

Epidemiology of nosocomial *Staphylococcus epidermidis* and *Acinetobacter baumannii* infections in a neonatal intensive care unit

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ABSTRACT

Background and Objectives: This study aimed to investigate epidemiology of *Staphylococcus epidermidis* (*S. epidermidis*) and *Acinetobacter baumannii* (*A. baumannii*) infections in neonatal intensive care unit (NICU) in a period of 8 years.

Materials and Methods: This retrospective cohort study was conducted on 46 cases of nosocomial infection by *S. epidermidis*, and 44 neonates with *A. baumannii* in NICU of Valiasr hospital, Iran.

Results: The trend of *A. baumannii* and *S. epidermidis* infection were as follows: 1 and 7 in 2014, 11 and 7 in 2015, 20 and 11 in 2016, 1 and 4 in 2017, 4 and 6 in 2018, 4 and 4 in 2019, 0 and 1 in 2020, and 3 and 6 in 2021-March 2022 respectively. Mortality proportion (%) in neonates with *S. epidermidis* and *A. baumannii* infection was at 8.3 and 32.1, respectively. There was a strong positive correlation between number of infected neonates in month and average of prescribed antibiotics before incidence of infection in every baby in that month. Fluconazole prescription before incidence of infection were associated with the *A. baumannii* infection in month too. Amikacin prescription had adjusted correlation on increasing of *A. baumannii* and *S. epidermidis* infection in month.

Conclusion: It seems reducing of hospitalization duration and medication prescriptions management plays an important role in reducing of nosocomial infections

Keywords: *Acinetobacter baumannii*; *Staphylococcus epidermidis*; Outbreak; Neonatal intensive care units; Nosocomial infections

INTRODUCTION

The isolation of an infectious species from two or more sterile site of different babies hospitalized in the same ward during a minimum of two weeks' period

is defined as an outbreak in the neonatology ward or neonatal intensive care unit (NICU). Nearly 38% of outbreaks in intensive care units (ICU) are reported from NICUs, also 87.6% of outbreaks happen in the neonatology wards (1). The underlying reasons for

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this high rate are speculated to be the prematurity of babies in these wards, inability to produce a strong immunologic defense, the nature of intensive care unit itself including prolonged length of stay, frequent invasive medical procedures, exposure to antibiotics and constant contact with healthcare staff (2-4). The most common pathogens which cause these NICU outbreaks are *Staphylococcus epidermidis* (*S. epidermidis*), *Klebsiella pneumoniae*, *Serratia marcescens* and *Acinetobacter baumannii* (*A. baumannii*). Furthermore, reports of NICU outbreaks with *Burkholderia cepacia*, *Escherichia coli* and *Staphylococcus aureus* have been published in the literature (5).

S. epidermidis is part of the normal microbiota, typically the skin flora, and less commonly in the mucosal flora. However in vulnerable patients using medical devices such as central-line or with predisposing conditions such as immunodeficiency, they can cause life-threatening infections (6, 7). The high level of antibiotic resistance and their ability to make biofilms allows them to endure and remain in hospital environment (8, 9). *S. epidermidis* is usually present in the nosocomial environment and can lead to the morbidity, mortality and economic burden (10).

A. baumannii is a Gram-negative, aerobic bacterium, which belongs to the family *Neisseriaceae*. *A. baumannii* is known to be an important nosocomial pathogen, chiefly in intensive care units (11, 12). This pathogen, is recognized as an agent of septicemia in outbreaks of NICUs worldwide (13-17). The global mortality rate from septicemia by *A. baumannii* has ranged from 34.0% to 43.4% in ICUs (18). Increasing rates of *A. baumannii* infections may be due to delays in infection control practices and greater prescription of wide-spectrum antibiotics (19, 20). In this study, we intend to describe epidemiology of two nosocomial infections due to *S. epidermidis* and *A. baumannii* in the Valiasr hospital NICU over the course of 8 years with the occurrence of several outbreaks and investigate the associated predisposing factors in the babies.

MATERIALS AND METHODS

Design. We detected outbreaks caused by *S. epidermidis* and *A. baumannii* in the NICU of Valiasr hospital, a tertiary center affiliated with Tehran University of Medical Sciences, located in Tehran, Iran, from March 2014 to March 2022. The NICU at Val-

iasr hospital has 35 beds and 2 isolated rooms, occupancy rates were estimated at 95%. The frequency of *S. epidermidis* occurred with 46 infants infected from March 2014 to March 2022, and the *A. baumannii* frequency between December 2014 and March 2022 including 44 cases. This study was approved by the Institutional Ethical Committee at Tehran university of medical sciences; R.TUMS.IKHC.REC.1397.138

Study variables. In this retrospective cohort study, the medical and demographic information documented by the hospital registry system was used for comparison. These variables included: gender, age, gestational age, birth weight, weight on admission day, cause of admission, type of culture test (source of nosocomial infection), Apgar score at first and fifth minutes, underlying diseases in either mother or the infant, duration of hospitalization, outcome of admission (expired or discharged), use of incubator care, mechanical ventilation, central or peripheral venous catheter, chest tube, prescribed antibiotics, and granulocyte colony stimulating factor (G-CSF) or surfactant.

The study included all admitted newborns to the NICU from March 2014 to March 2022 who remained as in-patients at least 72 hours after ICU admission and detected nosocomial infection by *S. epidermidis* and/or *A. baumannii*. Detection of nosocomial infection was based on guidelines of Centers for Disease Control and Prevention (CDC) and the National Health Surveillance Agency (21). Samples with incomplete medical records were excluded from the study.

Laboratory test and analysis. When obtaining blood cultures, the skin was cleaned using 70% isopropyl alcohol from the center to the margin of the needle insertion site after the vein was touched. This was followed by cleaning with 2% of iodine tincture, and the site was left to dry. When the vein needed to be palpated, sterilization of skin over the vein was conducted. For blood cultures, 3-5 ml of blood was obtained and inoculated into a sterile culture bottle. Blood culture bottles were processed by standard bacteriological techniques.

S. epidermidis was identified as coagulase-negative Gram-positive staphylococci on the basis of negative slide and tube coagulase reactions, susceptibility to Novobiocin on Mueller Hinton Agar and negative DNase results (22). *A. baumannii* as a Gram-negative

coccobacilli have positive results to a catalase test and negative to an oxidase test and has an absence of motility (20).

All isolates of a pathogen cultured from blood collected >48 h after hospitalization were considered as nosocomial bloodstream infections when they meet at least one of the following criteria signs or symptoms: fever (>38.5°C), hypothermia (<36.5°C), apnea and bradycardia.

Data are reported as mean and standard deviations (SD) or frequency (proportions). Continuous data was analyzed for normality using the Shapiro–Wilk test of normality. Spearman correlation, partial correlation and chi square tests were used for further analysis. The data was analyzed with SPSS-20 software (IBM, Armonk, NY, USA) and a P-Value of ≤ 0.05 was considered significant.

RESULTS

From March 2014 until March 2022, 6446 neonates were admitted to the NICU of Valiasr Hospital for various causes. Of those, 85 neonates developed nosocomial infection; 41 cases by only *S. epidermidis*, 39 neonates only by *A. baumannii*, and 5 neonates with both pathogens (*A. baumannii* and *S. epidermidis*).

The trend of *A. baumannii* infection in various years as followed: 1 infection in 2014, 11 in 2015, 20 in 2016, 1 in 2017, 4 in 2018, 4 in 2019, 0 in 2020, and 3 in 2021- March 2022. These amounts in *S. epidermidis* were 7 in 2014, 7 in 2015, 11 in 2016, 4 in 2017, 6 in 2018, 4 in 2019, 1 in 2020, and 6 in 2021 -March 2022.

Based on epidemic curves, *S. epidermidis* and *A. baumannii* are endemic, but outbreaks have been occurred in certain intervals. The beginning phases of outbreaks were different in cases of *S. epidermidis* and *A. baumannii*. Outbreaks of *S. epidermidis* had propagated curve most likely. The mode of this outbreak was 4 cases in November 2015. There was no special model of correlation in their distribution over time. *A. baumannii* outbreak had continues common source with the mode of 4 cases in November 2016 and 4 cases in May 2016. The correlation was cubic type and was calculated 0.68 ($R^2_{cubic}=0.688$) (Figs. 1a and 1b).

Almost all infants (97.65%) were admitted to the NICU within their first 48 hours from birth (73 babies on the first day of birth and 10 on the second day), 2

infants were admitted in the fourth day of their birth. The mean (SD) weight of neonates infected with *S. epidermidis* and *A. baumannii* was calculated at 1844 (982.65) and 1656.06 (812.32) gram respectively (Table 1).

Overall, 52.17% (24/46) and 47.72% (21/44) of the neonates had a birth weight of 1500 to 2,499 grams and, 45.65% (21/46) and 52.27% (23/44) had very low birth weight (VLBW) (<1500 grams) in *S. epidermidis* and *A. baumannii* group respectively. Also the gestational age mean (SD) was calculated at 34.62 (3.89) and 31.32 (4.57) weeks in neonates with infection of *S. epidermidis* and *A. baumannii* respectively. Overall, 78.26% (36 neonates) and 45.65% (21 cases) were born preterm (<37 weeks gestational age) and very preterm (<32 weeks gestational age) respectively in *S. epidermidis* group and, 84.09% (37 infants) of patients were born preterm and 36.36% neonates (16 cases) were born very preterm in *A. baumannii* group. Except for two of the cases, all neonates had cesarean delivery. In this study, all mothers participated in prenatal care during pregnancy and they reported to be non-smokers. The mean (SD) of Apgar score taken at the 1st and 5th minutes was 7.4 (1.84) and 9.07 (0.81) in *S. epidermidis* and 6.78 (2.50) and 9.1 (0.89) in *A. baumannii* groups respectively. The mean (SD) number of antibiotic prescribed per neonates before the onset of nosocomial infection in each baby was 7.9 (5.66) and 12.34 (9.3) in *S. epidermidis* and *A. baumannii* respectively (Table 2).

Overall, 4.88% (2/41) of neonates infected by *S. epidermidis* and, 33.33% (13/39) of those infected with *A. baumannii* expired in NICU. This difference was statistically significant ($X^2 = 10.62$; P-Value = 0.001). Also 60% (3/5) those infected both of them (*S. epidermidis*, and *A. baumannii*) expired in NICU. We found a positive correlation between the number of *A. baumannii* infection number in month and the average of days hospitalized before the onset of nosocomial infection in patient (Spearman's rho=0.746 P-Value= 0.02), but there was not statistical correlation between *S. epidermidis* infection number in month and the average of days hospitalized before the onset of nosocomial infection in patient (Spearman's rho=0.334, P-Value= 0.135).

In this study, 80.43% (37/46) and 79.55% (35/44) of *S. epidermidis* and *A. baumannii* agents were isolated from blood, 4.3% (2/44) and 25.0% (11/44) was isolated from respiratory tract respectively, and 6.18% (3/44) of *A. baumannii* agent was isolated from both

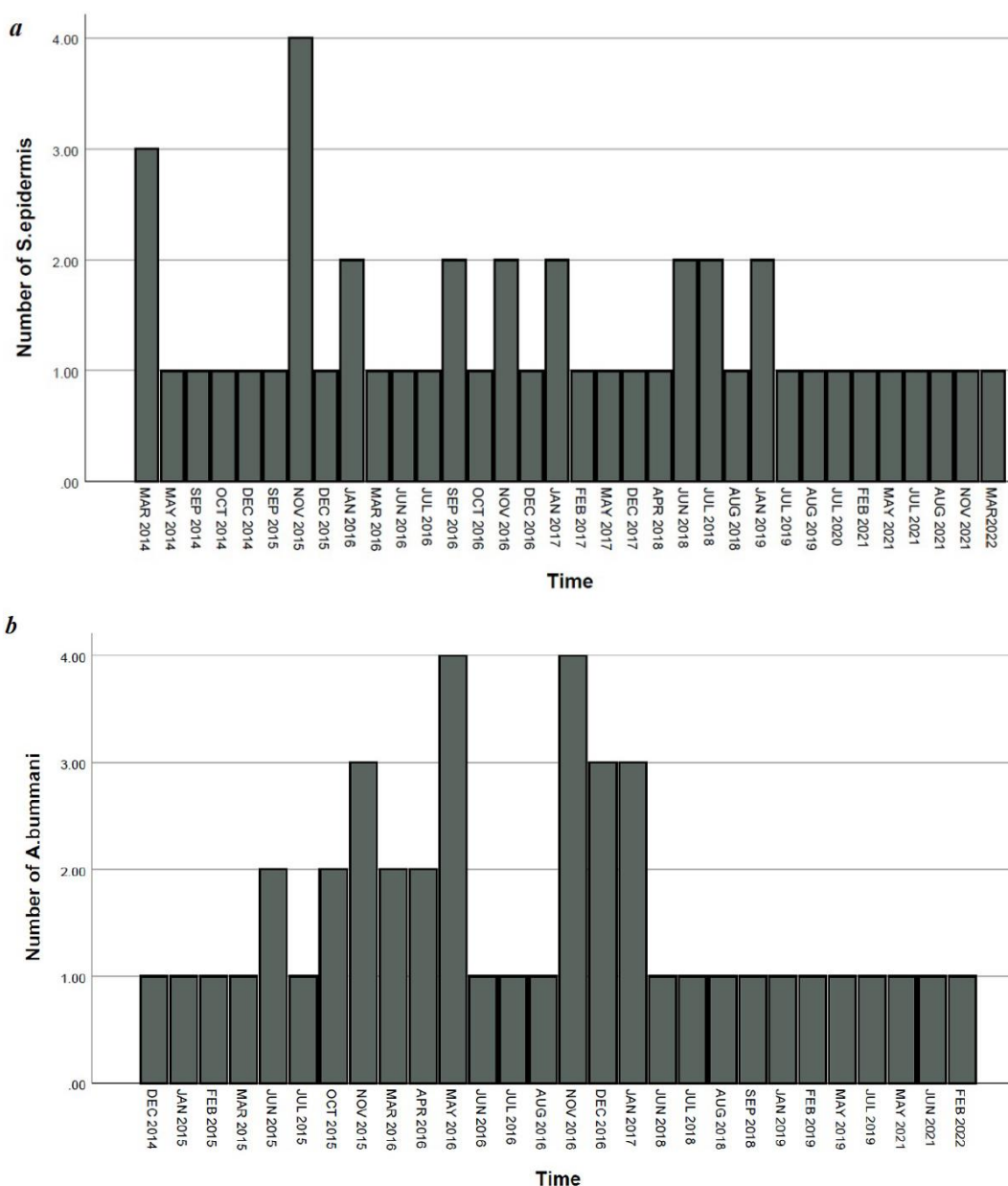


Fig. 1. The bar chart of occurrence nosocomial *S. epidermidis* (1a) and *A. baumannii* (1b) in NICU based on month

Table 1. The summary of descriptive information of weight of infected (*A. baumannii* and *S. epidermidis*) neonates by years

	<i>A. baumannii</i> (n)	Weight (gr) Mean (SD)	<i>S. epidermidis</i> (n)	Weight (gr) Mean (SD)
2014	1	1630.0	7	1791.43 (719.92)
2015	11	2103.0 (946.51)	7	2403.0 (906.92)
2016	20	1448.0 (658.40)	11	1673.18 (979.46)
2017	1	920.0	4	1570.0 (1401.79)
2018	4	1642.03 (742.01)	6	1581.09 (1289.1)
2019	4	1598.09 (988.39)	4	2447.0 (1009.8)
2020	0	-	1	2019.21
2021-March 2022	3	2113.78 (879.9)	6	1891.0 (841.0)
Total	44	1656.06 (812.32)	46	1844 (982.65)

Table 2. Distribution of neonates with outbreak of *S. epidermidis* and *A. baumannii* by Gestation age, Inpatient weight, Apgar-1 and 5th minute, Number prescribed antibiotics in per neonates, Number prescribed antibiotics in month and Number infected neonates in month

Number	Total		<i>S. epidermidis</i>		<i>A. baumannii</i>	
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Gestation age	33.12 (4.55)	33.0 (9.0)	34.62 (3.89)	34.0 (6.5)	31.32 (4.57)	34.0 (6.5)
Inpatient weight	1970 (903.74)	1910 (1785)	1844 (982.65)	1560 (3070)	1656.06 (812.32)	1470 (3000)
Apgar-1 st minute	7.0 (2.39)	8.0 (3.0)	7.7 (1.94)	9.0 (2.0)	6.76 (2.59)	9.0 (2.0)
Apgar-5 th minute	8.55 (1.47)	8.18 (1.53)	9.08 (0.86)	9.0 (1.0)	9.0 (1.0)	9.0 (1.0)
Number pre-scribed antibiotics in per neonates	4.7 (2.6)	4.0 (5.0)	3.66 (1.88)	3.0 (3.0)	5.9 (2.9)	3.0 (3.0)
Number pre-scribed antibiotics in month	9.89 (7.72)	7.0 (10.0)	7.9 (5.67)	7.0 (9.0)	12.33 (9.4)	7.0 (9.0)
Number infected neonates in month	2.0 (1.17)	2.0 (2.0)	1.93 (1.22)	2.0 (1.0)	2.08 (1.17)	2.0 (1.0)

blood and respiratory tract. In neonates with both pathogens (*S. epidermidis* and *A. baumannii*) the culture sample was positive in 3 cases of blood sample and in 2 cases of both blood and respiratory secretions.

In this analysis, infants who were hospitalized in NICU due to Neonatal Respiratory Distress Syndrome (NRDS) were more likely to be infected with *A. baumannii* than by *S. epidermidis*, (30 (68.18%) and 15 (32.61%) respectively), this difference was statistically significant ($X^2= 10.23$; P-Value=0.001) (Table 3).

A summary of aids and medical procedures administered for infected infants by *A. baumannii* and *S. epidermidis* is accessible in Table 4. The frequency of mechanical ventilation in infected infants by *A. baumannii* was higher than in neonates infected by *S. epidermidis* (47.72% and 21.74%) that there is statistically difference ($X^2= 6.37$; P-Value= 0.0009). In addition, 31.82% of patients in *A. baumannii* had chest tube insertion, while this proportion was 13.04% in *S. epidermidis* ($X^2= 4.58$; P-Value= 0.032).

Frequency of neonates received vancomycin, linezolid and colistin antibiotics before bacterial isolation is accessible in Table 5. In correlation analysis, there was a strong positive correlation between number of infected neonates in NICU in month and average number of prescribed antibiotics before occurrence nosocomial infection per neonate (*S. epidermidis*; Spearman's rho=0.64 P-Value= 0.003, and *A. baumannii*; Spearman's rho=0.843 P-Value< 0.001). Fluconazole was an antifungal drug that was correlated with number of infected neonates by *A. baumannii* in NICU (Spearman's rho=0.468 P-Value= 0.038), also prescription of ampicillin, amikacin, metronidazole, and vancomycin antibiotics before occurrence nosocomial infection had a positive correlation with number of infected neonates by *A. baumannii* in NICU in month (Spearman's rho, P-Value: 0.712, 0.01; 0.83, <0.001; 0.697, 0.002; and 0.574, 0.016 respectively) (Table 6).

In neonates infected by *S. epidermidis*, ampicillin

Table 3. Comparison of causes of inpatient with agent type of outbreak in NICU

Cause of inpatient#	<i>A. baumannii</i> (%)	<i>S. epidermidis</i> (%)	χ^2 (P-Value)*
Neonatal Respiratory Distress Syndrome	30 (68.18)	15 (32.61)	10.23 (0.001)
Endocrine Disorders	4 (9.09)	5 (10.87)	0.08 (0.78)
Metabolic Disorders	5 (11.36)	5 (10.87)	0.006 (0.94)
Congenital-Genetic Defects ‡	10.0 (22.73)	11 (23.91)	0.018 (0.894)
Septicemia and Meningitis	20.0 (45.45)	13 (28.26)	2.86 (0.091)
Congenital Heart Disease	12 (27.27)	10 (21.74)	0.37 (0.541)
Prematurity	26 (59.09)	21 (45.65)	1.63 (0.20)
Seizure	3 (6.81)	2 (4.35)	0.26 (0.609)

Each baby may have more than one cause for inpatient

‡Congenital-genetic defects except of heart diseases

*For cells with expected count less than 5, fisher exact test P- Value was considered

Table 4. The summary of medications or medical procedures used in two groups (*S. epidermidis* and *A. baumannii*)

Use of aids or medical procedures	cofactor	<i>A. baumannii</i>	<i>S. epidermidis</i>	χ^2 (P-Value)
Mechanical ventilation	Yes	21 (47.72)	10 (21.74)	6.73 (0.009)
Urinary tract catheterization	Yes	2 (4.55)	2 (4.35)	0.002 (0.963)
Central venous catheterization	Yes	10 (22.72)	5 (10.87)	2.28 (0.131)
G-CSF	Yes	5 (11.36)	4 (8.69)	0.12 (0.725)
Chest Tube insertion	Yes	14 (31.82)	6 (13.04)	4.58 (0.032)
Surfactant Using	Yes	11 (25.0)	5 (10.86)	3.07 (0.079)
Venous Catheterization	Yes	10 (22.72)	5 (10.86)	2.28 (0.131)

Table 5. Frequency of neonates received vancomycin, linezolid and colistin antibiotics before bacterial isolation

Antibiotics	<i>A. baumannii</i>	<i>S. epidermidis</i>	<i>A. baumannii</i> & <i>S. epidermidis</i>
	n (%)	n (%)	n (%)
Vancomycin	35 (89.74)	8 (38.0)	4 (80.0)
Linezolid	7 (17.94)	19 (46.3)	2 (40.0)
Colistin	22 (56.4)	14 (34.15)	4 (80.0)

Table 6. Correlation between number of nosocomial infection in month with average antibiotic number prescribed and types of antibiotic in *A. baumannii* and *S. epidermidis* A: before occurrence of nosocomial infection

Variables	Number of nosocomial infection in month	Correlation value‡	P-Value	Variables	Number of nosocomial infection	Correlation value‡	P-Value
	<i>S. epidermidis</i>	0.64	0.003		<i>S. epidermidis</i>	*	*
Colistin	<i>A. baumannii</i>	*	*	Amphotericin	<i>A. baumannii</i>	0.09	0.676
	<i>S. epidermidis</i>	0.33	0.89		<i>S. epidermidis</i>	0.169	0.49
Gentamycin	<i>A. baumannii</i>	*	*	linezolid	<i>A. baumannii</i>	0.119	0.649
	<i>S. epidermidis</i>	0.12	0.69		<i>S. epidermidis</i>	*	*
Clindamycin	<i>A. baumannii</i>	*	*	Tazocin	<i>A. baumannii</i>	-0.037	0.891
	<i>S. epidermidis</i>	0.084	0.734		<i>S. epidermidis</i>	0.228	0.33
Ampicillin sulbac-tam	<i>A. baumannii</i>	0.02	0.92	Flucunazole	<i>A. baumannii</i>	0.468	0.038
	<i>S. epidermidis</i>	*	*		<i>S. epidermidis</i>	0.0	1.0
Ampicillin	<i>A. baumannii</i>	0.712	0.01	Metronidazole	<i>A. baumannii</i>	0.697	0.002
	<i>S. epidermidis</i>	0.49	0.043		<i>S. epidermidis</i>	0.228	0.333
Amikacin	<i>A. baumannii</i>	0.83	<0.001	Vancomycin	<i>A. baumannii</i>	0.574	0.016
	<i>S. epidermidis</i>	0.585	0.007		<i>S. epidermidis</i>	0.082	0.73

Average of prescribed antibiotics in per neonates before occurrence of nosocomial infection

‡Correlation of number infected neonates in month and average antibiotic prescribed was calculated by Spearman correlation.

*No statistics were computed because of low sample size, other antibiotics with low sample size: Cefepim, Erythromycin, Sulfacetamide, Ciprofloxacin

and amikacin antibiotics prescription before occurrence nosocomial infection had a positive correlation with number of *S. epidermidis* infected neonates in NICU in month (Spearman's rho, P-Value: 0.49, 0.043; 0.585, 0.7; and 0.574, 0.016 respectively) (Table 6).

We used partial correlation for controlling of confounding effect of combinational treatment in association of antibiotics administration and occurrence *S. epidermidis* and *A. baumannii* number in month. Thus, only use of amikacin before the onset of nos-

nosocomial infection both in *S. epidermidis* and *A. baumannii* remained significant statistically (rho Partial= 0.469, P-Value=0.05, and rho Partial= 0.662, P-Value=0.01 respectively). Other result as follows: Partial correlation between ampicillin prescription and *S. epidermidis* occurrence (by controlling of Amikacin effect) = 0.46, P-Value=0.065: Partial correlation between ampicillin prescription and *A. baumannii* occurrence (by controlling of amikacin, vancomycin, and metronidazole effects) = -0.135, P-Value=0.644, vancomycin (by controlling of amikacin, ampicillin, and metronidazole effects)=0.022, P-Value=0.40, and metronidazole (by controlling of amikacin, ampicillin, and vancomycin effects)=0.066, P-Value=0.828.

DISCUSSION

This study describes epidemiology of *S. epidermidis* and *A. baumannii* infection in the NICU from 2014 to 2022 which affected 85 neonates. Over 95% of the infants affected were admitted to the NICU within their first 48 hours' birth. Based on the results of other studies, neonates younger than one week old are at greater risk for nosocomial infection (11, 23).

In this study, 45.65% (21 cases) and 52.27% (23 cases) of the neonates had a VLBW (<1500 gram) in *S. epidermidis* infected group and *A. baumannii* group respectively. Also 16 neonates (36.36%) were born very preterm (<32 weeks gestational age) in *A. baumannii* infection group and 21 babies (45.65%) in *S. epidermidis* group. Studies assert that neonates with VLBW and low gestational age are expected to have higher rates of nosocomial infections in NICUs. Premature neonates are at particularly high risk of nosocomial infection because of a flaw in their defensive maternal antibody and initial immature inherent immunity (23).

According to the results of our study, 31.82% of infected neonates had used chest tubes in NICU, 47.72% of neonates used mechanical ventilation, and 22.72% required central venous catheter in *A. baumannii* group. The majority of studies reporting *A. baumannii* outbreaks predominantly involved ICU patients requiring intubation and mechanical ventilation (20, 24). Unfortunately, we did not have access to auxiliary products or infection cultures.

Some studies mention that the duration of hospitalization is a risk factors related to outbreaks of *A. baumannii* (11, 24). In line with those findings, also

in our study, a strong correlation was observed between *A. baumannii* infections number in month and the number of days hospitalized before the onset of nosocomial infection in month.

Approximately 33% of neonates infected by *A. baumannii* died, while mortality rate for *S. epidermidis* was 4.88%. Fatality in infants with both nosocomial infections was 60% (3/5). The frequency of neonatal deaths following nosocomial infection in NICUs varied between 12% and 33.8% in studies (25, 26), fatality reaches 40% in developing countries (27). It is extremely difficult to establish the impact that nosocomial infections have on the death of a neonate who is admitted to the NICU. Infants are susceptible to various complications resulting from their initial condition and prematurity and several other coexisting factors can contribute to catastrophic consequences.

There is an ongoing discussion on the role of combinational treatment in order to find a balance in number of antibiotics prescribed and ensuring a healthy outcome (28). Some studies pointed that wide use of antibiotics increase the vulnerability of patients admitted in ICU and NICU to nosocomial infections, specially to microbial agents with multi-drug resistance (24, 29). In this study, the number of prescribed antibiotics before occurrence nosocomial per neonate positively influenced the number of *A. baumannii* and *S. epidermidis* infected patients in the month. In the present study, amikacin was one of the most commonly prescribed antibiotics: 81.81% (36 of 44) in the *A. baumannii* group and 82.61% (38 of 46) in the *S. epidermidis*. Use of Amikacin by controlling of confounding antibiotics had positive correlation with occurrence of both of *A. baumannii* and *S. epidermidis*.

Insufficient/overuse or inappropriate prescription is one of the main reasons for occurrence of drug resistance and nosocomial infections (30). Unfortunately, we did not have access to susceptibility pattern of *A. baumannii* in our study. However, we know that approximately 80% of the patients in our study were resistant to at least one drug. The use of fluconazole as antifungal medication had a positive correlation with number of infected neonates by *A. baumannii* in NICU in month. In the study of Alp et al. use of prophylactic fluconazole had reduced the systemic infections in extremely low birth weight and VLBW infants (11). While Manzoni et al did not recommend antifungal prophylaxis drugs such as fluconazole to

be administered for neonates (31). Also a Cochrane Review on 2015 reported that prophylactic of anti-fungal agents in VLBW neonates may reduce the risk of invasive fungal infections but the evidence is not sufficiently strong and needs to be cautiously implemented until the results of further trials provide enough evidence on the matter (32). In neonates infected by *A. baumannii*, metronidazole antibiotic prescription before occurrence nosocomial infection had a positive correlation with number of infected neonates too. In this study prescription of amikacin had adjusted positive correlation on increasing of *A. baumannii* and *S. epidermidis* infection in month.

CONCLUSION

Hospitalization duration, mechanical ventilation and chest tubes in NICU was correlated with the incidence of nosocomial infections by *A. baumannii*. Also number of prescription antibiotics was effective in increasing the incidence of *A. baumannii* and *S. epidermidis* infections. Use of fluconazole had a positive correlation with increasing the incidence of *A. baumannii* nosocomial infections. Amikacin prescription had adjusted correlation on increasing of *A. baumannii* and *S. epidermidis* infection in month. It seems hospitalization duration and medication prescriptions management play an important role in reducing the incidence of nosocomial infections.

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