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ASSESSMENT OF THE PATTERN OF ANTIBIOTIC USE IN THE NEONATAL INTENSIVE CARE UNIT (NICU) AT A TERTIARY HOSPITAL IN THE UAE

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ABSTRACT

Background: The use of antibiotics in NICU is considered to be essential either as a Prophylactic or empirical treatment for a number of diseases. Sepsis is considered as one of the major risk diseases and requires a variety of antibiotics. The proper selection of antibiotics is necessary to ensure a successful treatment outcome. **Objective:** To investigate the proper use of antibiotics. The type of infection, microbiological culture results, empirical and duration of antibiotic, antibiotic-resistant and risk factors associated with sepsis infection in NICU. **Methods:** This is a retrospective cross-sectional, non-probability study of all newborn babies admitted at NICU at a Tertiary Hospital in the UAE from 1 January 2018 to 31 December 2018. **Results**: A total of 256 neonates referred to the neonatal intensive care unit. 19 neonates (7.4%) were diagnosed with late-onset Sepsis (LOS), and none of them was diagnosed with early-onset Sepsis (EOS). About 9 neonates (3.5%) were diagnosed with other infections. All-cause infections in the NICU caused by 85.2% of gram-negative bacteria and 29.6% of gram-positive bacteria. There was a high bacterial prevalence of S.Haemolyticus and K.Pneumoniae by (18.5%) in the NICU. Of probable sepsis cases, 170 cases (91.4%) were prescribed Penicillin+Gentamicin.145 cases (78%) were prescribed an empirical antibiotic for ≤ 72 hours. There was a high prevalence of bacterial resistance of K. Pneumoniae and S.Haemolyticus by (18.5%) in the NICU. The central venous line in neonate major risk factor for sepsis as odds ratio 8.88% following by length of stay in NICU 1.03%, Gestational Age 0.82%, and Birthweight 0.23%. **Conclusions:** Sepsis represents the major reason for neonate morbidity and mortality. Wise choice of antimicrobial agents and optimal duration of treatment in neonatal with the suspected or culture-proven sepsis is critical in order to limit the use of unnecessary wide spectrum antibiotic treatment and to supply local solutions to the worldwide race against antimicrobial resistance.

KEYWORDS: Neonatal Intensive Care Unit, Empirical Antibiotic, Neonatal sepsis, Bacterial resistance.

INTRODUCTION

The use of antibiotics in NICU is significant either as a prophylactic or empirical treatment for a number of diseases. Sepsis is considered as one of the major risk diseases and requires a variety of antibiotics. The proper selection of antibiotics is necessary to ensure a successful treatment outcome. Nevertheless, many neonates are exposed to antimicrobial therapy, although they do not have an infection during a stay in the hospital, and there are serious adverse effects that use antibiotics in negative cultures such as antibiotic resistance. The suitable option of antibiotic and duration of treatment in NICU with suspected or culture-confirmed sepsis is essential to prevent serious adverse effects (Tzialla et al., 2012).

In Arab countries, Late-onset sepsis (LOS) and Early-onset sepsis (LES) is very common in NICU. Therefore, much effort is required to improve the specific uses of antibiotics during delivery in NICU to prevent unfavorable outcome (Hammoud, 2017).

The neonatal intensive care unit (NICU) is specially designed to care for new born babies that may require unique and highly specialized care. These new born babies may be premature, i.e., born before 37 weeks gestation, born with low birth weight (less than 2.5 kg) (Offenbacher et al.,1996; Drews et al.,1995). There are many risks and complications associated with a new born needing to be careful in a NICU. These may include intraventricular haemorrhage (Robinson., 2012), central nervous system involvement, severe respiratory complications (Ward & Beachy., 2003) and nosocomial infections (Su et al., 2007).

Infections are associated with increased morbidity and mortality, increased hospital cost, and increased length of hospitalization. Given that preterm infants have shown to

have compromised immune systems, infections can occur in as many as 65% of infants born with less than 1,000 grams birth weight (S toll et al., 2004). Sepsis, pneumonia, urinary tract infections, and meningitis are only some of the most commonly seen infections these neonates are at risk of acquiring (Ishii et al., 2013).

Furthermore, microorganisms interchange between mother and neonate at the time of delivery poses the neonate at significant risk of developing severe infections. Antibiotic use is common in NICU and intended as prophylaxis and treatment effect. Although survival of premature infants has significantly improved after the routine use of antibiotics in the NICU, negative consequences in both short and long term health outcomes such as haemorrhage (Zeissig et al.,2014; Schokker et al., 2014; Candon et al., 2015).

Researchers have investigated tools and attempted to identify biomarkers that may aid decision on the use of antibiotics. Regrettably, in neonates, the signs and symptoms at presentation are nonspecific, non-localized, and challenging to identify. Since neonates have significant risk factors for infection, physicians commonly utilize guidelines and scoring systems to adjust clinical decisions (Bender et al., 2008; Selimovic et al., 2010; Yang et al., 2012). One of these tools is the neonatal early-onset sepsis calculator (Simpson et al., 2018). Unnecessary antibiotic use in neonates may lead to the development of antimicrobial resistance, increased healthcare costs, and alter the developing microbiome of the neonate. On the other hand, withholding the use of antibiotics when it is otherwise necessary, may result in increased morbidity and mortality in those infants.

Morbidity and mortality connected considerably with nosocomial bloodstream infections (NBSIs) in neonatal intensive care units (NICUs) (BRODIE et al., 2000). Catheters are widely used in the inpatient setting of health care and it is the risk of bloodstream infection (BSI) such as peripherally inserted central venous catheters (PICCs) and central venous catheters (CVCs) used in Hospitalized Patients (Safdar & Maki, 2005; Fridkin et al., 1996).

Prematurity is also considered as an important risk factor for the survival of a newborn. Prevention of infection, as well as correct empirical antibiotic therapy, are key in the management of neonates (Ramasethu, 2017). Some studies have been done in the UAE in the neonatal population; the majority focused on investigating the causative pathogens of sepsis in this population group. Therefore, our study aim is to retrospectively, assess the pattern of antibiotic use in the neonatal intensive care unit in a tertiary hospital in the UAE to determine the common organism found in NICU, type of an infection, antibiotic uses, resistance and the risk factor associated with antibiotic-resistant in the neonatal intensive care unit.

METHODOLOGY

Research design and settings

This is a retrospective, cross-sectional, non-probability study. This study includes all preterm babies admitted at NICU at a Tertiary Hospital in the UAE. Demographic, Anthropometric, and baseline characteristics were obtained by reviewing the medical records of the neonates admitted to the neonatal intensive care unit from 1 January 2018 to 31 December 2018. The study aim is to investigate the use of antibiotics, presence of infection, microbiological culture results, antibiotic sensitivity patterns, and patient outcomes.

Data collection

The following information will be collected: patient demographics, current medical condition, mother comorbidity, infection risk factor and causative, APGAR at 5 min equal or more than 8, Culture, Pathogen, Multi-drug resistance, and medication used. The clinical outcome will be evaluated by the use of antibiotics, describe the microbiological and antibiotic resistance, the risk factors of infections, the most common causative organisms of LOS, and adequacy of the current empirical antibiotic plus duration. The outcome will consider rejecting when the outcome of the patients will be unknown. Then the useful treatment analysis will be performed by the health result of babies.

Apgar Score: is a fast test doing for neonatal soon after birth at one and five minutes, it checks a baby: Breathing effort, Heart rate, Muscle tone, Reflexes, and Skin color to see if need emergency care or extra medical care.

Inclusion criteria

Those admitted in NICU.
Newborn babies.

Exclusion criteria

Children with High bilirubin levels were excluded.

Sample technique

A convenience sample is a type of non-probability sampling method, contains all newborn babies admitted at NICU of Tertiary Hospital in the UAE from 1 January 2018 to 31 December 2018.

Data source, Management, and Measurements

Demographic, anthropometric, and baseline characteristics were obtained by reviewing the medical records (Wareed System) (demography: gender, nationality, gestational age, place of birth, birth weight, length of NICU stays, delivery mode, PROM, mother GBS, central line catheter, APGAR score, culture, pathogen, drug Resistance pathogen, and empirical antibiotics).

Data analysis and assessment

The data were analyzed using the Statistical Package for Social Sciences (SPSS, version 24). Qualitative variables were summarized using frequencies and percentages.

Chi-square test and Fisher exact test were used to study the association between neonatal sepsis, other infections, and significant related factors. Univariate and multivariate logistic regression models were used to investigate a set of risk factors that jointly influence the late-onset sepsis in the neonatal intensive care unit. A p-value < 0.05 was chosen as the criteria to make decisions regarding statistical significance.

Ethical Consideration

An ethical approval was granted from the Research and Ethical (REC) committee of the Ministry and Health and Prevention. The privacy and confidentiality of the participants was maintained.

RESULTS

Demographic, Anthropometric and Baseline characteristics

A total of 256 neonates referred to the neonatal intensive care unit and screened for sepsis and any other infections. Among these, 53.5% (n=137) were male and 46.5% (n=119) female. The patients were predominantly UAE national (n=189, or 73.8%). Most of the neonates were borne in a Tertiary Hospital in the UAE (n=233, or 91%). Of the total, 41% (n=105) were normal delivered and 59% (n=151) born by cesarean delivery. Giving birth to twins constituted about 16% (n=41). Among 256 neonates, 87.1% (n=223) scored equal and more 8 in Apgar score at 5 min. of the total, 129 neonates (50.4%) were borne before 37 weeks, 134 neonates (52.3%) were borne with birth weight less than 2.5 Kg, and 115 neonates (44.9%) were borne before 37 weeks with birth weight less than 2.5 Kg. Of the referred neonates, 79.3% (n=203) received no central venous line, 4.7% (n=12) received UVC venous line, 1.2% (n=3) received PICC venous line, 7.4% (n=19) received UAC+UVC venous line, 3.1% (n=8) received UAC+UVC+PICC venous line and 4.3% (n=11) received UVC+PICC venous line. The average neonatal weight at birth was 2.5 kg ± 2 SD. Average gestational age at birth 35.4 weeks ± 4.5. The average length of stay in the neonatal intensive care unit was 16.7 days ± 21.1 SD. For more details, see **Table 1.**

Table 1: Demographical characteristics of Neonates at baseline (n=256).

Baseline characteristics	Groups	Frequency	Percentage
Neonate gender	Male	137	53.5%
	Female	119	46.5%
Nationality	UAE national	189	73.8%
	Non UAE national	67	26.2%
Place of birth	Tertiary Hospital in the UAE	233	91.0%
	Transfer from another facility	23	9.0%
Delivery Mode	Normal Delivery	105	41.0%
	Cesarean Delivery	151	59.0%
Giving birth to twins	Yes	41	16.0%
	No	215	84.0%
Apgar score at 5 min	≥ 8	223	87.1%
	< 8	28	10.9%
	None	5	2%
Gestational Age	≥ 37 weeks	127	49.6%
	< 37 weeks	129	50.4%
Birthweight	≥ 2.5kg	122	47.7%
	< 2.5 kg	134	52.3%
Born before 37 weeks with birth weight less than 2.5 Kg	No	141	55.1%
	Yes	115	44.9%
Central venous line in the neonate	None	203	79.3%
	UVC	12	4.7%
	PICC	3	1.2%
	UAC+UVC	19	7.4%
	UAC+UVC+PICC	8	3.1%
	UVC+PICC	11	4.3%
Birthweight (kg)	Mean ± SD	2.5	± 2
Gestational age (weeks)	Mean ± SD	35.4	± 4.5
Length of stay in NICU (days)	Mean ± SD	16.7	± 21.1
Condition at discharge	Home	236	92.2%
	Died	9	3.5%
	Transfer to another facility	11	4.3%

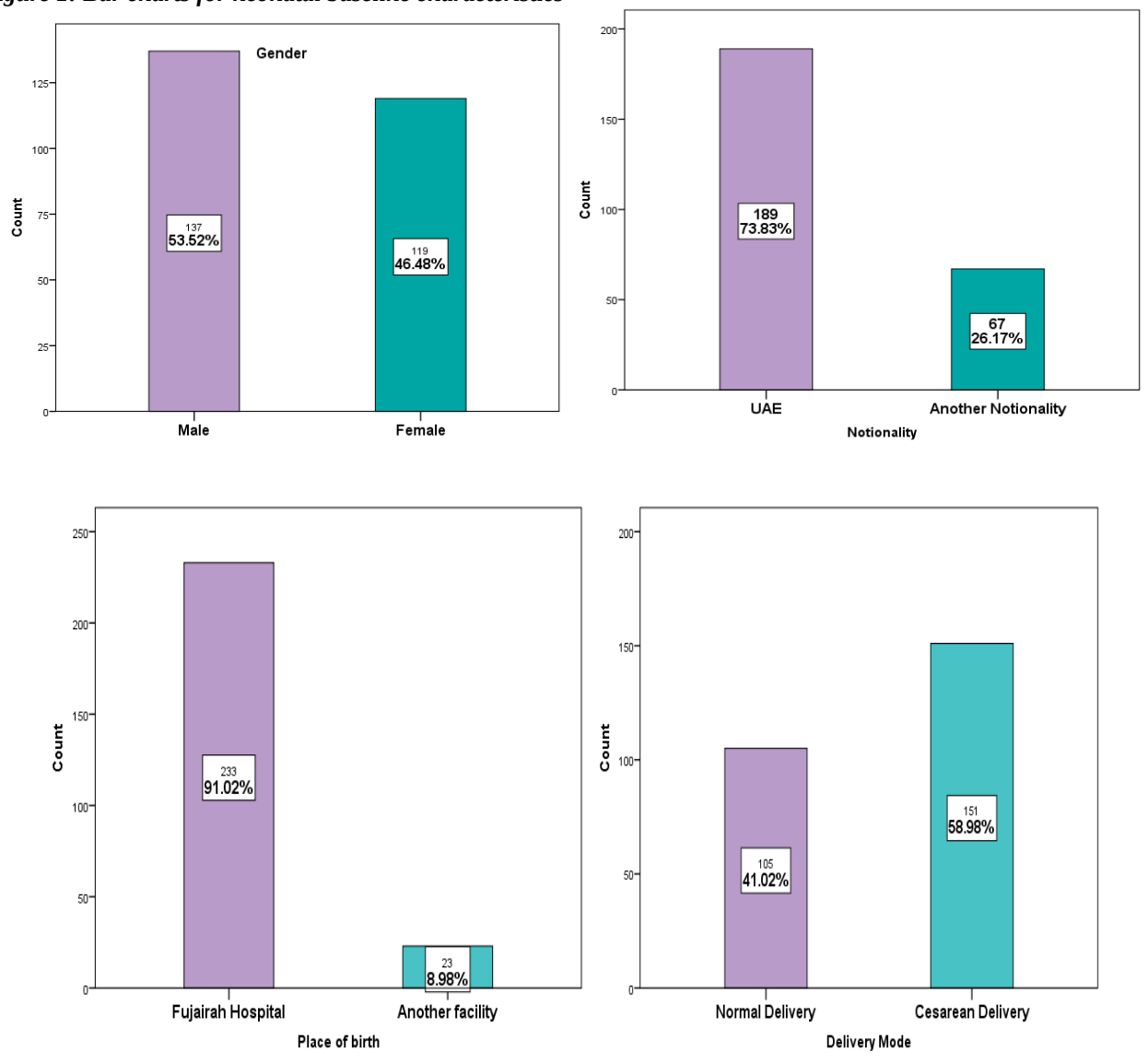
Abbreviations: UVC, **Umbilical Venous Catheter;** PICC, **Peripherally inserted central catheters;** UAC**, Umbilical Artery Catheter; Apgar,** "**A**ppearance, **P**ulse, **G**rimace, **A**ctivity, and **R**espiration."; **PROM,** Prelab or rupture of membranes

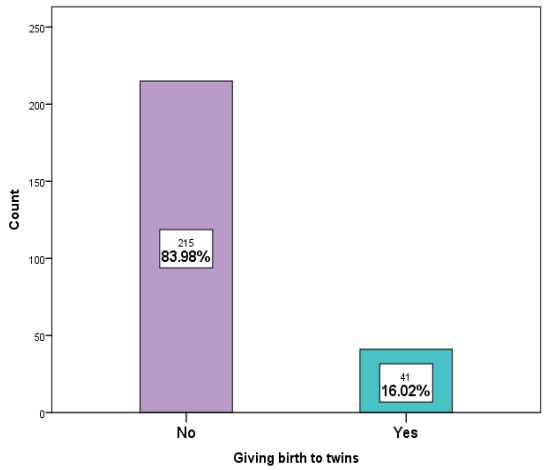
Table 2 and figure 2: summarizes the mothers' baseline characteristics. Group B Streptococcus was diagnosed in 1.6% (n=4) of mothers who gave birth. Among these four mothers, two of them received prophylaxis antibiotics for GBS (50%). Of the total, 155 mothers (60.5%) had no Prelab or rupture of membranes, 28 mothers (10.9%) had Prelab or rupture of membranes for ≥ 18 hours, 32 mothers (12.5%) had Prelab or rupture of membranes for <18 hours and 41 of them (16.0%) were Unknown.

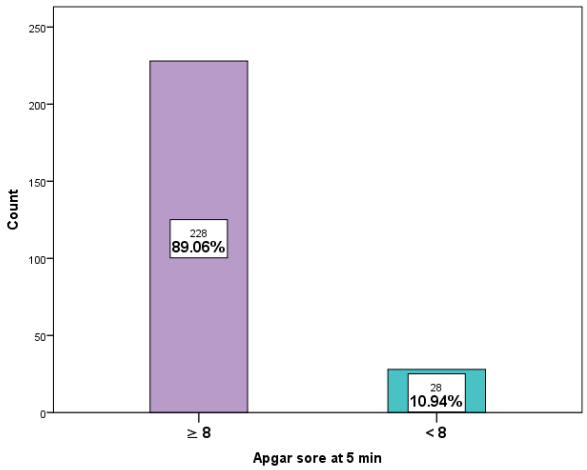
Table 2: baseline characteristics of Mother.

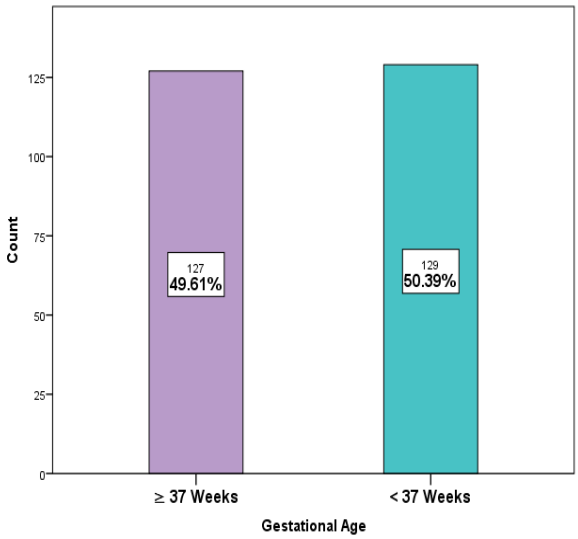
Baseline characteristics	Groups	Frequency	Percentage
Mother GBS infection	Positive	4	1.6%
	Negative	110	43%
	Unknown	142	55.5%
Prophylaxis antibiotic for GBS (n=4)	Yes	2	50%
	No	2	50%
PROM	Normal	155	60.5%
	≥ 18 hour	28	10.9%
	<18 hour	32	12.5%
	Unknown	41	16.0%
Abbreviations: GBS, Group B Streptococcus; PROM, Prelab or rupture of membranes			

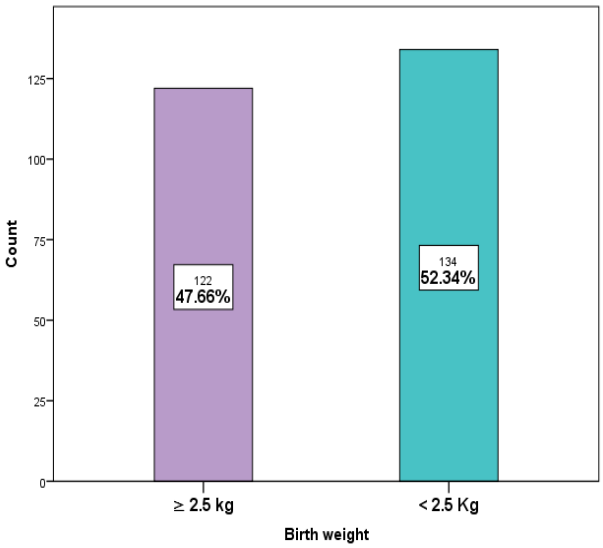
Figure 1: Bar charts for neonatal baseline characteristics

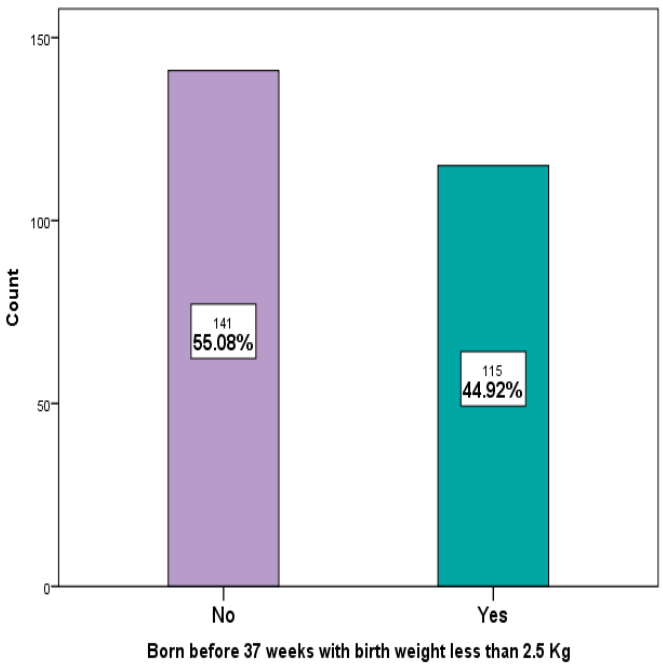



Count
215
83.98%
41
16.02%
No
Yes
Giving birth to twins


Count
228
89.06%
28
10.94%
≥ 8
< 8
Apgar sore at 5 min


Count
127
49.61%
129
50.39%
≥ 37 Weeks
< 37 Weeks
Gestational Age


Count
122
47.66%
134
52.34%
≥ 2.5 kg
< 2.5 Kg
Birth weight


Count
141
55.08%
115
44.92%
No
Yes
Born before 37 weeks with birth weight less than 2.5 Kg

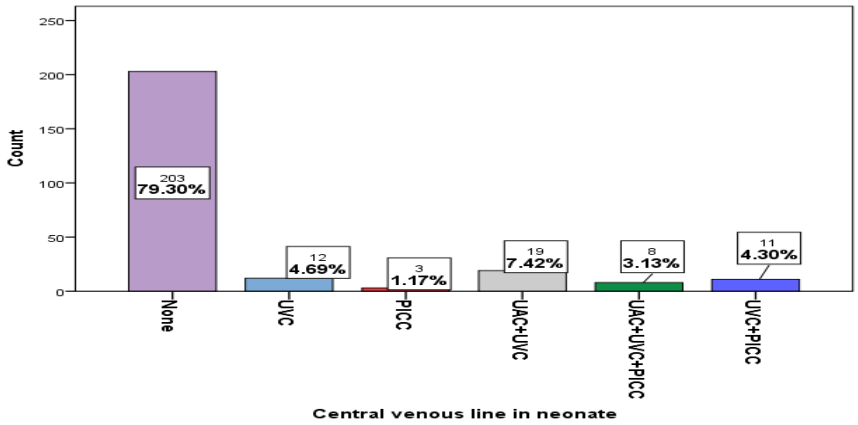
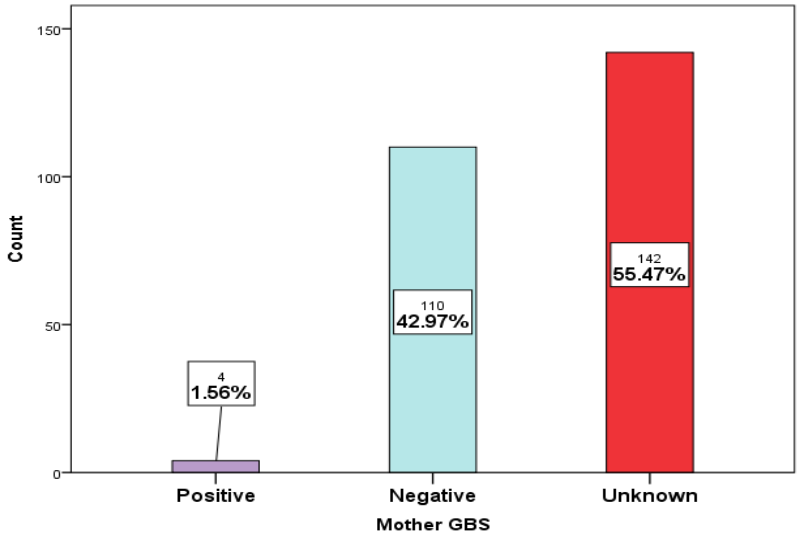
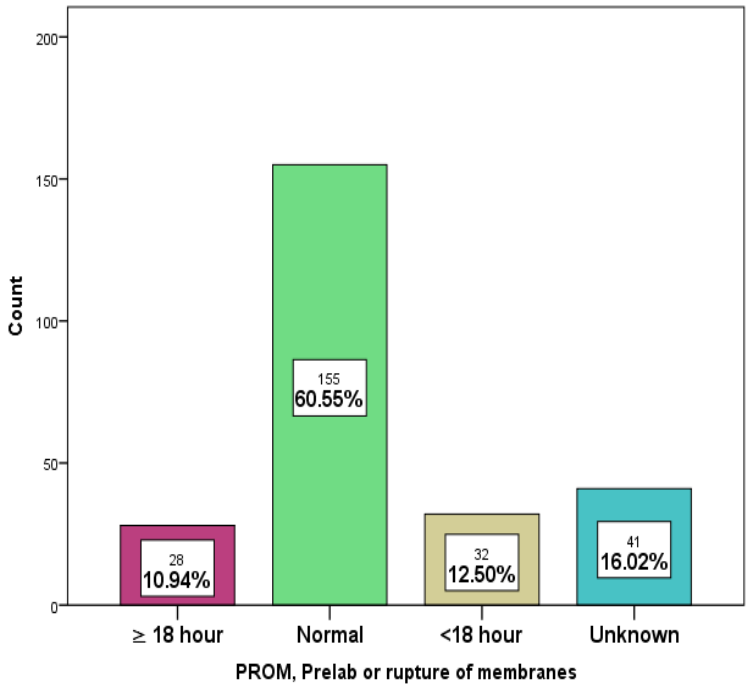


Figure 2: Bar charts for mothers' baseline characteristics.





The empirical antibiotic used and duration in the first 3 days of postnatal.

Assessment of Empirical antibiotic therapy for neonates suspected of early-onset sepsis

Of the 256 neonates referred to the neonatal intensive care unit, 186 neonates (72.6%) [95%CI: 67.2 – 78.2] were diagnosed with probable sepsis. Of probable sepsis cases, 12 cases (6.5%) were prescribed Ampicillin + Gentamicin, 170 cases (91.4%) were prescribed Penicillin + Gentamicin, 1 case (0.5%) were prescribed Ampicillin, 1 case (0.5%) were prescribed Penicillin + Cefotaxime, 1 case (0.5%) were prescribed Ampicillin + Cefotaxime and 1 case (0.5%) were prescribed Penicillin + Amikacin. Of probable sepsis cases, 145 cases (78%) were prescribed an empirical antibiotic for ≤ 72 hours, and 41 cases (22%) were prescribed empirical antibiotics for > 72 hours. **(Table 3)**

Table 3: Empirical antibiotic therapy and duration for neonates suspected of early-onset sepsis (n=186) or (72.6%)

Prevelance (CI 95%)	**72.6%**	**67.2% – 78.2%**
Empirical Antibiotic therapy	**Frequency**	**Percentage**
Ampicillin + Gentamicin	12	6.5%
Penicillin + Gentamicin	170	91.4%
Ampicillin	1	0.5%
Penicillin + Cefotaxime	1	0.5%
Ampicillin + Cefotaxime	1	0.5%
Penicillin + Amikacin	1	0.5%
	186	**100%**
Duration of Empirical antibiotic therapy		
≤ 72 hours	145	78%
> 72 hours	41	22%
	186	**100%**

Incidence of neonatal Sepsis and other infections in the Neonatal Intensive Care Unit

Among the total 256 neonates referred to the neonatal intensive care unit, 19 neonates (7.4%) [95%CI: 4.2 – 10.7] were diagnosed with late-onset sepsis, and none of them were diagnosed with early-onset sepsis. About 9 neonate (3.5%) [95%CI: 1.2 – 5.8] diagnosed with other infection. One neonate had both infection LOS and other infections. The overall incidence of infection in the neonatal intensive care unit was 27 neonate 10.5% [95%CI: 6.7 – 14.3], see **Table 4.**

Table 4: Incidence of late onset sepsis and other infections in NICU.

Infection type	**Incidence**	**95%CI**
Late onset sepsis (19 neonate)	7.4	[4.2 – 10.7]
Other infections (9 neonate)	3.5%	[1.2 – 5.8]
All cause infections (27 neonate)	10.5%	[6.7 – 14.3]

Table 5 shows the incidence of late-onset sepsis and other infection according to neonatal baseline characteristics. The incidence of late-onset sepsis increased with twins (26.8% vs. 3.7%) (P< 0.001), Neonates who scored < 8 at Apgar sore at 5 min (21.4% vs 5.7%) (P< 0.01), those with birth weight less than 2.5 Kg (13.4 vs 0.8%) (P< 0.001), those who born before 37 weeks (14% vs 0.8%) (P< 0.001), those who were born before 37 weeks with birth weight less than 2.5 Kg (15.7% vs 0.7%) (P< 0.001), neonates who received central venous line (32.1% vs 1%) (P< 0.001) and longer stay in the neonatal intensive care unit (P< 0.001).

On the other hand, neonates with birth weight less than 2.5 Kg (P< 0.05) reviving central venous line (P< 0.001) and a longer stay in the neonatal intensive care unit (P< 0.001) showing a higher incidence of other infections in the neonatal intensive care unit. Overall, the incidence of infections in neonatal intensive care unit increased with twins (29.3% vs 7%) (P< 0.001), Neonates who scored < 8 at Apgar score at 5 min (25% vs 8.8%) (P< 0.01), those with birth weight less than 2.5 Kg (18.7% vs 1.6%) (P< 0.001), those who born before 37 weeks (17.8% vs 3.1%) (P< 0.001), those who born before 37 weeks with birth weight less than 2.5 Kg (20% vs 2.8%) (P< 0.001), neonates who received central venous line (41.5% vs 2.5%) (P< 0.001) and longer stay in the neonatal intensive care unit (P< 0.001). Figure 3 shows bar chart of the incidence of neonatal sepsis and other infections in NICU.

Table 5: Incidence of late-onset sepsis and other infections in the Neonatal intensive care unit according to baseline characteristics.

Baseline characteristics	Groups	Sepsis (n=19) (7.4%)	Other (n=9) Infections (3.5%)	All cause infection (n=27) (10.5%)
Neonate gender	Male	10 (7.3%)	4 (2.9%)	13(9.5%)
	Female	9 (7.6%)	5 (4.2%)	14(11.8%)
Nationality	UAE national	12 (6.3%)	7 (3.7%)	19(10.1%)
	Non UAE national	7 (10.4%)	2 (3%)	8 (11.9%)
Place of birth	Fujairah Hospital	17 (7.3%)	7(3%)	23(9.9%)
	Another facility	2 (8.7%)	2 (8.7%)	4 (17.4%)
Delivery Mode	Normal Delivery	5 (4.8%)	3 (2.9%)	8 (7.6%)
	Cesarean Delivery	14 (9.3%)	6 (4%)	19(12.6%)
Giving birth to twins	Yes	11 (26.8%)***	1 (2.4%)	12(29.3%)***
	No	8 (3.7%)	8 (3.7%)	15(7%)
Apgar sore at 5 min	≥ 8 (no)	13 (5.7%)**	8 (3.5%)	20 (8.8%)**
	< 8 (yes)	6 (21.4%)	1 (3.6%)	7 (25%)
Birth weight less than 2.5 Kg	Yes	18 (13.4%)***	8 (6%)*	25 (18.7%)***
	No	1 (0.8%)	1 (0.8%)	2(1.6%)
Born before 37 weeks	Yes	18 (14%)***	6 (4.7%)	23 (17.8%)***
	No	1 (0.8%)	3 (2.4%)	4 (3.1%)
Born before 37 weeks with birth weight less than 2.5 Kg	Yes	18 (15.7%)***	6(5.2%)	23 (20%)***
	No	1 (0.7%)	3 (2.1%)	4 (2.8%)
Central venous line in neonate	Yes	17 (32.1%)***	6 (11.3%)***	22 (41.5%)***
	No	2 (1%)	3 (1.5%)	5 (2.5%)
Mother GBS infection	Positive	0	0	0
	Negative	6 (5.5%)	5 (4.5%)	10(9.1%)
	Unknown	13 (9.2%)	4(2.8%)	17(12%)
PROM	Normal	8 (5.2%)	6 (3.9%)	14 (9%)
	≥ 18 hour	4 (14.3%)	2 (7.1%)	6(21.4%)
	<18 hour	1 (3.1%)	1 (3.1%)	1 (3.1%)
	Unknown	6 (14.6%)	0	6 (14.6%)
Length of stay in NICU (days)		(Yes vs No)	(Yes vs No)	(Yes vs No)
	Mean	(51.7 vs 13.9)***	(40.8 vs15.8)***	(47.1 vs 13.1)***

Abbreviations: GBS, Group B Streptococcus; UVC, **Umbilical Venous Catheter;** PICC, **Peripherally inserted central catheters;** UAC**, Umbilical Artery Catheter;** PROM, Prelab or rupture of membranes
*, P values less than 0.05; **, P values less than 0.01; ***, P values less than 0.001

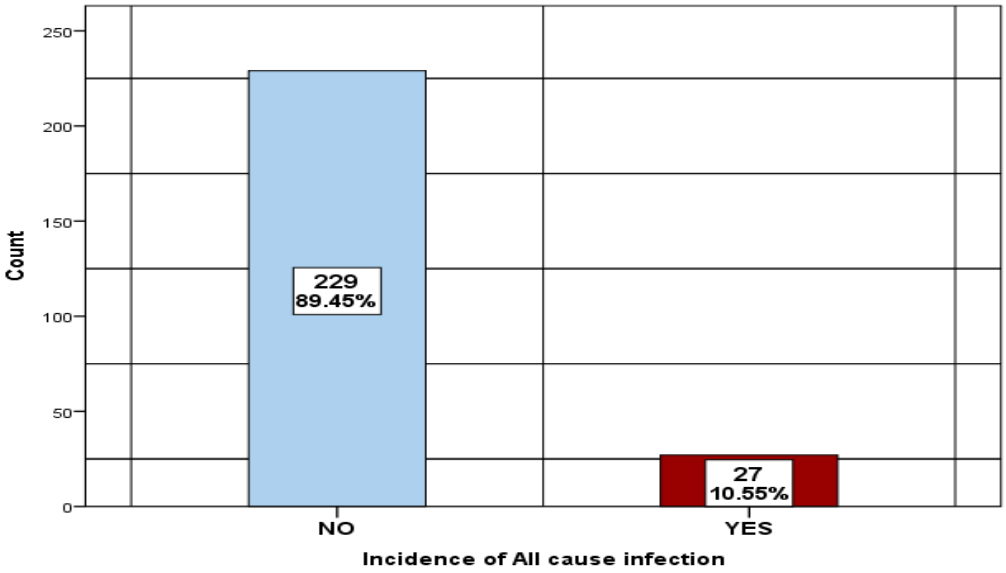
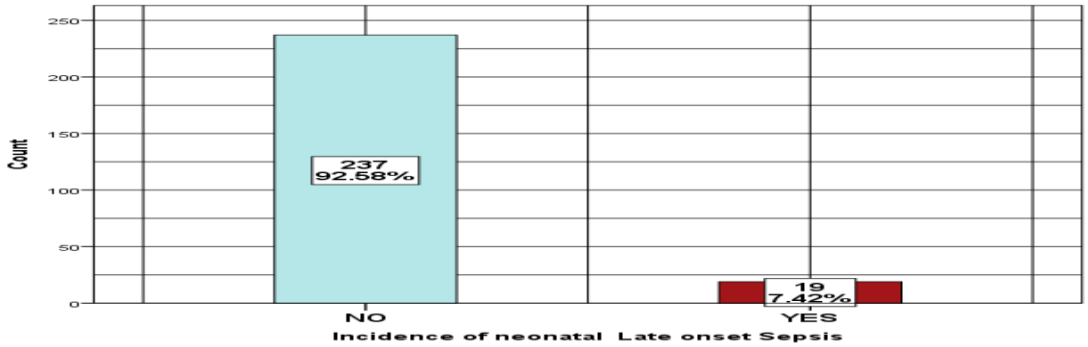
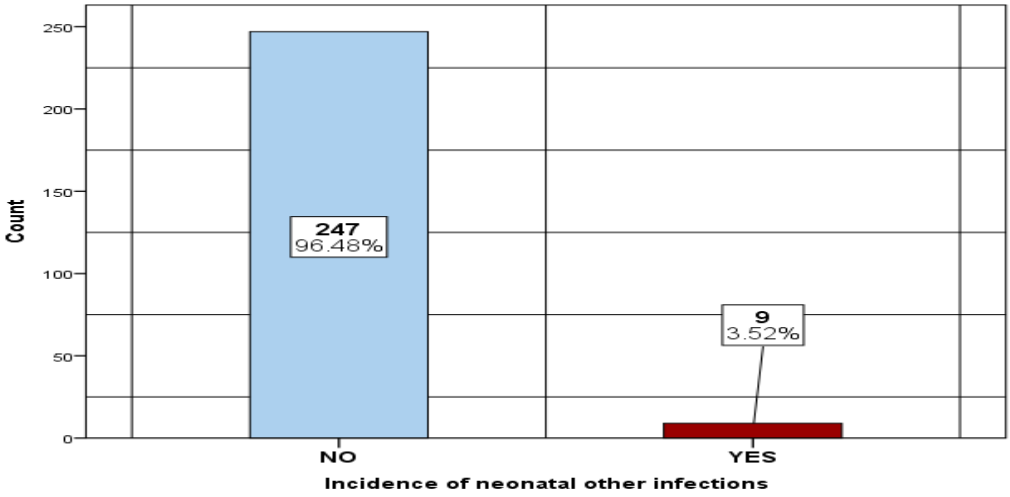
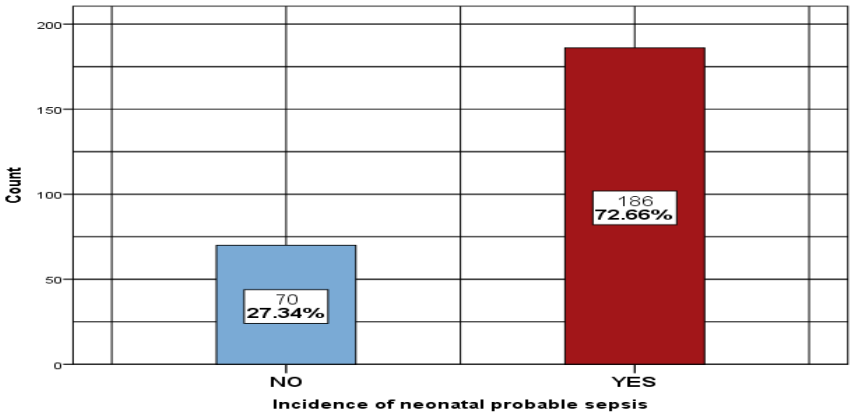


Figure 3: Bar charts for the incidence of neonatal sepsis and other infections in the Neonatal Intensive Care Unit.







Risk factor

Factors associated with neonatal Sepsis and other infections in Neonatal Intensive Care Unit

Table 6 displays the results of univariate and multivariate logistic regression analysis for the factors associated with the incidence of neonatal late-onset sepsis in the neonatal intensive care unit.

From the univariate analysis, significantly increased risks of neonatal late-onset sepsis in the neonatal intensive care unit were observed in twins (OR 9.5; 95 % CI 3.5– 25.5), scoring < 8 at Apgar score at 5 min (OR 4.5; 95 % CI 1.56– 13.05), low birth weight (OR 0.082; 95 % CI 0.03– 0.23), younger gestational Age (OR 0.692; 95 % CI 0.604– 0.793), receiving central venous line (OR 47.5; 95 % CI 10.5– 214.3), and length of stay in the neonatal intensive care unit (OR 1.05; 95 % CI 1.03– 1.07).

To identify the set of factors that jointly affect the incidence of neonatal late-onset sepsis, we used a stepwise procedure applied to the multiple logistic regression model. Accordingly, central venous line, low birth weight, younger gestational age, and Length of stay in the neonatal intensive care unit are jointly healthy determents of late-onset sepsis in the neonatal intensive care unit. Neonates who received central venous line showed incidence 8.88 times higher for late-onset sepsis when compared to those who did not receive a central venous line. If the length of stay in the neonatal intensive care unit increases by one day, then the odds of developing late-onset sepsis will be increases by 3%. If

the birth weight increases by 1 kg, then the odds of developing late-onset sepsis will decrease by 77%. If the gestational age increases by one week, then the odds of developing late-onset sepsis will be decreases by 18%.

Table 6: Univariate & Multivariate logistic regression analysis for the factors associated with neonatal Sepsis in the Neonatal Intensive Care Unit.

Factors	Neonatal Sepsis							
	Univariate				Multivariate			
	OR	95% CI		P.value	OR	95% CI		P.value
Giving birth to twins **(yes)**	9.5	3.5	25.5	**<0.001**	--------	--------	--------	--------
Apgar sore at 5 min **< 8**	4.5	1.56	13.05	**0.005**	--------	--------	--------	--------
Birthweight (kg)	0.082	0.03	0.23	**<0.001**	0.23	0.07	0.77	**0.017**
Gestational younger Age (weeks)	0.692	0.604	0.793	**<0.001**	0.82	0.69	0.97	**0.012**
Central venous line in neonate **(Yes)**	47.5	10.5	214.3	**<0.001**	8.88	1.41	55.89	**0.020**
Length of stay in NICU (days)	1.05	1.03	1.07	**<0.001**	1.03	1.003	1.05	**0.029**
Abbreviations: OR, odds ratio; CI, confidence interval; P values less than 0.05 were considered statistically significant, "---"not included in the multivariate logistic regression model.								

Comparison between organisms in NICU

The bacterial profile of neonatal Sepsis and other infections in the Neonatal Intensive Care Unit

Table 7 presents the main causative bacteria for neonatal sepsis and other infections in the neonatal intensive care unit. The results of the current study showed that 31.6% of Gram-positive bacteria and 84.2% of Gram-negative bacteria were responsible for neonatal late-onset sepsis. Similarly, other infections caused by 22.2% of gram-positive bacterial and by 77.8% of gram-negative bacteria. Overall, all-cause infections in the neonatal intensive care unit caused by 85.2% of gram-negative bacteria and 29.6% of gram-positive bacteria.

Staphylococcus Haemolyticus (26.3%) followed by Klebsiella Pneumoniae ESBL (21.1%), Staphylococcus Epidermidis (15.8%), Klebsiella.Pneumoniae (10.5%), Staphylococcus. Hominis (10.5%) and Pseudomonas. Aeruginosa (10.5%) were the most common causative bacteria for neonatal late-onset sepsis of the total cases in the neonatal intensive care unit. Regarding the other infections, Klebsiella Pneumoniae (33.3%) was the main causative bacteria. Overall, there was a high bacterial prevalence of Staphylococcus Haemolyticus (18.5%), Klebsiella Pneumoniae (18.5%), Klebsiella Pneumoniae ESBL (14.8%) and Staphylococcus Epidermidis (14.8%) of the total cases of neonatal infections in the neonatal intensive care unit.

Table 7: The main causative bacteria of Neonatal Sepsis and other infections in the Neonatal Intensive Care Unit (n=27).

Causative bacteria	Frequency (%) Late onset Sepsis (n=19)	Frequency (%) Other infections (n=9)	Frequency (%) All cause infection (n=27)
Klebsiella.Pneumoniae	2 (10.5%)	3 (33.3%)	5 (18.5%)
Klebsiella.Pneumoniae.ESBL	4 (21.1%)	0	4 (14.8%)
Escherichia.Coli.ESBL	0	1 (11.1%)	1(3.7%)
Staphylococcus.Hominis	2 (10.5%)	0	2(7.4%)
Staphylococcus.Epidermidis	3 (15.8%)	1 (11.1%)	4 (14.8%)
Morganella.Morganii	1 (5.3%)	0	1(3.7%)
Serratia.Marcescens	0	1 (11.1%)	1(3.7%)
Staphylococcus.Aureus.MRSA	1 (5.3%)	1 (11.1%)	2(7.4%)
Staphylococcus.Haemolyticus	5 (26.3%)	0	5 (18.5%)
Enterobacter.Cloacae	0	1 (11.1%)	1(3.7%)
Pseudomonas.Aeruginosa	2 (10.5%)	0	2(7.4%)
Enterobacter.Asburiae	1 (5.3%)	0	1(3.7%)
Haemophilus.Influenzae	0	1 (11.1%)	1(3.7%)
Stenotrophomonas.Maltophilia	1 (5.3%)	0	1(3.7%)
Enterococcus.Faecalis	1 (5.3%)	0	1(3.7%)
Staphylococcus.Capitis	1 (5.3%)	0	1(3.7%)
Gram positive bacteria	6 (31.6%)	2 (22.2%)	8 (29.6%)
Gram negative bacteria	16 (84.2%)	7 (77.8%)	23 (85.2%)

Table 8 demonstrates the patterns of empirical antibiotic prescribing for neonatal late-onset sepsis in the neonatal intensive care unit. Accordingly, Amikacin. piperacillin. tazobactam (57.9%), Vancomycin. Gentamicin (42.1%), Meropenem (15.8%) and Meropenem. Vancomycin (10.5%) were the most commonly prescribed antibiotics

for neonatal late-onset sepsis in the neonatal intensive care unit.

Table 8: Empirical antibiotics prescribed for neonatal late-onset Sepsis in the neonatal intensive care unit (n=19).

Antibiotic prescribed	Frequency	Percentage
Vancomycin. Gentamicin	8	**42.1%**
Amikacin.piperacillin.tazobactam	11	**57.9%**
Meropenem	3	**15.8%**
Meropenem.Vancomycin	2	10.5%
Metronidazole	1	5.3%
Gentamicin. Penicillin	1	5.3%
Meningitis.cefotaxime.vancomycin	1	5.3%
Gentamcin.Vancomycin.Tazobactam	1	5.3%
cefepime.meropenem	1	5.3%
Amikacin	1	5.3%
Cefepime.amikacin	1	5.3%
Ampicillin	1	5.3%
Ceftazidime. Ciprofloxacin	1	5.3%
Ampicillin. Gentamicin	1	5.3%
Amikacin.Tazobactam.cefotaxim.vancomycin	1	5.3%
Piperacillin.tazobactam.Gentamicin	1	5.3%

Bacterial and antibiotic resistance in Netoal Intensive Care Unit.

Table 9 shows the bacterial resistance patterns for neonatal late onset sepsis and other infections in the neonatal intensive care unit. Staphylococcus. Haemolyticus (26.3%), Klebsiella. Pneumoniae. ESBL (21.1%), Staphylococcus. Epidermidis (21.1%), Klebsiella. Pneumoniae (10.5%) and Staphylococcus. Hominis (10.5%) comprised of the highest prevalence of bacterial resistance profile for total cases of late-onset neonatal sepsis in neonatal intensive care unit for the other infections in the neonatal intensive care unit, Klebsiella. Pneumoniae (33.3%) showed the highest prevalence of bacterial resistance profile. Overall, there was a high prevalence of bacterial resistance of Klebsiella. Pneumoniae (18.5%), Staphylococcus. Haemolyticus (18.5%), Klebsiella. Pneumoniae. ESBL (14.8%), Staphylococcus. Epidermidis (14.8%), Staphylococcus. Hominis (7.4%) and Staphylococcus Aureus. MRSA (7.4%) in the neonatal intensive care unit.

Table 10 presents the sensitivity patterns of bacteria and antibiotic resistance in the neonatal intensive care unit.

Table 9: Bacterial resistance profile of neonatal Sepsis and other infections in the neonatal intensive care unit.

	Frequency (%)	Frequency (%)	Frequency (%)
Bacterial resistance	**Late onset Sepsis (n=19)**	**Other infections (n=9)**	**All cause infection (n=27)**
Klebsiella.Pneumoniae	2 (10.5%)	3 (33.3%)	5 (18.5%)
Klebsiella.Pneumoniae.ESBL	4 (21.1%)	----------	4 (14.8%)
Echerichia.Coli.ESBL	----------	1 (11.1%)	1 (3.7%)
Staphylococcus. Hominis	2 (10.5%)	----------	2 (7.4%)
Staphylococcus.Epidermidis	4 (21.1%)	1 (11.1%)	4 (14.8%)
Morganella.Morganii	1 (5.3%)	----------	1 (3.7%)
Serratia.marcescens	----------	1 (11.1%)	1 (3.7%)
Staphylococcus.Aureus.MRSA	1 (5.3%)	1 (11.1%)	2 (7.4%)
Staphylococcus.Haemolyticus	5 (26.3%)	----------	5 (18.5%)
Pseudomonas. Aeruginosa	----------	----------	----------
Enterobacter. Asburiae	----------	----------	----------
Haemophilus. Influenzae	----------	1 (11.1%)	1 (3.7%)
Stenotrophomonas.Maltophilia	1 (5.3%)	----------	1 (3.7%)
Enterococcus. Faecalis	1 (5.3%)	----------	1 (3.7%)
Staphyloccus.Capitis	1 (5.3%)	----------	1 (3.7%)
Enterobacter Cloacae	----------	1 (11.1%)	1 (3.7%)

Table 10: Antibiotic resistance profile of neonatal Sepsis and other infections in the neonatal intensive care unit. (n=27).

Antibiotic Resistance	KLEB. P	KLEB. P. ESBL	E.coli	SFCO. Hominis	SFCO. Epidermidis	MGNL. Morganii	SER. marcescens	SFCO. Aureus	SFCO. Haemolyticus	PSMN. Aeruginosa	ENBT. Asburiae	HMFL. Influenzae	S. Maltophilia	ENCO. Faecalis	SFCO. Capitis	ENBT. Cloacae
Ampicillin	**4(15.4)**	**3(11.5)**	**1(3.8)**	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
Cafalotin	--------	**3(11.5)**	**1(3.8)**	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	**1(3.8)**
Cefepime	--------	**3(11.5)**	**1(3.8)**	--------	--------	**1(3.8)**	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
Ceftazidime	--------	**3(11.5)**	**1(3.8)**	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
Ceftriaxone	--------	**3(11.5)**	**1(3.8)**	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------
Trimethoprim. Sulfamethoxazole	**1(3.8)**	**3(11.5)**	------	--------	**1(3.8)**	--------	--------	**2(7.7)**	**4(15.4)**	--------	--------	--------	**1(3.8)**	--------	--------	--------
Erythromycin	--------	--------	------	**2(7.7)**	**2(7.7)**	--------	--------	**1(3.8)**	**4(15.4)**	--------	--------	--------	--------	**1(3.8)**	**1(3.8)**	--------
Oxacillin.	--------	--------	------	**2(7.7)**	**3(11.5)**	--------	--------	**1(3.8)**	**4(15.4)**	--------	--------	--------	--------	--------	**1(3.8)**	--------
Clindamycin	--------	--------	------	--------	**2(7.7)**	--------	--------	**1(3.8)**	**5(19.2)**	--------	--------	--------	--------	--------	--------	--------
Gentamicin	--------	**1(3.8)**	------	--------	**2(7.7)**	--------	--------	**1(3.8)**	**2(7.7)**	--------	--------	--------	--------	--------	**1(3.8)**	--------
Piperacillin .Tazobactam	--------	--------	------	--------	--------	**1(3.8)**	--------	--------	**1(3.8)**	**1(3.8)**	--------	--------	--------	--------	--------	--------
Amoxicillin.Clavulanate	--------	**1(3.8)**	------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	**1(3.8)**
Cefoxitin	--------	--------	------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	--------	**1(3.8)**
Ciprofloxacin	--------	--------	------	**1(3.8)**	**1(3.8)**	--------	--------	**1(3.8)**	**3(11.5)**	--------	--------	--------	--------	--------	**1(3.8)**	--------
Levofloxacin	--------	--------	------	--------	--------	--------	--------	--------	**1(3.8)**	--------	--------	--------	--------	--------	--------	--------
Moxifloxacin	--------	--------	------	--------	--------	--------	--------	--------	**1(3.8)**	--------	--------	------	--------	--------	--------	--------
Doxycycline	--------	--------	------	--------	--------	--------	------	--------	--------	--------	------	--------	--------	**1(3.8)**	--------	--------
Tetracycline.	--------	--------	------	--------	--------	--------	------	--------	--------	--------	------	--------	--------	**1(3.8)**	--------	--------

Abbreviations: **KLEB. P**, Klebsiella.Pneumoniae;
KLEB. P. ESBL, Klebsiella.Pneumoniae.ESBL; E.coli, Echerichia.Coli.ESBL**;**
SFCO. Hominis, Staphylococcus. Hominis; SFCO**.**
Epidermidis, Staphylococcus.Epidermidis,
MGNL. Morganii, Morganella.Morganii; SER**.**
Marcescens, Serratia.marcescens; SFCO**. Aureus,** Staphylococcus.Aureus.MRSA; SFCO**.**
Haemolyticus, Staphylococcus.Haemolyticus; PSMN**.**
Aeruginosa, Pseudomonas. Aeruginosa; ENBT**.**
Asburiae, Enterobacter. Asburiae; HMFL**.**
Influenzae, Haemophilus. Influenzae;
S. Maltophilia, Stenotrophomonas.Maltophilia; ENCO**.**
Faecalis, Enterococcus. Faecalis;
SFCO. Capitis, Staphyloccus.Capitis; ENBT**.**
Cloacae, Enterobacter Cloacae.

DISCUSSION

Antibiotic is important to save the life of neonate in NICU in some situation such as infection. Nevertheless, one of the effects of the main issue in the newborn in NICU is the abuse of antibiotics that leads to antibiotic-Resistance. The results indicate that knowledge of assessment of empirical antibiotic therapy and duration, sensitivity patterns of bacteria and antibiotic resistance, causative organisms, identify the set of risk factors, and determine the type of infections in neonatal intensive care units support the improvement of healthcare treatment and safety of patients.

The empirical antibiotic used and duration in the first 3 days of postnatal

Our results show, the major Empirical antibiotic use in the first postnatal for Early-onset sepsis was Ampicillin (or penicillin) plus Gentamicin of probable sepsis cases, 12 cases (6.5%) were prescribed Ampicillin + Gentamicin, 170 cases (91.4%) were prescribed Penicillin + Gentamicin. They follow the guideline of empirical antibiotic use for EON in the first 3 days for neonate after born Ampicillin/penicillin+plus Gentamicin although there was 1 case (0.5%) were prescribed ampicillin, 1 case (0.5%) were prescribed Penicillin + Cefotaxime, 1 case (0.5%) were prescribed Ampicillin + Cefotaxime and 1 case (0.5%) were prescribed Penicillin + Amikacin. The World Health Organization (WHO) recommended the empirical antibiotic use as first-line antimicrobials neonatal for early-onset sepsis (EOS) during three (3) days after birth and Long-onset sepsis (LOS), or meningitis is Ampicillin (or penicillin) plus Gentamicin (Reference No. 28). On the other hand, Management for early and late sepsis in the neonate in NICU, the Initial empiric therapy depends on the newborn age, the type of organisms in an individual nursery, pathogens, and the causes of infection (Edwards et al., 2019).

In the present study, we found that of the suspected sepsis cases, 145 cases (78%) were prescribed as an empirical antibiotic for ≤ 72 hours, and 41 cases (22%) were prescribed as empirical antibiotics for > 72 hours. This finding is followed in agreement with the previous studies which showed that the duration of empirical antibiotic in the neonate is 48–72 hours until culture results for suspected sepsis (Astorga et al., 2018; Patel et al., 2009; Tzialla et al., 2015; Sivanandan et al., 2011). Commonly, the antimicrobial is stopping between (48–72 hours), as soon as blood culture are proven negative, and if lab outcome and the clinical signs and symptoms preclude the infection (Tzialla et al., 2015). Furthermore, an empirical antibiotic for neonatal early-onset sepsis must be stopped, with regular screening laboratory exams and no signs and symptoms of infection in the first postnatal (Cotten & Smith, 2013).

Received antibiotic with wrong diagnose sepsis in the first 3 days postnatal days.

A finding of the present study shows that among the 256 neonates referred to the neonatal intensive care unit, 168 neonates (72.6%) [95%CI: 67.2 – 78.2] were diagnosed with probable sepsis, and none of them was diagnosed with early-onset sepsis. These findings are consistent with previous studies of Human Development National Research Network and National Institute of Child Health. Assured in this observation on 6956 VLBW neonatal, view at least one course of antibiotic therapy was received by 56% of all new, only 21% of neonatal were diagnosed as sepsis. This significant correlation suggested the use of empirical antibiotic therapy although none of them diagnosed EOS There is no specific symptoms and signs for sepsis and empirical antibiotic treatment immediately used in high risk of symptom or sepsis (Tzialla et al., 2015).

Comparison between organisms in NICU

The result of the present study shows that 31.6% of Gram-positive bacteria and 84.2% of Gram-negative bacteria were responsible for neonatal late-onset sepsis. Similarly, other infections caused by 22.2% of gram-positive bacteria and by 77.8% of gram-negative bacteria. Overall, all-cause infections in the neonatal intensive care unit were caused by 85.2% of gram-negative bacteria and 29.6% of gram-positive bacteria. Staphylococcus Haemolyticus (26.3%) followed by Klebsiella Pneumoniae ESBL (21.1%), Staphylococcus Epidermidis (15.8%), Klebsiella.Pneumoniae (10.5%), Staphylococcus.Hominis (10.5%) and Pseudomonas. Aeruginosa (10.5%) were the most common causative bacteria for neonatal late-onset sepsis of the total cases in the neonatal intensive care unit. Regarding the other infections, Klebsiella Pneumoniae (33.3%) was the main causative bacteria. Overall, there was a high bacterial prevalence of Staphylococcus Haemolyticus (18.5%), Klebsiella Pneumoniae (18.5%), Klebsiella Pneumoniae ESBL (14.8%) and Staphylococcus Epidermidis (14.8%) of the total cases of neonatal infections in the neonatal intensive care unit. This finding is in agreement with the previous studies, which showed newborns had culture confirm septicemia and /or meningitis that Gram-ve bacteria (47.9%) was more considerably than Gram+ve (39.7%) caused sepsis. Klebsiella Pneumoniae (n=64, 16.8%) on the top followed by Coagulase Negative Staphylococci (CONS),Candida (n=42, 12.1%), Klebsiella Pneumoniae (ESBL) (n=41, 10.7%) and Staphylococcus Aureus (n=35, 9.2 %) in Latifa Woman and Children Hospital - Dubai, UAE (Elhalik et al., 2018). Another previous study in UAE show gram-negative organisms 104 (48.8 percent) more than gram-positive organism 98 (46 percent) (Al Khaaldi et al., 2017).

In our study, the type of organisms and percentage were different compared to other studies. Therefore, the empirical antibiotic therapy was considered different based up on hospital guidelines (Edwards et al., 2019).

Hence, determining the type of organisms that are spreading in neonatal intensive care unit is important to define the empirical antibiotic.

Bacterial and antibiotic resistance in Neonatal Intensive Care Unit

A finding of the present study shows the bacterial resistance patterns for neonatal late onset sepsis and other infections in the neonatal intensive care unit. Staphylococcus. Haemolyticus (26.3%), Klebsiella. Pneumoniae. ESBL (21.1%), Staphylococcus. Epidermidis (21.1%), Klebsiella. Pneumoniae (10.5%) and Staphylococcus. Hominis (10.5%) comprised of the highest prevalence of bacterial resistance profile for total cases of late-onset neonatal sepsis in neonatal intensive care unit for the other infections in the neonatal intensive care unit, Klebsiella. Pneumoniae (33.3%) showed the highest prevalence of bacterial resistance profile. Overall, there was a high prevalence of bacterial resistance of Klebsiella Pneumoniae (18.5%), Staphylococcus Haemolyticus (18.5%), Klebsiella Pneumoniae.ESBL (14.8%), Staphylococcus Epidermidis (14.8%) and Staphylococcus Hominis (7.4%) in the neonatal intensive care unit. Klebsiella Pneumoniae ESBL high grade of resistance to (Ampicillin, Cafalotin, Cefepime, Ceftazidime, Ceftriaxone, and Trimethoprim-Sulfamethoxazole), Staphylococcus Haemolyticus to (Erythromycin, Oxacillin, Clindamycin, and Ciprofloxacin), Klebsiella Pneumoniae (Ampicillin) and Staphylococcus Epidermidis to (Oxacillin).

We agree with, comparing data between several NICUs and geographic areas it is a complication because of total heterogeneities in the local epidemiology in each particular area, organizational models, logistic and the structure of the NICUs and their surveillance policies (Giuffrè et al., 2016).

The main of the World Health Organization (WHO) list is Gram-negative bacterial organisms. Because of their distinctive structure, Gram-negative bacteria are more resistant than Gram-positive bacteria, and cause enormous morbidity and mortality worldwide. The major reason of Gram-negative bacteria resistance is the outer membrane for extensive range of antimicrobial including colistins, β-lactams, quinilons and other antibiotics. Most antimicrobial should pass the outer membrane to arrival their aim, for instance, hydrophobis drugs can push through by a diffusion pathway, furthermore, hydrophilic antimicrobial like β-lactams push through porins, and vancomycin can't cross the outer membrane because of its structure that block it from using any of these passages. Can create resistance by any change in the outer membrane by Gram-negative bacteria like changing the mutations in porins or hydrophobic properties and other factors. Gram-positive bacteria shortage this important layer, which makes Gram-negative bacteria more resistant to antimicrobial than Gram-positive ones (Breijyeh, et al., (2020)). Staphylococcus aureus is one of the eminent medically important bacterial organism. Infections occasion by S. aureus strains with Methicillin resistance connected with increased aggressive course, multiple drug resistance, mortality and morbidity and hospital outbreaks (Kali, A. (2015)). In present study we found 2 infection causes by Staphylococcus aureus one causes LOS and second cause other infection (eye infection), in sepsis situation treated by vancomycin.

Risk factor

In the present study, we found that central venous line in neonate major risk factor for Sepsis as odds ratio 8.88% following by length of stay in NICU 1.03%, gestational age 0.82%, and Birthweight 0.23%. Among the total 256 neonates referred to the neonatal intensive care unit, 19 neonates (7.4%) [95%CI: 4.2 – 10.7] were diagnosed with late-onset sepsis, and none of them were diagnosed with early-onset sepsis. About 9 neonate (3.5%) [95%CI: 1.2 – 5.8] were diagnosed with other infection. A study by Zipursky el at\ (2019) found that 3306 (11.7%) present in hospital-acquired infections, it was considerable drop rate in 2010 as 14.2% and 2016 as 9.2%;P < .01), and the ratio of both central line-associated bloodstream infections CLABSIs and non-central line-associated bloodstream infections non-CLABSIs (P < .01) over the study term concomitant with an enormous decrease in the period of central line use (P = .01) in 30 Canadian Neonatal Network NICU. Risk factors for mortality were observed in nosocomial sepsis, low birth weight, and prematurity (Koutouby et al., 1995). Premature newborn infant in NICU has a high risk of hospital-acquired infections. one of commonly used in neonatal intensive care unit is centerline catheter that leads to bloodstream infection (McGowan, 2018).

Our study show, mother GBS infection Positive 4 (1.6%), Negative 110 (43%) and Unknown 142 (55.5%). The mother received prophylaxis antibiotics for GBS (n=4) 2 (50%). It is non-EOS. The result was zero, and the high ratio of unknown cases, 142 (55.5%). Findings of the previous study reported that it was the most common cause of EOS on a retrospective 12-year study in Latifa Women & Children hospital Dubai, UAE Group B Streptococcus (43- 58 percent) (Elhalik et al., 2018). Moreover, Early-onset group B streptococcal infection (EOGBS) is an elevated effect happening during delivery, in spite of it is low indecision, but it has an important life effect of the neonate (Braye et al., 2019).

The result of the present study shows that the prolonged rupture of membranes (PROM) Normal 155 (60.5%), leaking ≥ 18 hours 28 (10.9%), leaking <18 hours 32 (12.5%) and Unknown 41 (16%). Finding in the previous studies which showed that neonatal with mothers had risk factors like prolonged rupture of membranes, low gestational weight, preterm (<37 weeks) PROM, low Appearance and maternal colonization, Activity, Grimace, Pulse, Respiration score at birth had more ratio

of infection compared with neonates of a mother without these risk factors. There were 26 (13%) of the neonates had an early-onset neonatal infection, and in 5% of cases, sepsis was sure, provides more evidence marks a high level of EONI among neonatal of mothers complicated with prolonged rupture of membranes (PROM) (Ibishi et al., 2018). Onther study show, a total of 405 pregnant with prolonged rupture of membranes (PROM). Twenty-one cases (5.2%) of newborn sepsis. Of all PROM cases, one hundred eighty-six (45.9 percent) occurred in period pregnancy, of which fifty-six cases (30.1%) were suspected neonate sepsis and one hundred thirty cases (68.9 percent) were without neonate sepsis. The analyses present that the risk of neonate sepsis was higher in pregnant women with PROM for ≥ 18 hrs before hospital admission (OR 3.08) (Ocviyanti & Wahono, 2018). Preterm premature rupture of membranes (PPROM) is related to infection and inflammation associated with morbidity and mortality risks, and it may include the leakage of a membrane that leads correlated to infection (Drassinower et al., 2016; Ocviyanti & Wahono, 2018).

LIMITATION

This study was a retrospectively collected data from a routine clinic and not prospectively collected data. A group of patients had the critical disease, and congenital malformation was available in neonatal intensive care unit so measurement outcome of condition of discharge: Home, Died and another facility unfair if related to antibiotic use were not considered. Moreover, most of mother GBS infection unknown to measurement as a risk for group B streptococcus infection. Finally, this study was based on the population from one hospital; data from other centres are required to find out whether our results can be generalized to other neonatal intensive care unit settings.

There are multiple factors that support and strength the antimicrobial use in the setting such as availability of culture and sensitivity testing, availability of different antimicrobial options (as formulary medications), support from administration to promote antibiotic use, implementation of antimicrobial stewardship program within the facility that promote the appropriate use of antimicrobials, improves patient outcomes, reduces microbial resistance, and decreases the spread of infections caused by multidrug-resistant organisms. Moreover, the availability of clinical pharmacists is strongly supports the appropriate use of antimicrobials. However, the lack of other resources such as infectious disease physicians considered one of the limitations in the setting. Moreover, other limitations in the facility setting include lack of use of drug use evaluation measures such as defined daily dosing (DDD) or days of therapy (DOTs). This type of analysis of antimicrobial consumption is an important element of medical audit as it supports monitoring, evaluation, and applies necessary modification in the pattern of prescribing to the rational use of antimicrobials (Shankar et al., 2003).

CONCLUSION

In our study, we detected that ratio of EOS and LOS was less than has been reported in some nations. Moreover, the EOS was zero. Infections in the neonatal intensive care unit caused by 85.2% of gram-negative bacteria and 29.6% of gram-positive bacteria. There was a high bacterial prevalence of Staphylococcus Haemolyticus (18.5%), Klebsiella Pneumoniae (18.5%), Klebsiella Pneumoniae ESBL (14.8%) and Staphylococcus Epidermidis (14.8%) of the total cases of neonatal infections in the neonatal intensive care unit. Furthermore, there was a high prevalence of bacterial resistance of Klebsiella. Pneumoniae (18.5%), Staphylococcus. Haemolyticus (18.5%), Klebsiella. Pneumoniae. ESBL (14.8%), Staphylococcus. Epidermidis (14.8%) and Staphylococcus. Hominis (7.4%) in the neonatal intensive care unit. Klebsiella Pneumoniae ESBL high grade of resistance to (Ampicillin, Cafalotin, Cefepime, Ceftazidime, Ceftriaxone, and Trimethoprim-Sulfamethoxazole), Staphylococcus. Haemolyticus to (Erythromycin, Oxacillin, Clindamycin, and Ciprofloxacin), Klebsiella. Pneumoniae (Ampicillin) and Staphylococcus Epidermidis to (Oxacillin). The central venous line in neonate major risk factor for sepsis as odds ratio 8.88% is followed by length of stay in NICU 1.03%, Gestational Age 0.82%, and Birthweight 0.23%. Moreover, they follow the guideline of using empirical antibiotics and duration in the first 3 days postnatal and determine the type of organisms that are spreading in the neonatal intensive care unit is important to define the empirical antibiotic during a stay in the NICU.

Recommendation

Based on the findings of this study, the following recommendations are suggested:

- Improving EOS diagnose to limitate use unnecessary Empirical antibiotic in the first 3 days postnatal.
- Commitment to do mother GBS test.
- Healthcare worker should adhere to (CDC) 12-Step to prevention antibiotic resistance.
- The uses of the central venous line in the neonate in NICU should reduce.

Research implications

- A prospective study is needed in several NICUs to assess the pattern of organisms spread in NICUs for every hospital.
- Further research is suggested to investigate the reason for poor centerline control and find new safe way rather than central venous line in neonatal in NICU.
- Start to activate the technique as an automatic stop to use empirical antibiotics at 72 hours.
- Further research is suggested, to do more study for use empirical antibiotics in late-onset sepsis.

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