PN-01"Resistance Profile of Pathogens Causing Neonatal Sepsis in Neonatal Intensive Care Unit at Alexandria University Children Hospital"

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Introduction

Neonatal sepsis "a clinical manifestation of a systemic infection" is classified into early onset sepsis (EOS), if the onset of infection is before 72 hours of life and late onset sepsis (LOS), if it occurs from day four of life to three months of age. Antimicrobial resistance (AMR) is the ability of microbes by mutating to grow in the presence of a microbicidal or microbiostatic agents. Sepsis caused by multidrug resistant (MDR) pathogens is a significant cause of morbidity and mortality. When a neonate is infected with an AMR bacteria, treatment options are often limited, and healthcare professionals may need to use antibiotics that are less effective more expensive or associated with more side effects.

This study was conducted to estimate incidence rates of Multidrug resistant EOS and LOS, identify resistance profile of common pathogens causing neonatal sepsis in Neonatal Intensive Care Unit (NICU) at Alexandria University Children Hospital (AUCH) "El-Shatby" and guide antibiotic stewardship programs.

Materials and Methods

Data was collected as a part of a retrospective, cohort study conducted on a random sample of 754 medical records of neonates who received antibiotics in NICU at AUCH between December 2017 and December 2019. Data was analyzed using SPSS® for Windows, version 25, and Excel® for Microsoft® 365.

WHONET® software version 20.16.15. was used to generate a cumulative antibiogram and to describe types of resistance from all ordered cultures between January 2018 and December 2019.

Bacterial isolates non-susceptible to at least one agent in three or more antimicrobial categories were considered Multidrug Resistance (MDR). Those susceptible to only one or two categories were considered Extensive Drug Resistance (XDR) and those non-susceptible to all tested agents in all tested antimicrobial categories were considered Pan Drug Resistance (PDR).

Results

LOS was the most common form of neonatal sepsis. The incidence rate of multidrug resistant bacterial EOS and LOS were 27 and 101 per 1000 birth lives, respectively. Fungal sepsis caused by Candida was more common in late onset sepsis (22.8%) than early onset sepsis (11.4%).

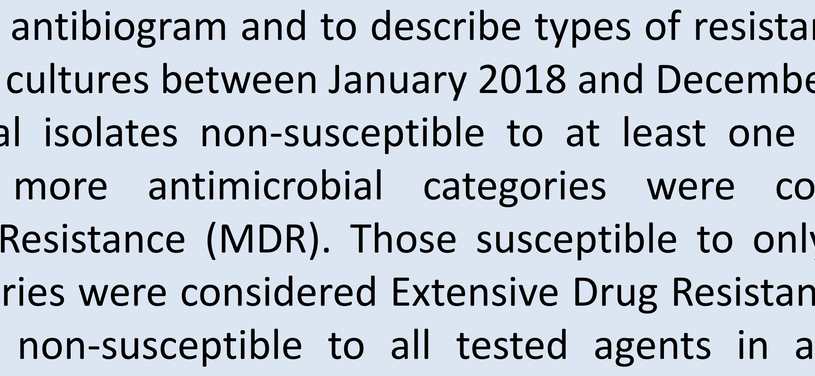
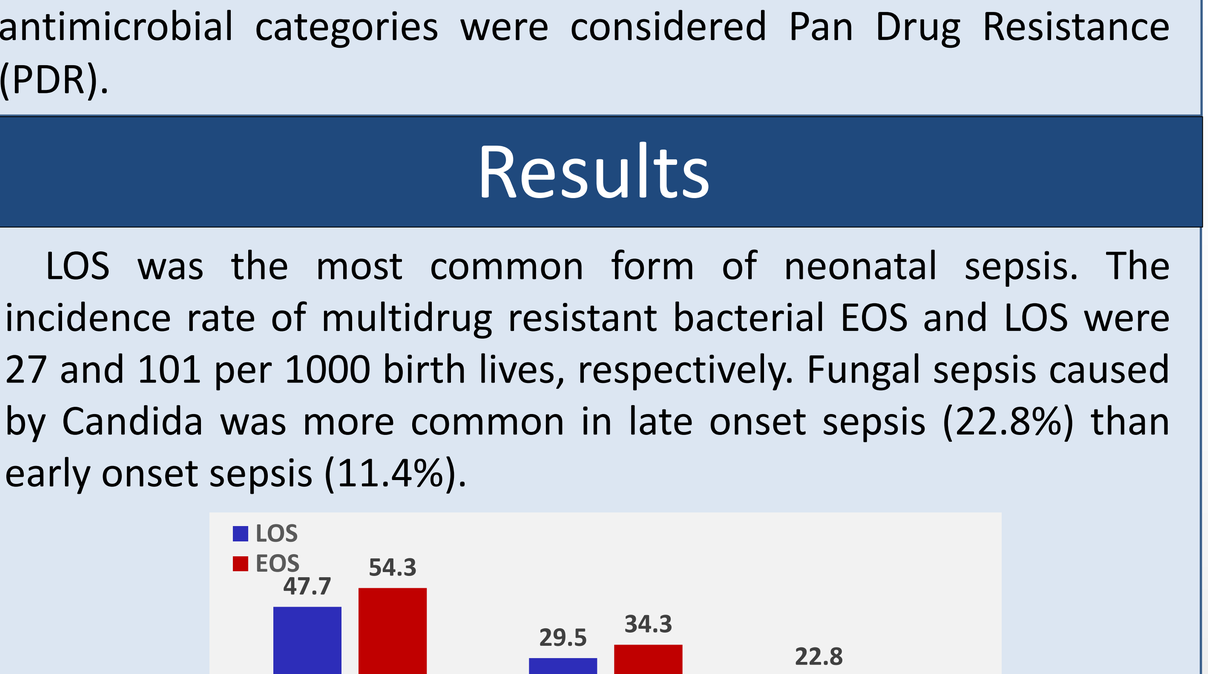


Figure 1. Distribution of El-Shatby NICU pathogenic organisms causing Neonatal Sepsis



Enterococcus (Ent), Staphylococcus aureus (sau), Streptococcus pneumoniae (spn), Streptococcus viridans (svi), Candida (can) Acinetobacter (ac-), Citrobacter (ci-), Escherichia coli (eco), Enterobacter (en-), Klebsiella pneumoniae (kpn),Pseudomonas aeruginosa (Pae).

Figure 2. Pathogenic organisms causing Neonatal Sepsis

There was no statistical difference in distribution of pathogens causing neonatal sepsis among EOS & LOS x^2=13.235,p = .194. they share the same nosocomial infection profile. In which Klebsiella pneumoniae was the main isolated Gram-negative pathogen and Staphylococcus aureus was the main isolated Gram-positive pathogen.

The difference in the distribution of different types of MDR among Late Onset MDR Bacterial Sepsis and Early Onset MDR Bacterial Sepsis was not statistically significant . (x^2= .637, *P= .837)*

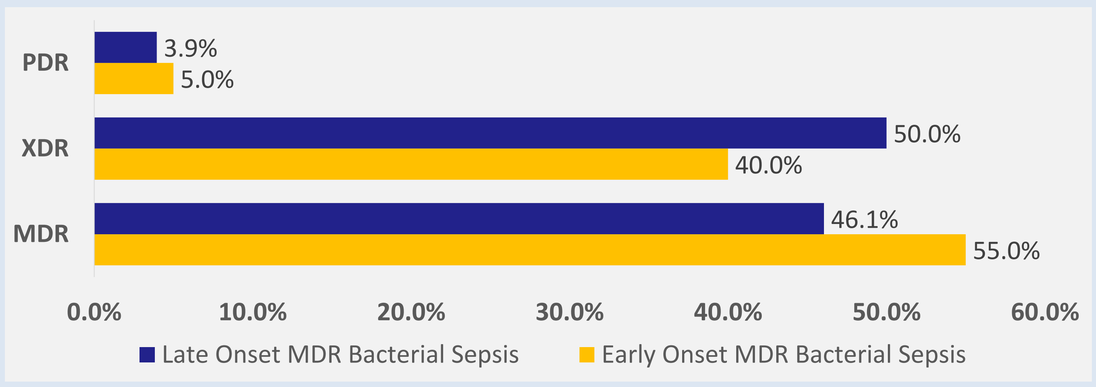
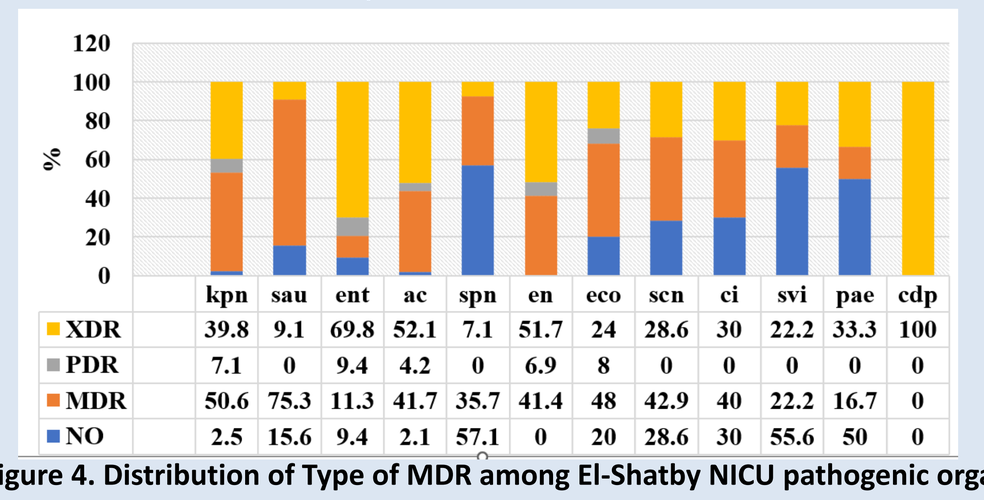


Figure 3. Distribution of type of MDR by type of MDR Bacterial Neonatal sepsis

Alarming XDR was found among *Enterococcus, Acinetobacter Enterobacter and Klebsiella pneumoniae* isolates.



	kpn	sau	ent	ac	spn	en	eco	scn	ci	svi	pae	cdp
XDR	39.8	9.1	69.8	52.1	7.1	51.7	24	28.6	30	22.2	33.3	100
PDR	7.1	0	9.4	4.2	0	6.9	8	0	0	0	0	0
MDR	50.6	75.3	11.3	41.7	35.7	41.4	48	42.9	40	22.2	16.7	0
NO	2.5	15.6	9.4	2.1	57.1	0	20	28.6	30	55.6	50	0

Figure 4. Distribution of Type of MDR among El-Shatby NICU pathogenic organisms

We noted emerging non-susceptibility to both Colistin and Tigecycline (Last resort antibiotic therapy for Gram-negative bacterial infections) and to linezolid (Last resort antibiotic therapy for Gram-positive bacterial infections). Urgent threats included **Carbapenem-resistant *Acinetobacter*** and **Carbapenem-resistant *Enterobacteriaceae***. While serious threats included: **Drug-resistant Candida**, *ESBL-producing Enterobacteriaceae*, vancomycin-resistant *enterococci* **(VRE)** and Methicillin-resistant *Staphylococcus aureus* **(MRSA)**

Table 1. Cumulative Antibiogram of Gram-positive organisms showing % non-susceptibility to different antibiotics.

Organism	N	AMP	PEN	PNV	OXA	AMK	GEN	TOB	GEH	STH	CRO	CTX	FEP	FOX	RIF	CIP	LVX	NOR	OFX	SXT	CLI	AZM	ERY	CLR	NIT	LNZ	VAN	TEC	CHL	DOX	TCY
sau	72		100	98		46	74	80						90	58	81	66		81	35	35	61	69	100	100	3	0	2		40	68
ent	49	91	89			100			88	100					100	100	86	100					95		100	10	82	75	0	41	50
spn	27				100										50		100		86	87	0		62			0	0			36	
scn	14			100		50	100	0						71	100	83	60		80	67	50	50	42			0	0	0		33	67
svi	9	40	29	29							100	88	67				33		100		63		43			13	22	11			

Sau=Staphylococcus aureus, ent=Enterococcus, spn=Streptococcus pneumoniae, scn, =Coagulase negatives Staphylococcus, svi=Streptococcus viridans

Ampicillin(AMP)-Penicillin G (PEN)- Penicillin V(PNV)-Oxacillin(OXA) Amikacin(AMK)-Gentamicin(GEN)-Tobramycin(TOB)-Gentamicin High(GEH)-Streptomycin High(STH)-Ceftriaxone(CRO)-Cefotaxime(CTX)-Cefepime(FEP) - Cefoxitin(FOX)-Rifampin(RIF)-Ciprofloxacin(CIP)-Levofloxacin(LVX)-Norfloxacin(NOR)-Ofloxacin(OFX)-Trimethoprim/-Sulfamethoxazole(SXT)-Clindamycin(CLI)-Azithromycin(AZM)-Erythromycin(ERY)-Clarithromycin(CLR)-Nitrofurantoin(NIT)-Linezolid(LNZ)-Vancomycin(VAN)-Teicoplanin(TEC)-Chloramphenicol(CHL)-Doxycycline (DOX)-Tetracycline(TCY)

Table .2 Cumulative Antibiogram of Gram-negative organisms showing % non-susceptibility to different antibiotics.

Organism	N	AMP	PIP	AMC	CSL	SAM	TZP	CZO	CFP	CXA	CAZ	CRO	CTX	FEP	FOX	ATM	ETP	IPM	MEM	AMK	GEN	TOB	CIP	LVX	OFX	SXT	COL	CHL	DOX	TCY	TGC
kpn	247	100	99	92	94	95	94	100	99	97	92	94	96	95	100	46	87	83	86	78	64	82	88	76	0	36	42	27	18	59	84
ac-	36		91	84		91	91				94	93	100	94				89	89	94	96	100	100	84		82	17		10	80	26
en-	27	100	96	100	92	95	92		91	100	96	96	100	96	100	67	100	89	93	100	80	100	92	81		50	48	100	6	60	93
eco	24	67	100	33	42	56	41		80	100	65	71	86	74		79	38	25	30	24	60	43	82	82		55	46	100	69	100	40
ci-	9	0	56	63	44	63	56		80	50	57	50	67	44	100	33	83	44	44	50	0	67	57	50		0	33	67	14	0	83
pae	5		50				20				25			20		50		20	20	0	0		50	50			0				

Klebsiella pneumoniae (Kpn), Acinetobacter (ac-) Enterobacter (en-), Escherichia coli (eco), Citrobacter (ci-) & Pseudomonas aeruginosa (pae)

Ampicillin(AMP)- Piperacillin(PIP)-Amoxicillin/Clavulanic acid(AMC)-Cefoperazone/Sulbactam(CSL)-Ampicillin/Sulbactam(SAM)-Piperacillin/Tazobactam(TZP)-Cefoperazone(CFP)- Ceftazidime(CAZ)-Ceftriaxone(CRO)- Cefotaxime(CTX)-Cefepime(FEP)-Cefuroxime(CXA)-Aztreonam(ATM)- Ertapenem(ETP)- Imipenem(IPM)- Meropenem(MEM)-Amikacin (AMK)- Gentamicin(GEN) -Tobramycin (TOB)- Ciprofloxacin (CIP)-Levofloxacin(LVX)- Trimethoprim/Sulfamethoxazole(SXT)-Colistin(COL)- Chloramphenicol(CHL)-Doxycycline (DOX)-Tetracycline(TCY)-Tigecycline(TGC)

Conclusions

- The most common form of neonatal sepsis in El-Shatby NICU was LOS.
- Gram-negative bacteria dominated in both EOS and LOS. Both EOS & LOS share the same nosocomial infection profile. In which *Klebsiella pneumoniae* was the main isolated Gram-negative pathogen and *Staphylococcus aureus* was the main isolated Gram-positive pathogen.
- *Candida* was the second most common pathogen in both EOS and LOS, but it was more common in LOS.
- Alarming XDR and PDX exists specially among *Enterococcus*, *Acinetobacter.* and *Klebsiella pneumoniae* isolates.

Recommendations

- Antibiotic stewardship program in El-Shatby NICU should focus on initiating empiric antibiotic therapy targeting multidrug resistant *Klebsiella pneumoniae* and Methicillin resistant *Staphylococcus aureus*, and to reserve last resort antimicrobials by preauthorization and restriction of Colistin, Linezolid and Carbapenems.
- Fungal stewardship program is needed.

References

Wynn JL. Defining neonatal sepsis. Curr Opin Pediatr. 2016 Apr;28(2):135-40.

World Health Organization-WHO. (2019). Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries: a WHO practical toolkit. JAC-Antimicrobial Resistance, 1(3).

Rafailidis, P. I., & Kofteridis, D. (2022). Proposed amendments regarding the definitions of multidrug-resistant and extensively drug-resistant bacteria. Expert Review of Anti-Infective Therapy, 20(2), 139–146.