ORIGINAL ARTICLE

Prevalence of Multidrug Resistant Organisms in Neonatal and Pediatric Intensive Care Units of Beni-Suef University Hospital

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ABSTRACT

Background: Hospital acquired infections are still a major cause of morbidity and mortality among neonates and children admitted to intensive care units Objectives: To determine the prevalence and clinical distribution of Multidrug resistant organisms (MDROs) in neonatal intensive care unit (NICU) and pediatric intensive care unit (PICU) of Beni-Suef University Hospital. Methodology: A cross-sectional study included 160 patients diagnosed with sepsis, 80 patients admitted at NICU and another 80 patients at PICU. Blood, sputum, urine were collected from each patient, to perform; CBC, CRP, culture and sensitivity. Identification of isolates was conducted by the various conventional methods. Thereafter, antimicrobial sensitivity tests were conducted for each isolate to detect MDROs. Results: Most of the isolates were MDROs (85.8%%) with high statistical significant difference regarding their frequencies. Most common Gram-negative isolate was klebsiella pneumoniae representing 36.7% of isolates. Candida albicans were significantly more frequent among PICU cases (p-value <0.05). MDR risk factors revealed that: length of stay (LOS) at the present ICU or LOS in another ICU before the current one were associated risk factors (p-value = 0.00001, 0.05 respectively). MDR Gram-negative isolates showed high resistance to ampicillin-sulbactam (98.8%) and were most sensitive to polymyxin (79.1%). In MDR Gram-positive yields, vancomycin (93%) and linozolide (100%) were the most effective, whilst, resistance was evident against ampicillin (93%). All Candida spp. isolates were most sensitive to amphotericin (93.1%) and most resistant to fluconazole (62%). The overall mortality rate was 32.5%: NICU deaths represented 52.5% and PICU deaths 12.5% with a significant difference between NICU and PICU. Conclusion: Prevalence rate of MDROs is extremely high among NICU and PICU patients even against newer categories of antibiotics, so, more strict infection control program should be applied.

INTRODUCTION

Healthcare associated infections (HCAI) are a worldwide threat in intensive care units. Infections in Pediatric and Neonatal intensive care units (PICU and NICU) range from 6 to 12% and 10 to 25% respectively[1].

Multidrug-resistant organisms (MDROs) pose one of the most serious challenges in healthcare associated and community-acquired infections[2]. MDROs include Vancomycin-resistant *Enterococci (VRE),* Methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum β-lactamase (ESBL) *Klebsiella pneumoniae,* carbapenemase producing Gram-negatives, *Enterococcus faecium, Acinetobacter baumannii,* in addition to multidrug resistant gram-negative rods[3].

Low gestational age, lengthy stay, abuse of antibiotics and invasive procedures in association with multidrug-resistant gram-negative bacilli are risk factors for infections in NICU. Global proliferation of multidrug resistant strains of bacteria is attributed to the abuse of antimicrobial agents[1,4].

Therefore, the aim of this study was to determine the prevalence and distribution of MDROs among patients admitted in NICU and PICU at Beni-Suef University Hospital.

METHODLOGY

The current study is a cross-sectional study; it involved 160 pediatric patients admitted in NICU (80 patients) and PICU (80 patients) of Beni-Suef University Hospital within duration of 10 months; from July 2016 to May 2017.

Inclusion criteria involved pediatric patients admitted to NICU or PICU at the time of the study, aged 1 day to 12 years, and suspected of having infection or sepsis. The patients were subjected to detailed history taking;

stressing on risk factors for MDROs and full clinical examination. All patients were followed up during the entire length of their stay at ICUs. The selected cases were divided into NICU and PICU groups depending on site of admission; also, they were divided into patients with no growth, cases with MDR organisms and non-MDR organisms (on the basis of the susceptibility patterns of the isolated organisms).

Specimens Collection

Blood samples were collected for CRP, CBC and blood cultures. Sputum (or deep tracheal aspirate) and urine samples were obtained from suspected cases, under complete aseptic conditions.

Processing of Specimens:

All samples admitted to the clinical microbiology laboratory were cultured and identified. Verifying the identity of the yields was conducted at the Medical Microbiology and Immunology laboratory, Faculty of Medicine, Beni-Suef University by various conventional methods including; culture on selective media, colony morphology, microscopic examination and different biochemical tests. Further identification was performed using an automated identification system (API ID32GN and ID32E systems, bio-Mérieux, Marcy-l'Etoile, France).

Antimicrobial Susceptibility Testing:

Antimicrobial susceptibility testing of all bacterial and yeast yields was performed by the Kirby-Bauer disc diffusion method on Mueller-Hinton agar and SDA (Oxoid, Basingstoke, UK) according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI) [5,6].

Commonly used antibiotic classes; penicillins, tetracyclines, cephalosporins, quinolones, lincomycins, macrolides, sulfonamides, glycopeptide antibiotics, aminoglycosides, carbapenems and oxazolidinones, were tested against Gram-positive and Gram-negative isolates e.g: ampicillin ($10\mu g$), oxacillin ($1\mu g$), amoxicillin-clavulanic acid ($30\mu g$), cefoxitin ($30\mu g$), cefotaxime ($30\mu g$), ceftriaxone ($30\mu g$), ceftazidime ($30\mu g$), imipenem ($10\mu g$), vancomycin ($30\mu g$), gentamicin ($10\mu g$), amikacin ($30\mu g$), erythromycin ($15\mu g$), azithromycin ($15\mu g$), ciprofloxacin ($5\mu g$) and norfloxacin ($10\mu g$).

Staphylococcus aureus (S.aureus), methicillin resistance was detected by the cefoxitin disk test (30 µg; Bio-Rad, Marnes-La-Coquette, France), as recommended by the Clinical and Laboratory Standards Institute (CLSI) [6]. However, methicillin-resistance in Coagulase negative *Staphylococci* (CONS) was detected by growth of the isolates on trypticase soy agar plates containing 6 µg of oxacillin per mL plus 4% NaCl [7]. All gram-negative isolates were screened for extended-spectrum β-lactamase (ESBL) activity using the double-disk approximation test [8].

For yeast isolates, CLSI M44A guidelines for fluconazole, voriconazole, ketoconazole, amphotericin-B and itraconazole were followed [6].

The yields isolated were considered Multidrug Resistant (MDR) organisms when they show resistance to three or more antimicrobial classes [9].

Ethical consideration:

An informed w r i t t e n consent was obtained from parents b e f o r e enrollment. The Scientific Research Committee of Community Department, Faculty of Medicine, Beni Suef University, revised and approved the study design.

Statistical analysis:

Analysis of data was carried out using an IBM computer utilizing statistical program for social science (SPSS) (version 23.0; Chicago, Illinois, USA). Data were expressed as Mean ± SD for quantitative parametric measures in addition to Minimum and Maximum for quantitative non-parametric measures and both number and percentage for categorized data.

The following tests were done:

1. Comparison between two independent mean groups for parametric data using Student t test.
2. Comparison between two independent groups for non-parametric data using Mann-Whitney test.
3. Chi-square test to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data.

The probability of error at 0.05 was considered significant, while at 0.01 and 0.001 were highly significant.

RESULTS

The present study included 160 patients; 80 patients admitted at NICU and 80 at PICU. The 1st group (NICU), out of the 80 patients selected, 54 were males (68%). Patients' ages ranged from 1 day to 41 days with mean ±SD (6.92 ± 9.57ds). While, 58 out of 80 cases were males in the second group (PICU), representing 72.5%. Patients' ages ranged from 2 months to 12 years with mean ±SD (5.32ys ± 8.325ys).

The culture results of different specimens examined revealed 169 yields isolated from 146 patients (91.2% of cases). Most of the isolated organisms were from the blood specimens (65/169 38.5%). Out of the 169 isolates, 29 (17.2%) were *Candida* spp., while, 140 (82.8%) were bacterial growths. Most of the bacterial isolates were Gram-negatives; (86/140 61.4%), most of which were *Klebsiella pneumoniae*; 62 isolates (62/86 72%) (Table1. Most of *Candida* spp were MDRO their number and distribution is shown in table 1.

Table 1: Distribution of different organisms among specimens examined

| Isolates		Specimens			Total
		Blood	Sputum	Urine	
S. aureus (MRSA)	Count	3	1	0	4
	% within Organism	75.0%	25.0%	0.0%	100.0%
	% within Culture type	4.5%	1.8%	0.0%	6.3%
	% of Total	1.8%	0.6%	0.0%	2.4%
CONS	Count	30	1	2	33
	% within Organism	90.9%	3.0%	6.1%	100.0%
	% within Culture type	46.2%	1.8%	4.1%	19.5%
	% of Total	17.8%	0.6%	1.2%	19.5%
VRSA	Count	1	0	0	1
	% within Organism	100.0%	0.0%	0.0%	100.0%
	% within Culture type	1.5%	0.0%	0.0%	0.6%
	% of Total	0.6%	0.0%	0.0%	0.6%
Enterococci faecalis	Count	5	0	8	13
	% within Organism	38.5%	0.0%	61.5%	100.0%
	% within Culture type	7.7%	0.0%	16.3%	7.7%
	% of Total	3.0%	0.0%	4.7%	7.7%
Streptococci pneumoniae	Count	2	1	0	3
	% within Organism	66.7%	33.3%	0.0%	100.0%
	% within Culture type	3.1%	1.8%	0.0%	1.8%
	% of Total	1.2%	0.6%	0.0%	1.8%
Klebsiella pneumoniae	Count	15	32	15	62
	% within Organism	24.2%	51.6%	24.2%	100.0%
	% within Culture type	23.1%	58.2%	30.6%	36.7%
	% of Total	8.9%	18.9%	8.9%	36.7%
Acinetobacter baumanni	Count	0	3	1	4
	% within Organism	0.0%	75.0%	25.0%	100.0%
	% within Culture type	0.0%	5.5%	2.0%	2.4%
	% of Total	0.0%	1.8%	0.6%	2.4%
Pseudomonas aeruginosa	Count	1	6	4	11
	% within Organism	9.1%	54.5%	36.4%	100.0%
	% within Culture type	1.5%	10.9%	8.2%	6.5%
	% of Total	0.6%	3.6%	2.4%	6.5%
E-coli	Count	1	0	3	4
	% within Organism	25.0%	0.0%	75.0%	100.0%
	% within Culture type	1.5%	0.0%	6.1%	2.4%
	% of Total	0.6%	0.0%	1.8%	2.4%
Enterobacter cloacae	Count	1	1	1	3
	% within Organism	33.3%	33.3%	33.3%	100.0%
	% within Culture type	1.5%	1.8%	2.0%	1.8%
	% of Total	0.6%	0.6%	0.6%	1.8%
Proteus mirabilis	Count	0	1	0	1
	% within Organism	0.0%	100.0%	0.0%	100.0%
	% within Culture type	0.0%	1.8%	0.0%	0.6%
	% of Total	0.0%	0.6%	0.0%	0.6%
Stenotrophomonas maltophilia	Count	0	1	0	1
	% within Organism	0.0%	100.0%	0.0%	100.0%
	% within Culture type	0.0%	1.8%	0.0%	0.6%
	% of Total	0.0%	0.6%	0.0%	0.6%
Candida albicans	Count	2	4	10	16
	% within Organism	12.5%	25.0%	62.5%	100.0%
	% within Culture type	3.1%	7.3%	20.4%	9.5%
	% of Total	1.2%	2.4%	5.9%	9.5%
Candida non albicans	Count	4	4	5	13
	% within Organism	30.8%	30.8%	38.5%	100.0%
	% within Culture type	6.2%	7.3%	10.2%	7.7%
	% of Total	2.4%	2.4%	3.0%	7.7%
Total	Count	65	55	49	169
	% within Organism	38.5%	32.5%	29.0%	100.0%
	% within Culture type	100.0%	100.0%	100.0%	100.0%
	% of Total	38.5%	32.5%	29.0%	100.0%

Comparison between frequency of MDR and non-MDR organisms shows that most of the isolates were MDRO 145/169 representing 85.8% and even higher percentage was recorded among bacterial isolates; MDR bacteria 126/140 (90%) and only 14/140 (10%) were non-MDRO with statistical significant difference for all types of organisms (*p*-value<0.05). *Klebsiella*

pneumoniae was the most frequent organism among all isolates (36.7%) and most of them were MDR; 59/62 representing 95.1%, followed by coagulase negative *Staphylococci* (CONS) (19.5%), which were mostly resistant; 24/33 isolated strains (72.7%) (Table 2 and Fig 1).

Table 2: Comparisons between frequency of MDR and non-MDR organisms

Organisms		Groups		Total	*P*-value
		Non MDR	MDR		
S. aureus (MRSA)	Count	0	4	4	**0.0001***
	% within Groups	0.0	2.7	2.3	
CONS	Count	9	24	33	**0.05***
	% within Groups	37.5	16.5	19.5	
VRSA	Count	0	1	1	**0.001***
	% within Groups	0.0	0.7	0.6	
Enterococci faecalis	Count	0	13	13	**0.0001***
	% within Groups	0.0	9	7.7	
Streptococci pneumoniae	Count	1	2	3	**0.044***
	% within Groups	4.1	1.3	1.7	
Klebsiella pneumoniae	Count	3	59	62	**0.001***
	% within Groups	12.5	40.6	36.7	
Acinetobacter baumanni	Count	0	4	4	**0.0001***
	% within Groups	0.0	3.2	2,3	
Pseudomonas aeruginosa	Count	0	11	11	**0.00001***
	% within Groups	0.0	8.8	6.5	
E-coli	Count	0	4	4	**0.00001***
	% within Groups	0.0	2.7	2.3	
Enterobacter cloacae	Count	0	3	3	**0.0001***
	% within Groups	0.0	2	1.8	
Proteus mirabilis	Count	1	0	1	**0.0001***
	% within Groups	4.1	0.0	0.6	
Stenotrophomonas maltophilia	Count	0	1	1	**0.0001***
	% within Groups	0.0	0.7	0.6	
Candida albicans	Count	5	11	16	**0.0001***
	% within Groups	20.8	7.5	9.5	
Candida non albicans	Count	5	8	13	**0.001***
	% within Groups	20.8	5.5	7.7	
Total	Count	24	145	169	
	% within total	14.3	85.7	100.0	

*P-value significant at ≤0.05.
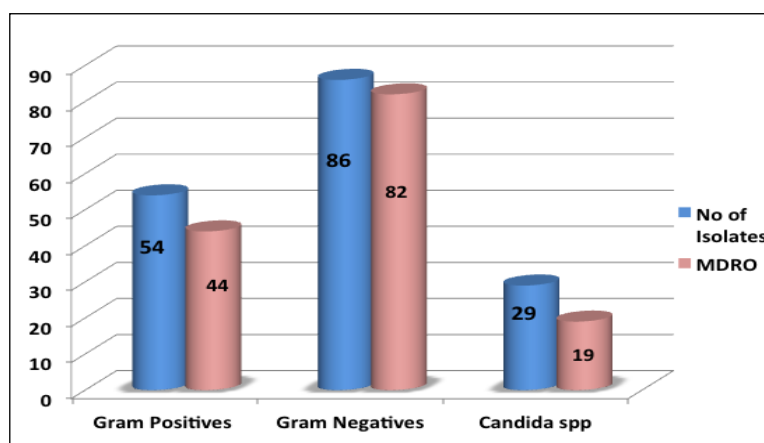
Fig.1: Distribution of different MDRO among the isolated growths

CRP and CBC results showed evidence for infection that were evidently higher in MDRO rather than in non-MDR organisms and no growth patients (*p*-value <0.05).

Comparison between NICU and PICU regarding frequency of organisms shows that the most common Gram-negative isolated organism was *Klebsiella pneumoniae* representing 62 (36.7%) isolates; in NICU were 34 (54.8%) and 28 (45.2%) in PICU. Meanwhile, frequency of *Candida albicans* was evidently higher among PICU cases (*p*-value <0.05) **(Table 3).**

Table 3: Comparison between NICU and PICU as regarding organisms' frequency

Organism		Groups		Total	*P*-value
		NICU	PICU		
S. aureus (MRSA)	No.	2	2	4	0.824
	% within Groups	2.8	2.0	2.4	
CONS	No.	14	19	33	0.981
	% within Groups	19.4	19.6	19.5	
VRSA	No.	0	1	1	0.388
	% within Groups	0.0	1.0	0.6	
*Enterococci faecali*s	No.	3	10	13	0.138
	% within Groups	4.2	10.3	7.7	
Streptococci pneumoniae	No.	1	2	3	0.752
	% within Groups	1.4	2.1	1.8	
Klebsiella pneumoniae	No.	34	28	62	0.120
	% within Groups	47.2	28.9	36.7	
Acinetobacter baumanni	No.	1	3.0	4	0.497
	% within Groups	1.4	3.1	2.4	
Pseudomonas aeruginosa	No.	6	5	11	0.852
	% within Groups	8.3	5.2	6.5	
E-coli	No.	2	2	4	0.824
	% within Groups	2.8	2.1	2.4	
Enterobacter cloacae	No.	1	2	3	0.388
	% within Groups	1.4	2.1	1,8	
Proteus mirabilis	No.	0	1	1	0.391
	% within Groups	0.0	1.4	0.6	
Stenotrophomonas maltophilia	No.	0	1	1	0.391
	% within Groups	0.0	1.0	0.6	
Candida albicans	No.	3	13	16	**0.043***
	% within Groups	4.3	13.4	9.4	
Candida non albicans	No.	5	8	13	0.753
	% within Groups	6.9	8.2	7.7	
Total	No	72	97	169	
	% of total	42.6	57.4	100.0	

*P-value significant at ≤0.05.

The length of stay ranged from 1 day to 45 days with mean ± SD (11.65ds ± 9.63). Only 61 patients had a stay at their original admission setting (origin; before the current ICU) and 99 cases came from the emergency room and community, the mean length of stay at origin was 8.45 ± SD 9.69, ranged from 1 day to 41 days.

Univariate and multivariate regression analysis of MDR risk factors revealed that: LOS at the present ICU or LOS in another ICU before the current one were associated risk factors (*p*-value = 0.00001, 0.05 respectively) (Table 4,5).

Table 4: Univariate analysis of different risk factors that affect MDR acquisition among patients under the study

		No	Mean	SD	*P-value	95% Confidence Interval for Mean		Min	Max
						Lower Bound	Upper Bound		
Length of stay at the current ICU (Days)	No growth	41	6.195	6.3609	***0.00001**	4.187	8.203	1.0	25.0
	MDR	46	16.522	10.3661		13.443	19.600	2.0	45.0
	Total	87	11.655	10.0959		9.503	13.807	1.0	45.0
In ICU (Stay in ICU before our ICU) (Days)	No growth	39	10.85	18.980	***0.05**	4.69	17.00	1.0	106
	MDR	34	18.29	12.547		13.92	22.67	1.0	47
	Total	73	14.32	16.622		10.44	18.19	1.0	106

*P-value significant at ≤0.05

Table 5: Multivariate analysis of risk factors that affect the developing of MDR among all patients under the study:

Risk factors of MDR	#B	*P-value	⌘OR	95% Confidence Interval for OR	
				Lower Bound	Upper Bound
Invasive procedure					
Mechanical Ventilation	0.031	0.701	1.031	0.880	1.208
Urinary catheter	0.031	0.853	1.032	0.742	1.435
Intravascular catheter	-6.862	0.999	0.001	0.000	0.0004
Operative drain	0.148	0.797	1.159	0.376	3.572
Chest tube	0.080	0.665	1.083	0.754	1.557
Nephrostomy tube	1.577	0.999	4.840	0.00001	0.00001
Antimicrobial empirical use	-10.269	0.99	52.82	0.00001	0.00001
Previous colonization by MDR organisms	-11.005	0.536	0.446	0.0003	0.002
Delivery risk factors					
IUGR	-0.0016	0.108	1	0.99	1
Type of delivery	-.559	0.380	.572	0.164	1.991
Site of delivery	-.290	0.682	.748	0.188	2.986
PROM	-.058	1.000	.944	0.00001	0.0001
DM	16.159	0.297	0.293	0.009	1.002
Preeclampsia	-14.311	0.991	.0006	0.00001	0.00001

*P-value significant at ≤0.05; #B=Beta coefficient; ⌘OR=Odds Ratio

Regarding antimicrobial sensitivity in the current study: Gram-positive organisms (4 organisms) were tested against 24 antibiotic and Gram-negative (7 organisms) against 25 antibiotics. MDR Gram-negative isolates showed high resistance to ampicillin-sulbactam (98.8%), cefoxitin (94.2%), amoxicillin-clavulanic acid (93%), and piperacillin-tazobactam (90.7%). Best sensitivity was observed with polymyxin (79.1 %), colistin (75.6%) and imipenem (68.6 %). MDR Gram-positive culture findings revealed vancomycin (93%) and linozolide (100%) sensitivity, whilst, resistance was evident against ampicillin (93%) and piperacillin (84.8%). Meanwhile, all *Candida* spp. isolates were most sensitive to amphotericin (93.1%) and most resistant to fluconazole, with a percentage of (62%).

Regarding the fate of patients; the overall mortality rate was 32.5% (52 patients): NICU deaths represented 52.5% (42 patients), and PICU deaths represented 12.5% (10 patients) with a significant difference between NICU and PICU (*p* value = 0.00001) (Table 6).

Table 6: Fate of patients attended the NICU and PICU during the study

Fate		Groups		Total	P-value
		NICU	PICU		
Discharged from hospital	Count	35	35	70	
	% within groups	43.7	43.7	43.7	
Referred to pediatric ward	Count	2	32	34	
	% within groups	2.5	40.0	21.2	**0.000001***
Referred to another hospital	Count	2	3	5	
	% within groups	2.5	3.75	3.1	
Death	Count	42	10	52	
	% within groups	52.5	12.5	32.5	
Total	Count	80	80	160	
	% within groups	100.0	100.0	100.0	

*P-value significant at ≤0.05.

DISCUSSION

MDR organisms pose a worldwide threat in ICU for hospitalized children; hinders disease control and is associated with high mortality rates. Treatment cost is correspondingly increased secondary to the prevalence of resistant pathogens requiring more expensive therapies [10].

In the present study, MDR-HAI prevalence was 85.8%; this was comparable to the reported prevalence (92.45%) in 2 pediatric ICUs in Pediatric Hospital-Cairo University [11] and higher than the reported prevalence in King Chulalongkorn Memorial Hospital-Thailand (52%)[12]. The difference might be explained by different sample size, demographic variations and inadequate adherence to infection control measures.

In this study, distribution of *Klebsiella pneumoniae* 62 (36.7%) was 34 in NICU (54.8%) and 28 (45.2%) in PICU culture results. The predominance of *Klebsiella pneumoniae* in NICU was also reported in other National studies (40 %)[13], (42.8%)[14], (14.29%)[15], and international studies (ranged from 12%-34%) [16-19]. Unlike our study, *E. coli* [20,21], *P.aeruginosa* [23, 24] and *Enterobacter* spp [23] were identified as the most common Gram-negative isolates in other studies.

Moreover, *Klebsiella pneumoniae* were the most common MDR yields 59/62 (95.1%), followed by CONS 24/33 (72.7%) and *Pseudomonas aeruginosa* 11/11 (100%); representing 40.6%, 16.5%, 8.8% respectively of all MDRO. Similar to our *Klebsiella* findings, reports came from other reports [1,16,17,24] and other studies revealed similar results to those of *Acinetobacter* and *Pseudomonas infections* [25, 26].

In the present study 86.8% of the isolates were CONS. The vast majority of them were MDR. Most of CONS isolates were detected at blood cultures (69.7%); and vancomycin susceptibility of all isolated CONS was 93.9%. Similar findings were obtained in other studies in Egypt [1,15,27] and other different countries (including China, Mexico, South Africa, and Kenya) [14,18,20]. Possible explanations for the high percentage of MDRO

in the studied group can be extrapolated by; abuse of antibiotics in the outpatient settings, treating viral infections with antibiotics, inappropriate dose and incomplete course of antibiotics.

In this study, univariate and multivariate analysis of MDR risk factors revealed that: LOS at the present ICU or LOS in another ICU before the current one were associated risk factors (*p*-value = 0.00001, 0.05 respectively), while, the other risk factors showed no statistical significance (table 4,5). Similarly; in a study done in Tahran, LOS was an evident risk factor, while, antibiotic therapy due to absence of clear history regarding antibiotic therapy in one-third of studies participants was unclear, like our own work [28]. On the contrary, other study reported that empirical therapy, intravenous catheterization and parenteral nutrition were risk factors among neonates [29,30].

Regarding antibiotic sensitivity, MDR Gram-negative isolates showed high resistance to ampicillin-sulbactam (98.8%), cefoxitin (94.2%), amoxicillin-clavulanic acid (93%), and piperacillin-tazobactam (90.7%). Best sensitivity was observed with polymyxin (79.1 %), colistin (75.6%) and imipenem (68.6 %). This agrees with another study, which reported that all the isolates of *Klebsiella pneumoniae,* our main isolate, had the same antibiogram, showing resistance to ampicillin and piperacillin and susceptibility to colistin and imipenem [13,29,31].

The Gram-positive cultures findings revealed that vancomycin (93%) and linozolide (100%) were the most effective, whilst, resistance was evident against ampicillin (93%) and piperacillin (84.8%). In Egypt, Shehab El-Din et al. found that best sensitivity among Gram-positive isolates was to vancomycin, followed by imipenem, amikacin, and finally quinolones. In addition, vancomycin sensitivity was also reported by other studies [20,21,30].

Our data showed that, 29 out of the 169 isolates were *Candida* spp (17.2%). (*C. albicans* 54.2%, *C.non albicans* 44.8%), most of them were MDRO (Table 1). They were most sensitive to amphotericin B (93.1%) and

most resistant to fluconazole (62%). Though other studies found that *C. albicans* was most prevalent yeast isolate in NICU similar to our data, nevertheless, the total percentage of the *C.non albicans* were more, unlike the present findings [32,33]. However, another study found that *C. glabrata* exceeded in number *C. albicans* contradicting the present results[34]. Regarding antifungal sensitivity, our data were comparable to other reports [32,34], who found that their yeast isolates were highly sensitive to amphotericin B and relatively resistant to azoles.

In the present study, the overall mortality rate was 32.5% (52 patients): NICU deaths represented 52.5% (42 patients), and PICU deaths represented 12.5% (10 patients) with a significant difference between NICU and PICU (Table 4). Similarly; previous national study reported high mortality rates (51%) [35], and several international studies reported overall mortality of HAI in pediatric intensive care unit ranged between 10%-53.6 % [12,36]. In contrast, very low mortality rates were reported in the developed countries[18], which can be explained by the high quality of life and high standard measures of health care and hospital services in these countries.

CONCLUSION

To sum it up, MDROs frequencies (85.7%) were very high among NICU and PICU cases. Most common MDROs were *Klebsiella, CONS, Candida* and *Pseudomonas* spp. respectively. Frequency of Gram-negative organisms is much more common than Gram-positive organisms. The high rate of antimicrobial resistance is in continuous increase; even for new categories, so, strict infection control programs should be implemented.

Conflicts of interest: The authors declare that they have no financial or non financial conflicts of interest related to the work done in the manuscript.

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