where indicated. Other supportive laboratory investigations such as hemogram including white cell count, absolute neutrophil count, platelet count, band cell count, immature to total neutrophil ratio, C- reactive protein and procalcitonin were also done to corroborate the diagnosis of neonatal sepsis. If different species were cultured in the same patient more than two weeks apart, they were considered as separate episodes. Phenotypically similar micro-organisms grown from body fluids and culture samples taken from other parts of the body were considered to be concordant.

## Laboratory methods

Blood culture was obtained under sterile precautions. One ml of blood by venipuncture was inoculated directly in blood culture bottle containing Tryptisoya and Thiogluconate growth media. Processing for blood culture was done with BD BACTEC system and the antibiotics sensitivity testing were conducted on the VITEK-2 platform. The presence of a positive culture was indicated by an audible alarm produced by blood culture system. MacConkey's media was used for subculture on day 1, 2, 3 & 7 of incubation. For cerebrospinal fluid (CSF) (0.2ml) cultures, centrifuged deposits were plated on the blood agar, MacConkey's media and chocolate agar. If multiple cultures obtained from the same infant, who grew identical organism with the similar antibiotic susceptibility, it was considered as a single case. Two consecutive positive blood cultures with CONS were required for the clinical diagnosis of sepsis.<sup>10</sup>

After thawing the transport swab, the sample was plated on MacConkey agar and blood agar with addition of ampicillin 16mg/ml and gentamycin 6mg/ml was added with Mueller-Hinton agar. The sample was then incubated for 24-48hrs at 37°C in air. Standard laboratory methods were used for each morphologically different colony types and were identified to species and genus level.<sup>11</sup>

Descriptive analyses were used with results presented as proportions. Data were analyzed using Microsoft excel 2016 and online calculators. This is retrospective collection of data; general consent was obtained during admission. The study is approved by Dubai Scientific Research Ethics Committee, Dubai Health Authority with reference number DSREC-10/2022\_07.

## Inclusion criteria

All the neonates admitted to NICU, Latifa Women and Children Hospital between January 2011 to December 2021.

## Exclusion criteria

We excluded the babies who were transferred from other Hospital to our NICU and culture positive within 5 days of admission.

## Results

During the study period starting from January 2011 until December 2021, there were 9835 admissions to the NICU. Of them 6626 were preterm (<37 weeks gestation) and 1526 were less than 28 weeks gestation. Over the 11 years of study, 4849 microbial culture positive isolates were identified from the NICU. These isolates included samples taken from, blood, cerebrospinal fluid, endotracheal aspirates, throat/nasopharynx, urine, rectal, fecal, eyes, and other wound cultures.

Prevalence of positive cultures is noted to be declining steadily during the study period, from 1055 isolates in 2011 to 226 in 2021 with occasional fluctuations. This is correlated with the increase number of total NICU admissions and increase numbers of preterm admissions. During the study period, isolation of Gram-negative bacteria (n= 2730, 56.3%) were more compared to Gram positive bacteria (n=2119, 43.7%). Most common isolated bacterial species were Klebsiella pneumoniae (15.7%), Coagulase Negative Staphylococcus - CONS (14.6%), Stenotrophomonas maltophilia (11.5%) and Pseudomonas aeruginosa (11.1%). Although, preponderance in growth of Gram-Negative Bacilli was observed, rate of isolation of both gram-negative bacilli (GNB) and gram-positive cocci (GPC) were showing declining trend (Table 1, Figure 1). Among GNB, most common isolates grew K. pneumoniae (n=758, 15.7%), S. maltophilia (n=557, 11.5%) and P. aeruginosa (n=536, 11.1%). Growths of other GNB like, Serratia spp., A. baumannii, Enterobacter spp. and Citrobacter spp. E. coli, etc. were observed less frequently (combined n = 879, 18.2%). Among gram-positive cocci, CONS (n=704, 14.6%), Staph aureus (n=386, 8%) and E. faecalis (n=214, 4.4%) were the most common organisms. (Table 1) GBS, on the contrary, was rarely isolated (n=33, 0.7%). Candida spp. was most common fungi isolated with preponderance of Candida albicans. Among the non albicans, C. glabrata, C. kruseii and C. parapsilosis were rarely grown. ESBL producing K. pneumoniae was noted to be the most common MDRO (n= 208, 4.3%). There is a steady decline in number of MRSA over the year (Table 1, Figure 2) and its number accounts for 3% (n=145) of total isolates.

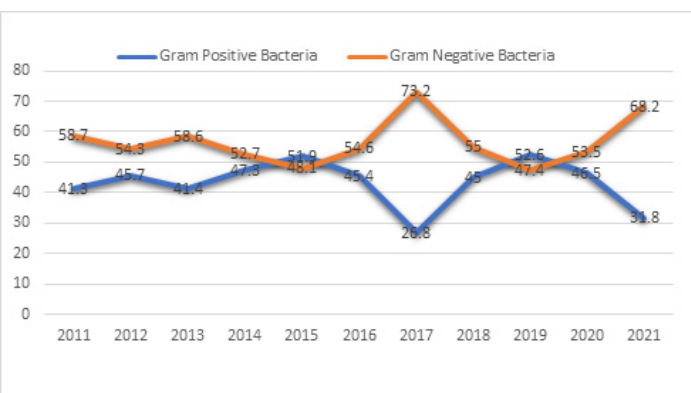


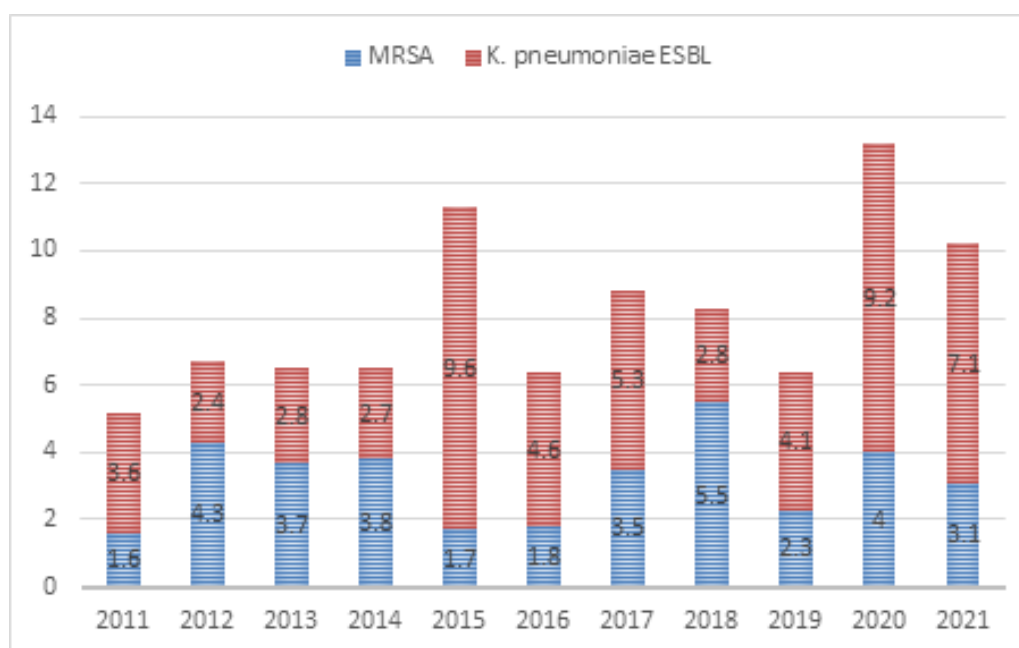
Figure 1 Trend of Gram Positive/ Gram Negative Microbes over last 11 years (%).

**Table 1** Microbial prevalence over last 11 years in the NICU (January 2011 to December 2021)

Year	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	Total
	(No and %)	(No and %)	(No and %)	(No and %)	(No and %)	(No and %)	(No and %)	(No and %)	(No and %)	(No and %)	(No and %)	(No and %)
<b>Total isolates</b>	1055	628	743	556	478	324	284	180	171	174	226	4849
<b>Gram Positive Bacteria</b>	436 (41.3)	287 (45.7)	308 (41.4)	263 (47.3)	248 (51.9)	147 (45.4)	76 (26.8)	81 (45)	90 (52.6)	81 (46.5)	72 (31.8)	2119 (43.7)
S. epidermidis (CONS)	120 (11.4)	109 (17.3)	77 (10.4)	85 (15.3)	40 (8.4)	69 (21.3)	32 (11.3)	35 (19.4)	53 (31)	48 (43.2)	36 (15.9)	704(14.6)
S. aureus	76 (7.2)	37 (5.9)	33 (4.4)	34 (6.1)	54 (11.3)	39 (12)	18 (6.3)	25 (13.9)	28 (16.4)	14 (12.6)	28 (12.4)	386 (8)
E. fecalis	30 (2.8)	18 (2.9)	62 (8.3)	46 (8.3)	35 (7.3)	7 (2.2)	6 (2.1)	3 (1.7)	3 (1.8)	2 (1.8)	2 (0.9)	214 (4.4)
Others*	203 (19.2)	121 (19.2)	126 (16.9)	92 (16.5)	118 (24.8)	30 (9.2)	20 (7.1)	17 (9.4)	6 (3.5)	16 (9.2)	3(1.3)	782 (16.2)
GBS	7 (0.7)	2 (0.3)	10 (1.3)	6 (1.1)	1 (0.2)	2 (0.6)	0	1 (5.5)	0 (0)	1 (0.6)	3 (1.3)	33 (0.7)
MRSA	17 (1.6)	27 (4.3)	28 (3.7)	21 (3.8)	8 (1.7)	6 (1.8)	10 (3.5)	10 (5.5)	4 (2.3)	7 (4.0)	7 (3.1)	145 (3)
<b>Gram Negative Bacteria</b>	619 (58.7)	341 (54.3)	435 (58.6)	293 (52.7)	230 (48.1)	177 (54.6)	208 (73.2)	99 (55)	81 (47.4)	93 (53.5)	154 (68.2)	2730 (56.3)
K. pneumoniae	110 (10.4)	73 (11.6)	117 (15.7)	73 (13.1)	85 (17.8)	60 (18.5)	62 (21.8)	54 (30)	27 (15.8)	28 (25.2)	69 (30.5)	758 (15.7)
S. maltophilia	147 (13.9)	127 (20.2)	98 (13.2)	36 (6.5)	14 (2.9)	39 (12.0)	58 (20.4)	5 (2.8)	5 (2.9)	3 (2.7)	25 (11.1)	557 (11.5)
P. aeruginosa	64 (6.1)	64 (10.2)	136 (18.3)	68 (12.2)	32 (6.7)	43 (13.3)	54 (19)	5 (2.8)	35 (20.5)	18 (16.2)	17 (7.5)	536 (11.1)
Others*	298 (28.2)	77 (12.3)	84 (11.3)	116 (20.9)	99 (20.7)	35 (10.8)	34 (12)	35 (19.4)	14 (8.2)	44 (25.3)	43 (19.0)	879 (18.2)
<b>K. pneumoniae ESBL</b>	38 (3.6)	15 (2.4)	21 (2.8)	15 (2.7)	46 (9.6)	15 (4.6)	14 (5.3)	5 (2.8)	7 (4.1)	16 (9.2)	16 (7.1)	208 (4.3)

\*Includes: other gram positive and gram-negative bacteria like: Group B streptococcus, other streptococcus spp., Escherichia coli, Acinetobacter, Citobacter, Enterobacter, serratia, Fungus (Candidia, Aspergillus etc.). These organisms are found to be in less numbers mostly grown in cultures other than from blood culture.

**Legends:** K pneumoniae, Klebsiella pneumoniae; S maltophilia, Stenotrophomonas maltophilia; P aeruginosa, Pseudomonas aeruginosa; ESBL, Extended Spectrum Beta Lactamase producer; E coli, Escherichia coli; A baumannii, Acinetobacter baumannii; spp, species; CONS, Coagulase Negative Staphylococcus spp; S epidermidis, Staphylococcus epidermidis; S aureus, Staphylococcus aureus; E fecalis, Enterococcus fecalis; GBS, Group B Streptococcus (Streptococcus agalactiae); MRSA, Methicillin Resistant Staphylococcus Aureus



**Figure 2** Trend of Multidrug Resistant Microbes over 11 years (%).

On analyzing the antimicrobial susceptibility profile (Table 2), only 74% of *Klebsiella pneumoniae* isolates were noted to be sensitive to 2<sup>nd</sup> and 3<sup>rd</sup> generation cephalosporins. Aminoglycosides were not uniformly effective (Gentamicin 86%, Amikacin 100%). Ciprofloxacin susceptibility was around 82%. As expected, *S. maltophilia* responded only to Trimethoprim+Sulfamethoxazole (100%) and Gentamicin (100%). There was emerging resistance noted toward Ceftazidime (sensitive= 89%) for *Pseudomonas aeruginosa*, the only sensitive antibiotics being Piperacillin + Tazobactam (sensitive 96%) and the aminoglycosides (sensitive 92-100%). Other gram-negative organisms also showed a similar profile of emerging resistance to 3<sup>rd</sup> generation Cephalosporins, retaining sensitivity to Aminoglycosides and Ciprofloxacin.

**Table 2** Antibiotics sensitivity pattern during the study period (from January 2011 to December 2021)

Organisms	Sensitivity	Resistance
<i>Stenotrophomonas maltophilia</i>	Cotrimoxazole (100%) + Gentamicin (100%)	Resistant to all other antibiotics
<i>Pseudomonas aeruginosa</i>	Piperacillin + Tazobactam (96%) ± Amikacin (100%)/ Gentamicin (92%)	Ceftazidime (11%) Meropenem (11%)
<i>Staph aureus</i>	Flucloxacillin (100%) ± Gentamicin (100%) / Amikacin (100%) Vancomycin (100%) / Linezolid (100%) / Teicoplanin (100%)	Clindamycin 26% Ciprofloxacin & Moxifloxacin 22%
<i>Kl. pneumoniae</i>	Piperacillin + Tazobactam (93%) ± Amikacin (100%) Gentamicin (86%)	Ceftazidime 26 % Ceftriaxone 25% Ciprofloxacin & Moxifloxacin 18%
<i>Staph epidermidis (CONS)</i>	Vancomycin (100%) / Linezolid (100%) / Teicoplanin (100%)	Gentamicin 47 % Amoxicillin + Clavulanate 44% Clindamycin 52%
<i>Enterococcus fecalis</i>	Vancomycin (100%) / Linezolid (100%) / Teicoplanin (100%)	Ciprofloxacin 20 %
<i>Group B streptococcus (GBS)</i>	Ampicillin 100% Penicillin 100% Cefuroxime 100% Amoxicillin + Clavulanate 100%	Erythromycin 44% Clindamycin 47%
<i>Klebsiella pneumoniae ESBL</i>	Meropenem (100%) ± Amikacin (100%) Ertapenem 100%	Ceftazidime 97 % Ceftriaxone 96% Ciprofloxacin 18% Piperacillin + Tazobactam 26 %
<i>AMPC producer (Serratia and pseudomonas)</i>	Meropenem (100%) ± Amikacin (100%) Ertapenem 100%	Mostly resistant to all other antibiotics
<i>MRSA</i>	Vancomycin (100%) / Linezolid (100%) / Teicoplanin (100%)	Gentamicin 20%

On the other hand, among the CONS species 66 % were susceptible to Amoxycillin + Clavulanate and 53% of them were susceptible to Gentamicin, and all of them were susceptible to Vancomycin, Teicoplanin and Linezolid. All *Staph aureus* were sensitive to Gentamicin, Oxacillin, Vancomycin, Linezolid and Teicoplanin. Ciprofloxacin sensitivity of *Staph aureus* was 78%. *E. fecalis*, third most common GPC was universally sensitive to Vancomycin, Teicoplanin and Linezolid (100%) but around 80% of them are sensitive to Ciprofloxacin. All the GBS isolates are sensitive

to Penicillin, Ampicillin and Cefuroxime. Whereas, 47% and 44% were resistant to Clindamycin and Erythromycin respectively.

All ESBL producers were sensitive to Meropenem, Ertapenem and Amikacin, most being sensitive to Piperacillin+ Tazobactam (74%) and Ciprofloxacin (82%). On the contrary, Amp C producers were only sensitive to Meropenem (100%), Ertapenem (100%) and Amikacin (100%). MRSA were only sensitive to Vancomycin (100%), Teicoplanin (100%) and Linezolid (100%) and some to Gentamicin (80%).

## Discussion

In the current study, we noted a general preponderance of GNB over GPC (Table 1 & Figure 1). Among the GNB, *Klebsiella pneumoniae* (15.7%) was the most frequently isolated and CONS (14.6%) among the GPC, which is similar to pattern noted in the middle eastern region and other Countries.<sup>4,7,12</sup> The findings from a large systematic review indicated that, *Klebsiella*, *Enterobacter* species, *Escherichia coli*, and *Pseudomonas* species, were recognized as the most common bacterial pathogens of neonatal sepsis in the Middle East region, which is similar to our observation.<sup>7,13</sup> It is known that most GNB are water borne and very easily colonize medical devices and equipment and hence are ready threat to neonatal population world wide.<sup>14</sup>

On the contrary, GPC dominate in most Western countries, Australia, North America, UK, Brazil and even in Europe.<sup>15</sup> Our data is comparable to the data reported from other centers but much higher than some from the other regions.<sup>9</sup> Increasing prevalence of CONS worldwide are attributable to multiple invasive procedures, central venous catheters use and lipid emulsions.<sup>14,16</sup> Although, CONS infections are relatively benign as compared to GNB or *S. Aureus*, in preterm neonates, they can be lifethreatening.<sup>2,14</sup>

There have been opposing findings too; GNB have been reported by developed countries and CONS by Middle Eastern regions as well.<sup>5</sup> However, there is a wide variation in the patterns between different regions. In Africa, *S. aureus* and *Streptococcus pneumoniae* are most prevalent ; *Klebsiella* is dominant in South-East Asia; in Europe and Western pacific regions, *S. aureus* and *Klebsiella pneumoniae* are more common, and finally *S. aureus* and *Haemophilus influenzae* are more in Americas region.<sup>7,14</sup> These results support the fact that, there is wide regional variation in the diversity of organisms causing neonatal sepsis and changes over time even in the same place.<sup>7,14</sup> In almost all countries of Latin America, the frequency of gram-negative pathogens varied from 31% to 63% with *K. pneumoniae*, *P. aeruginosa* and *E. coli* being the predominant organisms.<sup>14</sup> Although evidence showed that gram-positive bacteria are the most commonly encountered in NICU patients, case fatality rate are highest for gram-negative infection.<sup>17</sup>

To further complicate the understanding, there exists wide variation in the microorganism profile and sensitivity pattern in different NICUs which consistently changes with time. There is lack of evidence to demonstrate species specific causal association between neonatal infection and environmental contamination.<sup>2</sup> Our study used a mix of sterile body fluid (Blood, CSF, urine) and mucosal surfaces (Throat, nasopharyngeal etc.) to analyse the existing and dynamic nature of microbial profile. We do understand that surveillance cultures detect only a 3<sup>rd</sup> of pathogens that would cause invasive disease<sup>18</sup> and are aware of the poor association between susceptibility profiles of microbes grown from environmental surfaces and those found in body fluid cultures.<sup>14</sup> Despite this, we could observe similar findings reported by studies that included mucosal swabs. However, mucosal swabs may help in cohorting, occasionally making antimicrobial

choice during outbreak based on duration and frequency of mucosal colonization especially for invasive disease.<sup>11</sup>

It was alarming to note very high prevalence of *Stenotrophomonas maltophilia* (*S. maltophilia*) (11.5%) in our study, which is one of the highest among peers. *Stenotrophomonas* is a multidrug resistant, pathogenic organism which rarely causes invasive disease but has specific implications to neonatal population as it is directly related to use of invasive devices and length of stay.<sup>19</sup> We could curb its prevalence down to 2.7% recently with efficient use of antimicrobial stewardship program, while 2021 being an exception. None of the cases of *S. maltophilia* over these years was found responsible for invasive disease.

Another surprising observation is a low rate of prevalence of GBS (0.7%). Variability in GBS prevalence has been observed worldwide, (less than 1% to 40%).<sup>2,7,14</sup> Some studies have not reported any case of isolation of Group B *Streptococcus*.<sup>7,16</sup> Maternal Intrapartum Antibiotic prophylaxis, frequent isolation of GNB and other GPC, population dynamics, diagnostic modalities are considered the reasons for its variable occurrence.<sup>20</sup> The clearly evident resistant pattern of GBS to erythromycin (44%) and clindamycin (47%) are consistent with other published literature.<sup>21,22</sup>

Antimicrobial resistance is an emerging pandemic. In our study, not only did we notice an increasing trend of Antimicrobial resistant GNB and GPC, we also noted that these *Klebsiella* and other GNB were increasingly resistant to Cephalosporins, however more than 90% were still susceptible to Piperacillin + Tazobactam combination. All the GNB were sensitive to Amikacin but not to Gentamicin. Carbapenems retained maximum susceptibility for GNB whereas not all GNB were susceptible to Ciprofloxacin. Recent evidence showing emergence of high resistance to amoxicillin, ampicillin, aminoglycosides, and cephalosporins.<sup>5</sup> Even within the aminoglycoside spectrum, amikacin (which was less used in their units) sensitivity is more than gentamicin (which was more commonly used).<sup>1,5,14</sup> Although, several studies suggest that piperacillin-tazobactam could be effective for ESBL Enterobacteriaceae infections.<sup>23</sup> Some studies indicate better survival rates with carbapenems.<sup>24,25</sup> Other studies observed ESBL production in 69% of Enterobacteriaceae.<sup>1,9</sup> There was about 50% resistance of *E. coli* and *K. Pneumoniae* to third generation cephalosporins.<sup>17</sup>

There was relatively uniform susceptibility pattern and a higher rate of ESBL organisms. Among ESBL organisms low susceptibility rates observed to ciprofloxacin, indicating the coexistence of fluoroquinolone and ESBL producing Enterobacteriaceae. Thus fluoroquinolones are not the appropriate empiric therapy for patients with suspected ESBL producing Enterobacteriaceae.<sup>13,23</sup> Susceptibility of *P. aeruginosa* to carbapenems noted to be remained very high. Many previous evidences also showed a similar findings even among ESBL-producing Enterobacteriaceae.<sup>4,13</sup> Carbapenem resistant organisms emerged as a concern throughout the globe. The pattern of antibiotic use and the location of the isolates within the hospital have an impact on variable antimicrobial susceptibility pattern.<sup>13</sup> During the study period, we did not observe a single case of Vancomycin resistant Enterococci (VRE) or Carbapenam resistant pseudomonal aerogenosa in our NICU.

Our findings and other evidences support the fact that there is wide spread regional variation in the organisms causing sepsis and also change over time even in the same place.

## Conclusion

Strict implementation of infection control measures and rational use of broad-spectrum antibiotics, along with continuous surveillance

to retard our journey towards the pre-antibiotic era. Our NICU antibiotics policy changes time to time based on the surveillance data, which enable us to keep a control over antibiotics use and prevention of MDROs. This eventually leads to better short and long-term outcome.

**Limitations of the study:** Retrospective observational study, mix of cultures (mucosal and sterile body fluids), molecular typing of bacterial not done, maternal cultures correlation not there, single centre study, no subgroup analysis, substantial heterogeneity, true infections and colonization not differentiated.

**Strengths:** Our sample size is large. There is a definite trend in microbiological profile and antimicrobiological susceptibility seen over time. Infection control measures and their success could be seen i.e. restricted use of broad spectrum antibiotics, strictly following antimicrobial stewardship program, continuous surveillance of emergence of MDROs, invasive lines restrict time policy.

Despite these limitations, we believe that this study has provided a useful characterization of the burden and impact of existent microbial profile and antimicrobial sensitivity patterns in our NICU. This is one of the largest microbiological profile surveillance studies in the Middle Eastern region. The data from this study can be considered as a baseline guide for any future study or formulating antimicrobial guidelines.

## Acknowledgments

None

## Statements

**Statement of Ethics:** The study is approved by Dubai Scientific Research Ethics Committee, Dubai Health Authority with reference number DSREC-10/2022\_07.

**Consent to participate statement:** This is a retrospective study and data were collected as part of continuous surveillance, for which general consent was obtained from the parents at the time of admission.

## Author contributions

MSE: Original concept design, acquisition of data, analysis and interpretation of data, and evaluation of manuscript, patient management. JH: Acquisition of data, analysis and interpretation of data, and evaluation of manuscript, patient management. SKD: Acquisition of data, analysis and interpretation of data, drafting and evaluation of manuscript, patient management. EAATE: Acquisition of data, interpretation of data, evaluation of manuscript, patient management. All authors approved the final manuscript.

**Data Availability statement:** The data that support the findings of this study are available on request from MSE or the Corresponding Author. Due to privacy and to maintain confidentiality data not available publicly.

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## Conflicts of interest

The authors have no conflicts of interest to declare.

## References

1. Gandraa S, Alvarez-Uriab G, Murkic S, et al. Point prevalence surveys of antimicrobial use among eight neonatal intensive care units in India: 2016. *International Journal of Infectious Diseases*. 2018;71:20–24.
2. Kumar S, Shankar B, Arya S, et al. Healthcare associated infections in neonatal intensive care unit and its correlation with environmental surveillance. *Journal of Infection and Public Health*. 2018;11(2):275–279.
3. Baier C, Pirr S, Ziesing S, et al. Prospective surveillance of bacterial colonization and primary sepsis: findings of a tertiary neonatal intensive and intermediate care unit. *Journal of Hospital Infection*. 2019;102(3):325–331.
4. Al-Matarya A, Heena H, S Al Sarheed A, et al. Characteristics of neonatal Sepsis at a tertiary care hospital in Saudi Arabia. *Journal of Infection and Public Health*. 2019;12(5):666–672.
5. Eshetu B, Gashaw M, Solomon S, et al. Bacterial Isolates and Resistance Patterns in Preterm Infants with Sepsis in Selected Hospitals in Ethiopia: A Longitudinal Observational Study. *Glob Pediatr Health*. 2020;7:1–8.
6. Weldu Y, Naizgi M, Hadgu A, et al. Neonatal septicemia at intensive care unit, Ayder Comprehensive Specialized Hospital, Tigray, North Ethiopia: Bacteriological profile, drug susceptibility pattern, and associated factors. *PLoS ONE*. 2020;15(6):e0235391.
7. Akbarian-Rad Z, Riahi SM, Abdollahi A, et al. Neonatal sepsis in Iran: A systematic review and meta-analysis on national prevalence and causative pathogens. *PLoS ONE*. 2020;15(1):e0227570.
8. Almohammady MN, Eltahlawy EM, Reda NM. Pattern of bacterial profile and antibiotic susceptibility among neonatal sepsis cases at Cairo University Children Hospital. *J Taibah Univ Med Sc*. 2020;15(1):39–47.
9. Sana F, Satti L, Zaman G, et al. Pattern of Blood Stream Infections and their antibiotic susceptibility profile in a Neonatal intensive care unit of a tertiary care hospital; a current perspective. *J Pak Med Assoc*. 2019;69(11):1668–1672.
10. Mahmoud ElHalik M, Habibullah J, El-Atawi K, et al. Epidemiology of sepsis in NICU; A 12 years study from Dubai, U.A.E. *J Pediatr Neonatal Care*. 2018;8(2):84–88.
11. Parm Ü, Metsvaht T, Sepp E, et al. Mucosal surveillance cultures in predicting Gram-negative late-onset sepsis in neonatal intensive care units. *J Hosp Infect*. 2011;78(4):327–332.
12. Alp E, Orhan T, Kürkcü CA, et al. The first six years of surveillance in pediatric and neonatal intensive care units in Turkey. *Antimicrob Resist Infect Control*. 2015;4:34.
13. Al-Tawfiq JA, Rabaan AA, Saunar JV, et al. Antimicrobial resistance of gram-negative bacteria: A six-year longitudinal study in a hospital in Saudi Arabia. *Journal of Infection and Public Health*. 2020;13(5):737–745.
14. Rastogi S, Shah R, Perlman J, et al. Pattern of bacterial colonization in a new neonatal intensive care unit and its association with infections in infants. *Am J Infect Control*. 2012;40(6):512–515.
15. Abdel-Wahab F, Ghoneim M, Khashaba M, et al. Nosocomial infection surveillance in an Egyptian neonatal intensive care unit. *Journal of Hospital Infection*. 2013;83(3):196–199.
16. Gul A, Takci S. Analysis of late-onset neonatal sepsis cases in a level three neonatal intensive care unit. *North Clin Istanbul*. 2020;7(4):354–358.
17. Mohsen L, Ramy N, Saied D, et al. Emerging antimicrobial resistance in early and late-onset neonatal sepsis. *Antimicrobial Resistance and Infection Control*. 2017;6:63.
18. Mariani M, Bandettini R, La Masa D, et al. Bacterial invasive infections in a neonatal intensive care unit: a 13 years microbiological report from an Italian tertiary care centre. *J Prev Med Hyg*. 2020;61(2):E162–E166.
19. Mutlu M, Yılmaz G, Aslan Y, et al. Risk factors and clinical characteristics of *Stenotrophomonas maltophilia* infections in neonates. *Journal of Microbiology, Immunology and Infection*. 2011;44(6):467–472.
20. Dong Y, Basmaci R, Titomanlio L, et al. Neonatal sepsis: within and beyond China. *Chin Med J*. 2020;133(18):2219–2228.
21. Raabe VN, Andi LS. Group B *Streptococcus* (*Streptococcus agalactiae*). *Microbiol Spectr*. 2019;7(2):10.1128/microbiolspec.GPP3-0007-2018.
22. Ding Y, Wang Y, Hsia Y, et al. Systematic review and meta-analyses of incidence for group B *Streptococcus* disease in infants and antimicrobial resistance, China. *Emerg Infect Dis*. 2020;26(11):2651–2659.
23. Yoon YK, Kim JH, Sohn JW, et al. Role of piperacillin/tazobactam as a carbapenem-sparing antibiotic for treatment of acute pyelonephritis due to extended-spectrum  $\beta$ -lactamase-producing *Escherichia coli*. *Int J Antimicrob Agents*. 2017;49(4):410–415.
24. Tamma PD, Han JH, Rock C, et al. Carbapenem Therapy Is Associated With Improved Survival Compared With Piperacillin-Tazobactam for Patients With Extended-Spectrum  $\beta$ -Lactamase Bacteremia. *Clinical Infectious Diseases*. 2015;60(9):1319–1325.
25. Seidel J, Haller S, Eckmanns T, et al. Routine screening for colonization by Gram-negative bacteria in neonates at intensive care units for the prediction of sepsis: systematic review and metaanalysis. *Journal of Hospital Infection*. 2018;99(4):367–380.