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Nosocomial Infection in an Egyptian Neonatal Intensive Care Unit.

Sally AF El- Sahrigy[1]*, Azza MO Abdel Rahman[1], Hala Youssef[1], Ahmed A Talaat[1], Dalia A Khairy[2], Howayda E Gomaa[3], and Sohad M Dorgham[4].

[1]Pediatrics' Department, Medical Research Division, National Research Centre, Cairo, Egypt.
[2]Pediatrics' Department, Faculty of Medicine, Cairo University, Cairo, Egypt.
[3]Clinical pathology Department, Medical Research Division, National Research Centre, Cairo, Egypt.
[4]Microbiology and Immunology department, National Research Center, Cairo, Egypt.

ABSTRACT

We examined the etiology of nosocomial infection in a neonatal intensive care unit and determined antibiotic susceptibility of the isolated organisms to detect changes in infection patterns. The study included 56 neonates who developed nosocomial infection (10.93±11.2 days) from neonatal intensive care unit, Cairo University hospital. Four samples were collected from each neonate before treatment: blood, tracheal aspirate, urine and skin swab. Blood agar, Mac Conkey, CLED agar media and Thioglycolate broth bottles were used. For rapid identification of enterobactericae family we used API for enteric and non- enteric non-fermenter organism identification. Antimicrobial susceptibility tests were done. Nosocomial infections presented as neonatal septicemia (46.4%), pneumonia (14.3%), skin infection (10.7%) and mixed infections (28.6%). Gram-negative organisms were isolated from 42 neonates (75%), while 20 neonates showed Gram-positive septicemia (35.7%). Major isolated pathogens were Klebsiella species (39.3%), staphylococcus aureus (21.4%), coagulase negative staphylococci (14.3%), Acinetobacter species (14.3%), and pseudomonas aeroginosa (7.14%). The most encountered risk factors associated with nosocomial sepsis was prematurity (adjusted OR=9.444, 95CI=1.433-62.238). The Gram negative and positive organisms showed a high degree of resistance to commonly used antibiotics: third generation cephalosporines, amoxicillin/clavulanic acid, oxacillin, ciprofloxacin, gentamycin and trimethoprim/sulphamethaxzole. Both types of organisms were sensitive to amikacin and imipenem.

Keywords: neonates, nosocomial infection, bacteria, antibiotic resistance

Corresponding author

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INTRODUCTION

Nosocomial infection (NI) is a serious problem in neonates who are admitted to the neonatal intensive care units (NICUs), and is associated with increase in mortality, morbidity, and prolonged length of hospital stay [1].

They are defined as those infections that occur beyond 48 hours after birth and are caused by pathogens that are not maternally derived [2].

The rate of NI increases with the degree of both prematurity and low birth weight, and risk factors in this group of patients include immaturity of the immune system, barrier functions of the skin and gastrointestinal tract, in addition to the invasive diagnostic and therapeutic procedures undergone by neonates [3,4].

Pathogens vary considerably between different neonatal units. In developing countries, gram-negative organisms may be far more prevalent as neonatal pathogens with a higher incidence of antimicrobial resistance [5].

Overuse of antibiotics results in the development of antimicrobial resistant organisms (ARO). Infection with ARO results in delay in starting effective antibiotic therapy, increased morbidity and mortality, and prolonged hospital stay [6,7].

Therefore, ongoing surveillance of microbiological isolates and their sensitivity patterns is mandatory to guide the selection of empiric antibiotic therapy.

PATIENTS AND METHODS

This study was carried out on 56 neonates (36 males, 20 females) who stayed at least 48 hours in the unit and developed NI with mean age (10.93±11.2 days). They were recruited from NICU, Cairo University hospital in the period from (2010- 2011).

Nosocomial infection has been defined by the US Department of Health and Human Services for Disease Control and Prevention as an infection occurring during hospitalization which was not present or incubating at the time of admission [8].

Late onset sepsis (LOS) was defined as positive microbial growth on one or more bloodstream cultures or any sterile body fluid obtained after 72 hours of life accompanying clinical signs of sepsis [9]. The study protocol was approved by the ethical committee of the National Research Center (NRC). All neonates were included after a written consent from their parents.

Clinical samples:

Four samples were collected from each neonate as follows:

1. Throat swab or tracheal aspirate was obtained for microbiological assay. The samples were collected in sterile containers and sent to the lab. (NRC) within 1 hour of collection. Samples collected at night were stored at 4°c overnight and sent to the lab. by 10 a.m next day.

2. Concomitant blood sample for blood culture was collected; from each patient 3 ml of blood was withdrawn, and added to thioglycolate broth bottle, for aerobic and anaerobic culture. Blood samples were taken just before the next dose of the prescribed antibiotic.

3. Urine samples were collected in a sterile container and sent to the lab. as in no.1

4. Skin swabs were taken from umbilical area. Samples collected at night were kept in the incubator at 37ºc after adding 2drops of sterile saline.

For each patient the following investigations were completed:

1. Full history taking and complete clinical examination with special emphasis on maternal pregnancy history and antenatal care, details of delivery, the infant's status at delivery, diagnosis, procedures , duration of hospital stay and complications during hospitalization and the outcome at discharge.

2. Complete blood picture, erythrocyte sedimentation rate (ESR), C- reactive protein (CRP), total bilirubin and blood urea and creatinine.

3. Microbiological study using: Blood agar medium, Mac Conkey medium, CLED agar medium (for urine examination), Thioglycolate broth bottles for blood culture and Muller Hinton agar (for antibiotic susceptibility tests).

4. Biochemical tests:

    a. Rapid identification of enterobactericae family in 4 hours using API (20) kit.
    b. Rapid identification of non-fermenter (non-enteric) Gram-negative organisms (Acinetobacter) within 24-48 hours using API (20 NE) kit.

5. Antimicrobial susceptibility tests using disc diffusion method for all enterobactericae. Antimicrobial susceptibility testing were performed on the isolates according to the method established by the CLSI (formerly NCCLS) and interpreted with criteria published in 2005 (Clinical and Laboratory Standards Institute, 2005).

Isolates were tested using Mueller-Hinton agar . Meropenem, imipenem, ampicillin, ampicillin-sulbactam, ciprofloxacin, ceftazidime, cefepime, amikacin, and tobramycin disks (Oxoid Microbiology Systems) were used.

Statistical Analysis:

Standard computer program SPSS for Windows, release 13.0 (SPSS Inc, Tulsa, USA) was used for data entry and analysis. All qualitative variables were expressed as count and percent. Chi-square (χ^2) test was used to compare frequency of qualitative variables among the different groups. Risk analysis was calculated as odds ratio(OR) and confidence intervals(CI). For all tests a probability (p) less than 0.05 was considered significant. Graphic presentation of the results was also done. [10]

RESULTS

During the study period, 56 neonates (64.3% were males and 35.7% were females) developed NI after 48 hours of stay at NICU. The three primary reasons for admission to NICU were preterm and hyaline membrane disease (64.3%), prematurity only (14.3%), and transient tachypnea of newborn (21.42%). Twenty-two neonates (39.3%) were born through unassisted vaginal delivery and 34 (60.7%) by caesarean section. The mean length of stay was (24.4± 3.8) days. During the study period, 18 neonates died (32.1%). Risk estimate was done to identify risk factors associated with NIs (Table 1), the only significant risk factor identified was prematurity, mechanical ventilation, nasogastric intubation and mortality were not associated with development of NIs. Since all patients were subjected to central line access, therefore this factor was not included in the table I as a risk factor. Data showed non- significant relationship between prevalent organisms (Klebsiella and Staph. Aureus) and type of delivery or mortality outcome in studied neonates (Table 2). The most frequent isolated organisms in all specimens were Klebsiella (39.3%), Staphylococci (21.4%), Acinetobacter spp.(14.3%), and Coagulase Negative Staphylococci (CONS) (14.3%). Distribution of organisms in blood cultures and tracheal specimens were illustrated in figure (1) and (2) respectively.

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Table 1: Risk Estimate for variable factors related to nosocomial septicaemia

Risk Factors	Nosocomial Sepsis N %	Adjusted OR	95% CI
Prematurity	34 (60.7%)	9.444	1.433-62.238
Mechanical Ventilation	22(39.3%)	8.556	.881- 83.057
Nasogastric Intubation	18 (32.14%)	5.727	.590- 55.600
Mortality	16 (28.57%)	4.667	.478- 45.54

OR= Odds Ratio, CI= Confidence Interval

Table (2): Relation of prevalent organisms; Klebsiella species and Staphylococcus aureus to type of delivery and mortality of studied neonates

Nosocomial infection		Mode of Delivery		Fisher's exact test p-value	Death		Fisher's exact test p-value
		Vaginal N%	Caeserean N%		Positive N%	Negative N%	
Klebsiella	Positive	6(27.3%)	12 (35.3%)	1.000	6 (33.3%)	12 (31.6%)	1.000
	Negative	16(72.7%)	22 (64.7%)		12 (66.7%)	26 (68.4%)	
Staphylococcus	Positive	4 (18.2%)	6 (17.6%)	1.000	4 (22.2%)	6 (15.8%)	1.000
	Negative	18 (81.8%)	28 (82.4%)		14 (77.8%)	32 (84.2%)	

Table 3: Antibacterial susceptibility pattern of selected micro-organisms

Antibiotic	Staph aureus	CONS	Klebsiella spp	Acineto. spp	E. coli	Pseudo -monus
Meropenem						
Imipenem	80%	60%	85%	40%	100%	
Ampicillin						
Amp-Sulbactam						
Amikacin	80%	60%	77%	60%	100%	100%
Tobramycin	20%	40%		20%		
Ciprofloxacine			23%	40%		
Ceftazidime						
Cefepime						100%
Cefotoxime	20%	40%				
Cefobid						100%
Chloramphenicol	20%			40%		
Ofloxacin	20%	40%				
Rifampicin	20%	40%				

CONS= coagulase negative staphylococci

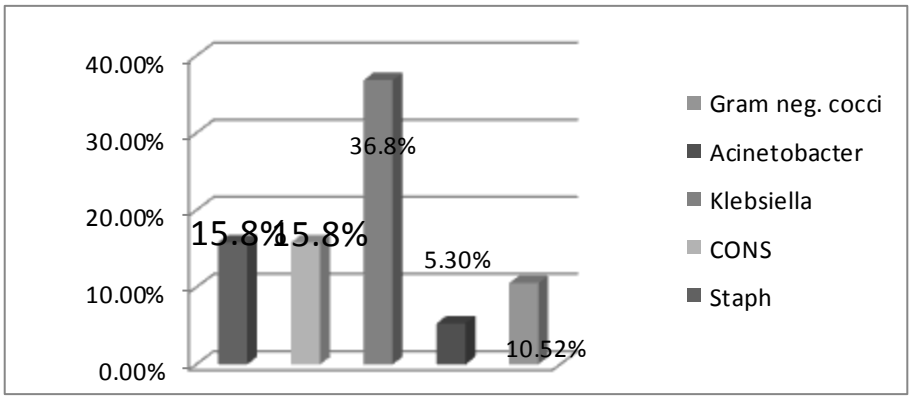

Figure 1: Distribution of organisms in blood culture

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CONS= coagulase negative staphylococci

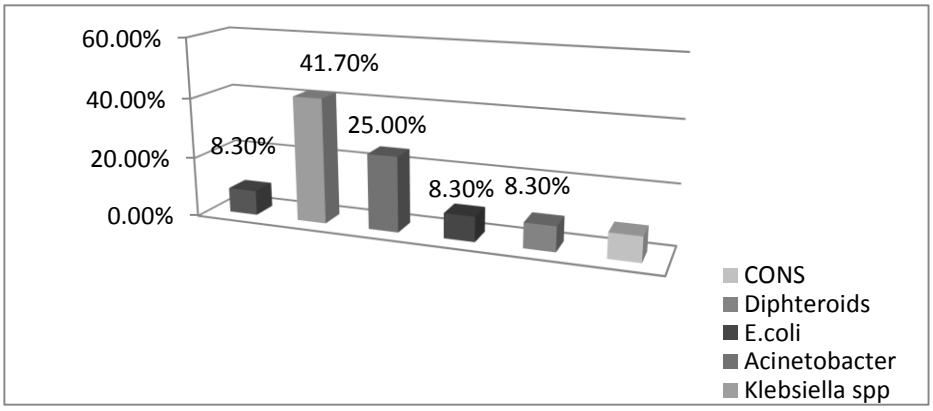

Figure (2: Distribution of organisms in tracheal specimens.

DISCUSSION

Neonates admitted to the NICUs are at high risk for developing nosocomial infection. Therefore, ongoing infectious disease surveillance is essential to minimize the occurrence of this problem [9].

In this study, we evaluated 224 samples from 56 neonates admitted to NICU, Cairo University Hospital who developed NI. Forty- six (46.4%) of patients developed neonatal septicemia. Therefore, we studied the risk estimate for different variables associated with the development of septicemia as prematurity, invasive procedures used and mortality. Sixty (60.7%) of cases were preterm neonates with low birth weight. This was in agreement with previous studies [9,11,12] .They identified low birth weight and prematurity as risk factors associated with increased NI rates as they have increased susceptibility to infection due to immature immune system, inefficient neutrophil function and lack of antigen type- specific antibodies to pathogens in their environment. In addition to their inability to mount a mature immune response, premature infants are exposed to multitude of therapies during their NICU stay that places them at risk for acquiring infection.

One of the therapies that provide a portal of entry for pathogens include intubation and mechanical ventilation [13]. In our study 39.3% of neonates with NI were on mechanical ventilation, central venous lines were used in 25% and 32% have undergone nasogastric intubation. Although these factors increase the risk for NI development in this vulnerable group of neonates, our results did not prove their risk in developing NIs. These results were in disagreement with previous studies [11, 12, 14, and 15]. Hwang et al, [16], found that endotracheal intubation and assisted ventilation were recognized factors in NICU due to colonization of humidified air with hydrophilic micro-organisms, physical trauma of passing an endotracheal tube and transient bacteremia during routine suction. Samanta et al, [17], had reported that the only independent risk factor found for late onset Gram negative neonatal infection was the duration of total parenteral nutrition after adjusting gestational age. Whereas, in another retrospective case control study by Gupta et al, [18], it had shown that the only independent risk factor for late onset infections was the duration of ventilatory support.

The present work showed that the most frequent NI was blood stream infections; neonatal septicaemia (46.4%), pneumonia (14.3%), skin infection (10.7%) and mixed infections (28.6%). We reported no urinary tract infections. These results came in accordance with previous work [14,15,19, and 20] , they showed that these types of NIs were strongly related to the use of invasive devices.

To determine different types of NIs, four samples were obtained from each neonate namely: blood, tracheal aspirate, urine and skin swab samples. Gram- negative organisms were isolated from 42 neonates (75%); whereas Gram – positive bacteria were obtained from 20 neonates (35.7%). Klebsiella species were the most commonly isolated pathogens from blood cultures (36.8%), and tracheal aspirates (41.7%). These results were in agreement with previous studies [21], they reported Klebsiella pneumoniae to be the most commonly isolated pathogen from bloodstream infection (29%) thus implicating these infections as hospital acquired

versus maternally transmitted. These data are consistent with other reviewers of neonatal sepsis in developing countries where Gram- negative infections are more frequently encountered. Zaidi et al, [22], demonstrated that 60% out of 11,471 bloodstream samples throughout the developing world were caused by Gram- negative organisms with K. pneumonia accounting for 20%, Pseudomonas 7%, Acinetobacter 3.5% and other Gram- negatives 14%. The studies conducted in Asia demonstrated that the rate of hospital- acquired infections with multi-resistant Gram- negative organisms were high. The same study revealed that the type of isolated organisms and the mortality rate were similar to those in developed countries [23].

The present work showed that the most common second isolated organism from blood cultures was coagulase negative Staphylococci (CONS) (15.8%), Staph. Aureus (15.8%) followed by Gram negative cocci (10.5%), and Acinetobacter species (5.3%). In developed countries, blood stream infections with CONS was reported to be the most common NI with incidence as high as 78% of total infections [5,19,24, and 25]. Worth to mention that bloodstream bacterial isolates in the current study are considerably different from those obtained in a similar review in the same unit in year 2007 throughout 2008, where Gram- positive isolates constituted 56.7% with CONS(13%) followed by S. Epidermis (12%). Gram- negative isolates formed 43.3% of total isolates with Klebsiella species predominance (25%) followed by E.coli (10%) and Pseudomonus (10%) [26].

In the current study, tracheal aspirate cultures revealed Gram -negative organisms in 42.9% of cases with prevalent organisms in the form of Klebsiella species (41.7%), followed by Acinetobacter (25%) and E.coli (8.3%). Gram- positive organisms formed only 8.3% from the prevalent organisms presented as S. Aureus. These results came in agreement with previous studies [1, and 27]. They showed that healthcare- associated pneumonia is more often caused by Gram -negative organisms.

Skin swab culture revealed 21.4% positive results. Staphylococcus aureus and Pseudomonus aeruginosa are the most common isolated organisms. This is mostly due to direct transfer of hospital pathogens and skin flora of caregivers' hands to the neonates and their environment [15].

The patterns and rates of resistance for both Gram -negative and Gram -positive organisms were surprisingly high and cause a great deal of concern with respect to antibiotic prescription and to infection control measures. Eighty five percent of Klebsiella isolates were susceptible to imipenem and 77% to amikacin. Amikacin showed the greatest activity against Acinetobacter spp. (60% susceptibility) followed by imipenem (40%), ciprofloxacine (40%) and chloramphenicol (40%). All E.coli tested were susceptible to imipenem and amikacin (100%). All Pseudomous aeruginosa were susceptible to amikacin and cefoperazone (100%). All Gram -negative organisms showed great resistance to second, third and fourth generation cephalosporines. This came in agreement with previous work [21], who showed a similar pattern of extensive resistance for the Gram -negative organisms to cephalosporines.

As for Gram –positive organisms, 80% of Staphylococcus aureus and 60% of CONS were sensitive to imipenem and amikacin. Only 20% of isolated Staphylococcus aureus species and 40% of CONS were susceptible to cefotoxime, ofloxocillin and rifampicin. However, all showed resistance to ceftazidime, cefepime and cefobid.

CONCLUSION

The commonest encountered organisms in NICU were Klebsiella species, followed by Staphylococcus aureus, CONS and Acinetobacter species. Based on the bacterial profile in the present study, the suitable empiric antibiotic therapy for neonatal NI would be imipenem plus amikacin. Both types of antibiotics will provide adequate cover for both Gram- negative organisms, Staph. aureus and CONS. Once the offending pathogen is known, descalation of treatment is imperative.

Ongoing surveillance of NI is essential in monitoring trends in infection, ensuring up to date appropriate antibiotic therapy, early outbreak detection and institution of preventive measures.

Further studies recommended on large-scale multi-center to determine organism distribution in NICUs over Egypt, and to identify the genes associated with multi-drug resistant phenotypes of prevalent organisms.

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REFERENCES

[1] Sadowska-Krawczenko I, Jankowska A and Kurylak A. Arch. Med Sci .2012; 8(5): 854-858.
[2] Richard A and Polin . Journal of Pediatric and Child Health.2005; 44:62-66.
[3] Couto RC, Pedrosa TM, Tofani Cde P, and Pedroso ER. Infect Control Epidemiol .2006; 27: 571-5.
[4] Bartels DB, Schwab F, Geffers C, Poets CF, and Gastmeier P. Arch Dis Child Fetal Neonatal Ed.2007; 92: F449-53.
[5] Ballot DE, Nana T, Sriruttan C, and Cooper PA . International Scholarly Research Network ISRN Pediatrics. Article ID 508512; 1-6.2012.
[6] Siddiqi A, Khan DA, Khan FA, and Razzaq A . Singapore Med J.2009; 50: 486 – 489.
[7] Thaver D, Ali SA,and Zaidi AKM. Pediatr Infect Dis J.2009; 28:S19 – S21.
[8] Lopez Sastre JB, Coto CD, and Fernandez CB. J Perinat Med 2002;30:149-57.
[9] Joseph CJ,Lian WB, and Yeo CL. Proceedings of Singapore Healthcare.2012; 21(4):238-244.
[10] Daniel WW: Biostatistics: A foundation for analysis in the health sciences. 6th edition. John Wiley and sons, Inc., New York 1995.
[11] Payman S, Masood Y, and Mohsen N. Hospital J. Pediatr. 2006;73(3): 197-200.
[12] Ahmed A, Ezzat I, and Baghagho E. Researcher 2012;4(5):40-45.
[13] Newby J. J Perinat. Neonat. Nurs. 2008; 22(3):221-227.
[14] Nagata E., Brito ASJ, and Matsuo T. Am J Infect Control.2002; 30:26-31.
[15] Polak JD, Ringler N, and Daugherry B. Newborn Infant Nurs Rev.2004; 4:38-45.
[16] Hwang I, Choi C, and Chang Y. J. Korean Med. Sci.2004; 20:177-81.
[17] Samanta S, Farrer K, Breathnach A, and Health PT. Arch. Dis. Child Fetal Neonatal 2011; Ed 96: F15-F18.
[18] Gupta N, Crocket DC, Anthony M, and Webster CP. Arch Dis Child Fetal Neonatal 2011; Ed. 96(3):F234-7.
[19] Efird MM, Rojas MA, Lozano JM et al. J Perinatol.2005; 25: 531-536.
[20] Jeong IS, Jeong JS, and Choi EO. BMC Infectious Diseases.2006; 6(article 103).
[21] Macharashvili N, Kourbatova E, Butsashvili M, Tsetsvadze T, McNutt LA, and Leonard MK. Int J Infect Dis. 2009;13(4):499-505.
[22] Zaidi AK,Huskins WC, Thaver D, Bhutta ZA, Abbas Z, and Goldmann DA. Lancet. 2005;365(9465):1175-88.
[23] Tiskumara R, Fakharee SH, Liu CQ, Nuntnarumit P, Lui KM, and Hammoud M . Arch. Dis. Child Fetal Neonatal Ed.2009; 94(2):F144-8.
[24] Kawagoe JY, Segre CAM,Pereira CR,Cardoso MF,Silva CV, and Fukushima JT. Am J Infect Control.2001; 29:109-114.
[25] Clark R, Powers R, White R, Bloom B, Sanchez P, and Benjamin DK Jr. J Perinatol.2004; 24:382-388.
[26] Mohsen LM, Mourad AAF, Iskander IF, El-Sahrigy SAF,Abd El-Maksoud S, and Mohy El—Deen A. Australian J of Basic and Applied Sciences. 2012;6(12):530-536.
[27] Van der Zwet WC, Kaiser AM, Van Elburg RM et al. J Hosp Infect 2005; 61:300-11.