Multidrug resistance pattern in bacteriological isolates of neonatal septicemia in NICU of a tertiary care center

Fareya Haider[1,*], Zahida Parveen Dar[2], Aman Gupta[3], Shadma Yaqoob[4], Mastan Singh[5]

[1]Assistant Professor, [3]Resident, [4]Associate Professor, [5]Professor and Head, Dept. of Microbiology, Era's Lucknow Medical College and Hospital, Lucknow, Uttar Pradesh, India, [2]Senior Resident, Dept. of Microbiology, King Khalid Civilian Hospital, Tabuk, Saudi Arabia

***Corresponding Author:**
Email: fareyahaider@gmail.com

Received: 5th July, 2018 **Accepted:** 7th July, 2018

Abstract

Introduction: Multidrug resistance pathogens have been found to be an increasing cause of neonatal sepsis in developing country like India. The present study was conducted to study the multidrug resistant pattern in bacterial isolates of neonatal septicaemia in Neonatal intensive care unit (NICU) of a tertiary referral hospital, Northeastern part of U.P., India.

Material and Methods: It was a prospective study in which blood culture sample was taken from 450 neonates who had clinical features of sepsis or had presence of risk factors (one major–prolonged rupture of membranes/evidence of chorioamnionitis, intrapartum fever, foul smelling liquor or two minor–febrile illness of mother 2 weeks prior to delivery, meconium stained liquor amnii, more than 3 vaginal examinations during labour, low birth weight or prematurity, prolonged labour, low Apgar score) over a period one year.

Results: A total of 102 (22.7%) suspects were found to be positive for sepsis. In present study, among positive cases of neonatal sepsis, the prevalence of early onset was around three forth as compared to late onset sepsis. Among all gram positive and gram negative isolates *Klebseilla pneumoniae* was found to be maximum followed by *Grp B streptococcus.* Out of total isolates only five isolates were MDR, whereas 4 MRSA and 17 ESBL.

Conclusion: Presence of Multidrug resistant isolates as well an increasing rate of ESBL producers among neonates noted in this study is alarming. Thus regular monitoring of susceptibility profile of bacterial pathogen is the need of the hour to treat and curtail the increasing trend of neonatal septicemia.

Keywords: Neonatal sepsis, Antibiotic susceptibility, *Klebseilla pneumoniae Grp B streptococcus.*

Introduction

Neonatal sepsis or sepsis neonatorum refers to systemic infection of the newborn. It is characterized by a constellation of a nonspecific symptomatology in association with bacteremia. Prompt recognition, appropriate antimicrobial therapy and judicious supportive care are the key determinants of positive outcome in this serious pediatric emergency. In many developing countries neonatal mortality rates (deaths in the first 28 days of life) are as high as 40–50 per 1000 live births,[1,2] with infections being the major cause of death.[3,4] Sepsis is a significant cause of morbidity and mortality in neonates.[5,6]

Not surprisingly, sepsis is the commonest diagnosis of inpatients among neonates at referral facilities.[7] A very wide spectrum of organisms has been described for cases of neonatal septicemia and this septicemia is subject to geographical alterations.

Gram positive cocci causing neonatal septicemia are *Staphylococcus aureus, Coagulase negative Staphylococcus (CoNS), Enterococci, Group B Streptococcus, Streptococcus pneumoniae, Listeria monocytogens and Streptococcus viridans*.

Gram negative bacteria causing neonatal septicemia are *Escherichia coli, Klebsiella spp, Enterobacter spp., Pseudomonas spp., Neisseria meningitidis, Neisseria gonorrhoeae, Salmonella spp*. etc. The inadvertent use of broad-spectrum antibiotics has led to the emergence of multidrug resistant Gram-negative bacteria.[8,9] Pathogens causing neonatal infections and their antibiotic susceptibility patterns may change over time[10] and differ between countries[11] and so it is essential to diagnose the cases in time to provide with appropriate antibiotic treatment. Considering the high infection rate among patients, their high treatment expenses, the high rate of mortality and the resistance of these microorganisms to antibiotics, specific attention and proper measurement is necessary.[12]

Considering the relevance of changing spectrum of pathogens responsible for neonatal septicaemia and their equally variable antibiotic susceptibility pattern, the present study was planned to be carried out to study the multidrug resistant pattern in bacterial isolates of neonatal septicaemia in NICU of Era's Lucknow Medical College and Hospital, Lucknow.

Materials and Methods

Evaluation of blood samples from the neonates having clinical features of sepsis or suspected or at risk (one major and two minor) of neonatal septicemia were taken into study. The major risk factors included prolonged rupture of membranes (>24 hours), evidence of chorioamnionitis, intrapartum fever >100.4degF and foul smelling liquor, whereas minor included febrile illness in the mother within 2 weeks prior to delivery, meconium stained liquor amnii, more than 3 vaginal examinations during labour, low birth weight (<2500 grams) or prematurity, prolonged labour (sum of first and second stage >24 hours), and neonates with Apgar score at 1 minute < 4. Neonates with congenital and chromosomal anomalies and those whose guardians refused to give consent were not taken.

Evaluation of a total of 450 suspected cases over a period of one year from 2017 May to 2018 May was done. Using aseptic technique, 1-2ml of blood was collected from each patient, was inoculated immediately into brain heart infusion (BHI) broth and was incubated for 24hr under aerobic conditions at 37^0C. First subculture was done on 5% Sheep blood agar and MacConkey agar plates incubated for 14-24 hrs. A negative result followed by examining the broth daily, for the appearance of turbidity and a final subculture was done at the end of 7 days. Identification of isolates upto species level was done by using standard biochemical tests. Minimum inhibitory concentration (MIC) was set on for antimicrobials using dehydrated Microscan broth dilution method. Susceptibilty was interpreted on the basis of CLSI guidelines of corresponding years. Antibiotic agents tested for gram negative isolates were as follows: cephalosporins (ceftriaxone, cefotaxime); β-lactam/β-lactamase inhibitor (amoxicillin/clavulanic acid) carbapenem (imipenem); aminoglycosides (amikacin, gentamicin,); aminopenicillin (ampicillin); cotrimoxazole, and for gram positive isolates, the drugs included were cepholosporins (cefoxitin, cefotaxime, ceftriaxone); β-lactam/β-lactamase inhibitor (amoxicillin/clavulanic acid); aminoglycosides (amikacin, gentamicin, netilmicin,); aminopenicillin (ampicillin); vancomycin, linezolid and cotrimoxazole. The Quality control strains (QC) recommended by CLSI which were used with each isolate were *Escherichia coli* ATCC 25922, *E.coli* ATCC 35218, *Pseudomonas aeruginosa* ATCC 27853, *Klebseilla pneumoniae* ATCC 700603 (ESBL positive strain) and *S.aureus* ATCC-43300 (MRSA positive) Bacterial isolates from blood samples were only considered if QC strains MICs were within the acceptable ranges. Methicillin resistant staphylococcus aureus (MRSAs) were classified by standard cefoxitin Disk diffusion test and extended spectrum beta-lactamases (ESBLs) by using the phenotypic method where ≥5mm increase in zone diameter for cefotaxime tested in combination with clavulanate was observed against the zone diameter when tested alone where considered ESBL positive. The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD.

Results

Among the total (n=450) clinically suspected cases, a total of (n=102) were culture positive, hence prevalence of neonatal sepsis was found to be 22.7%. Around three fourth (n=75; 73.5%) were found to be early onset type while remaining 27 (26.5%) as late onset.

Table 1: Distribution of cases according to presence of different risk factors

S. No	Risk Factor	Total (n=102)		Early onset (n=75)		Late onset (n=27)		Significance of difference	
		No.	%	No.	%	No.	%	χ^2	P
1.	Fever	32	31.4	26	34.7	6	22.2	1.428	0.232
2.	PROM								
	No PROM	48	47.1	30	40.0	18	66.7	5.737	0.057
	No meconium	44	43.1	37	49.3	7	25.9		
	Meconium +ve	10	9.8	8	10.7	2	7.4		
3.	Mode of delivery								
	Vaginal	47	46.1	30	40.0	17	63.0	4.213	0.040
	LSCS/Vacuum	55	53.9	45	60.0	10	37.0		
4.	Preterm	63	61.8	48	64.0	15	55.6	0.599	0.439
5.	Low birth weight (<2.5 kg)	46	45.1	29	38.7	17	63.0	4.733	0.030
6.	Low Apgar (<7)	84	82.4	63	84.0	21	77.8	0.529	0.467

A significant difference in proportion of patients with risk factors between two onset types was observed for mode of delivery and low birth weight only with significantly higher proportion of early onset cases having LSCS/instrumented delivery as compared to those with late onset (p=0.040) and significantly higher

proportion of late onset cases with low birth weight as compared to those with early onset (p=0.030).

Table 2: Distribution of bacterial pathogen among the two case groups

S. No.	Organism	Total (n=102)		Early onset (n=75)		Late onset (n=27)	
		No.	%	No.	%	No.	%
Gram Positive							
1.	*S.aureus*	7	6.9	6	8.0	1	3.7
2.	*Enterococcus spp.*	3	2.9	2	2.7	1	3.7
3.	*Grp B streptococcus*	15	14.7	11	14.7	4	14.8
Gram Negative							
4.	*P. aeruginosa*	6	5.9	4	5.3	2	7.4
5.	*Acinetobacter spp.*	10	9.8	7	9.3	3	11.1
6.	*C.fruendii*	2	2.0	2	2.7	0	0.0
7.	*Citrobacter spp.*	3	2.9	3	4.0	0	0.0
8.	*E. coli*	11	10.8	8	10.7	3	11.1
9.	*Enterobacter spp.*	8	7.8	6	8.0	2	7.4
10.	*K. oxytoca*	3	2.9	2	2.7	1	3.7
11.	*K. pneumoniae*	32	31.4	22	29.3	10	37.0
12.	*Proteus mirabilis*	2	2.0	2	2.7	0	0.0

Among Gram positive isolates *Grp. B streptococcus* was most common in both early and late onset groups. *Staphylococcus aureus* was the next most common isolate followed by *Enterococcus spp.* Among Gram negative isolates, *K. pneumoniae* was the most common followed by *E. coli* and *Acinetobacter* spp.

Table 3: Comparison of antibiotic susceptibility testing by Microscan broth dilution method showing Gram positive and Gram negative clinical isolates susceptible to various antibiotics

S. No.	Antibiotic (disk content in µg)	Gram Positive (n=25)		Gram Negative (n=77)			Significance
		Tested	No of sensitive isolates	Tested	No of sensitive isolates	χ^2	P
1.	Ampicillin(10)	25	3 (12.0)	77	5 (6.5)	0.792	0.374
2.	Gentamicin(10)	24	10 (41.7)	77	34 (44.2)	0.046	0.830
3.	Amoxycalvulinic acid (20/10)	24	12 (50.0)	76	43 (56.6)	0.319	0.572
4.	Ceftriaxone(10)	24	12 (50.0)	76	29 (38.2)	1.057	0.304
5.	Amikacin (30)	22	18 (81.8)	76	48 (64.0)	2.384	0.115
6.	Linezolid(30)	25	21 (84.0)	-	-	-	-
7.	Cefoxitin(30)	23	14 (60.9)	-	-	-	-
8.	Vancomycin (30)	18	18 (100)	-	-	-	-
9.	Netilmicin (30)	22	19 (86.4)	-	-	-	-
10.	Cotrimoxazole(25)	23	11 (47.8)	68	23 (33.8)	1.440	0.230
11.	Cefotaxime(30)	25	16 (64.0)	71	32 (45.1)	2.650	0.104
12.	Imipenem(10)	-	-	71	62 (87.3)	-	-

Among Gram positive isolates, Vancomycin, Amikacin and Linezolid showed maximum sensitivity. Among Gram negative isolates Imipenem showed maximum sensitivity. Ampicillin was least sensitive antibiotic against both the types. Statistically, no significant difference was observed between two types wherever common antibiotics were used for assessment of sensitivity pattern.

Table 4: Percentage sensitivity of various antibiotics against clinical isolates

S. No.	Antibiotics (disk content in µg)	Gram Positive			Gram Negative								Total
		S..aureus	*Enterococcus. spp.*	*Grp..B streptococcus*	*P. aeruginosa*	*Acinetobacter spp.*	*C. freundii*	*Citrobacter sp.*	*E. coli*	*Enterobacter spp.*	*K. oxytoca*	*K. pneumoniae*	*Proteus mirabilis*	
1.	Ampicillin(10)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	27.3	12.5	0.0	3.1	0.0	7.8
2.	Gentamicin(10)	57.1	33.3	35.7	50.0	30.0	50.0	66.7	54.5	62.5	66.7	37.5	0.0	43.6
3.	Amoxycalvulinic acid(20/10)	42.9	50.0	53.3	33.3	60.0	50.0	66.7	72.7	37.5	66.7	61.3	0.0	55.0
4.	Ceftriaxone(10)	66.7	33.3	46.7	50.0	20.0	50.0	33.3	63.6	50.0	66.7	29.0	0.0	41.0
5.	Amikacin(30)	66.7	50.0	92.9	83.3	70.0	100.0	33.3	50.0	62.5	100.0	61.3	50.0	68.0
6.	Linezolid(30)	85.7	100	80.0	50.0	0.0	100	100	100	50.0	73.2	61.3	50.0	73.2
7.	Cefoxitin(30)	85.7	100.0	46.7	20.0	33.3	0.0	0.0	44.4	62.5	0.0	28.6	50.0	39.1
8.	Vancomycin(30)	-	100	100	-	-	-	-	-	-	-	-	-	100
9.	Netilmicin(30)	100	100	76.9	33.3	33.3	-	-	0.0	66.7	0.0	42.9	-	63.4
10.	Cotrimoxazole(25)	57.1	0.0	46.7	50.0	50.0	50.0	0.0	40.0	20.0	100	25.0	0.0	37.4
11.	Cefotaxime(30)	57.1	66.7	66.7	33.3	60.0	50.0	33.3	40.0	75.0	50.0	35.7	50.0	50.0
12.	Imipenem(10)	-	100	-	83.3	90.0	100	100	66.7	85.7	100	93.3	50.0	87.5

Table 5: Prevalence of ESBL and MDR positivity

S. No.	Organism	Total	MDR Positive		ESBL Positive	
			No.	%	No.	%
1.	*CoNS*	7	0	0	0	0
2.	*Enterococcus spp.*	3	0	0	0	0
3.	*S. aureus*	15	0	0	0	0
4.	*P. aeruginosa*	6	1	16.7	0	0
5.	*Acinetobacter spp.*	10	1	10.0	1	10.0
6.	*C.freundii*	2	0	0	0	0
7.	*Citrobacter spp.*	3	0	0	1	33.3
8.	*E. coli*	11	2	18.2	2	18.2
9.	*Enterobacter spp.*	8	0	0	1	12.5
10.	*K. oxytoca*	3	0	0	0	0
11.	*K. pneumoniae*	32	0	0	12	37.5
12.	*Proteus mirabilis*	2	1	50.0	0	0

Prevalence of MDR was maximum in *P. mirabalis* (50%) and, maximum ESBL positivity was observed for *K. pneumoniae* (37.5%).

Table 6: Distribution of early onset and late onset cases according to their outcome

S. No.	Outcome	Total (n=102)		Early onset (n=75)		Late onset (n=27)	
		No.	%	No.	%	No.	%
1.	Recovered	97	95.1	72	96.0	25	92.6
2.	Expired	5	4.9	3	4.0	2	7.4

χ^2=0.494; p=0.482

A total of 5 (4.9%) mortalities took place. There were 3 (4%) early onset cases who expired whereas a total of 2 (7.4%) late onset patients also expired. Statistically, there was no significant difference in rate of mortality between two groups (p=0.482).

Table 7: Association between MDR, MRSA and ESBL positive isolates and neonatal outcome

S. No.	Variable	Total	Alive		Expired	
			No.	%	No.	%
1.	MDR	5	2	40.0	3	60.0
2.	MRSA	4	4	100	0	0
3.	ESBL	17	16	94.1	1	5.9

Discussion

The present study evaluates the multi-drug resistant pattern of bacterial isolates among septicemic neonates admitted in NICU of a tertiary care hospital in Lucknow, (U.P), India. The study revealed the prevalence of neonatal sepsis to be 22% (102/450). Prevalence of neonatal sepsis among clinically suspect cases has been reported to be varying from 10% to 50% in various studies from India. Low APGAR (82.4%) and Preterm delivery (61.8%) were the most common predictors of neonatal sepsis.

Vaidya et al.[13] reported this incidence to be 40.9% among clinically diagnosed cases of sepsis. Kaistha et al.[14] in a retrospective analysis reported this incidence to be 13.17%. The variability in prevalence rate is dependant on the regional location, season, infrastructural facilities and most importantly on inclusion criteria. In present study, the inclusion criteria was much relaxed, thereby the number of suspects was higher and positivity rates were relatively lower.

In present study, Gram positive organisms isolated out of total were 25 (24.5%) whereas the remaining were Gram negative organisms 77 (75.5%). The findings in present study are in agreement with those reported in literature[15-19] who reported presence of Gram negative organisms to be more common. Among Gram positive isolates *Grp B streptococcus* was most common in both early and late onset groups. *Staphylococcus aureus* was the next most common isolate followed by *Enterococcus spp.* Among Gram negative isolates, *K. pneumoniae* was the most common followed by *E. coli* and *Acinetobacter* spp. which showed similarity with the study of Tallur et al., Karunasekara et al., Moreno et al., Karthikeyan and Premkumar, Lim et al.,[15-19] On evaluation of sensitivity pattern among Gram positive isolates – Ampicillin was found to be least sensitive for both Gram positive (12%) as well as Gram negative (6.5%) isolates whereas Vancomycin was most sensitive (100%) for Gram positive isolates followed by Netilmicin (86.4%), Linezolid (84%) and Amikacin (81.8%). Except for Ampicillin, Gentamicin, Amoxicillin-clavulinic acid, Ceftriaxone and Cotrimoxazole, all the antibiotics showed more than 50% sensitivity. The sensitivity pattern in the present study appeared to be similar to that reported by Kaistha et al. In present study, more than two third *K. pneumoniae* were resistant against third generation cephalosporins which is similar to the observations made by Maramba-Lazarte et al. at St. Louis University.[20] In present study 97.1% of *Klebsiella* spp. (31 *K. pneumoniae* + 3 *K. oxytoca*) and 87.5% of *Enterobacter spp.* were resistant against ampicillin. Similar observations were made by Ale-Tayeb et al.[21] that all the *Klebsiella* and *Enterobacter* strains were resistant against Ampicillin.

Prevalence of ESBL positivity was 37.5% among *Klebsiella spp.* which is similar to that reported by Kolar et al.[22] and Shayanfar et al.[23]

In present study, MRSA was not associated with any mortality while 60% of MDR positive neonates expired and in ESBL positive patients was 5.9%.

The findings in present study indicated the changing pattern of drug sensitivity of microbial organisms responsible for neonatal sepsis and need of a renewed protocol for treatment of neonatal sepsis. The lower mortality rates in present study show that timely intervention with correct strategy is helpful in reducing mortality, although the high mortality rates in MDR cases (60%) indicate the need to explore new antibiotic regimens. Further studies on larger sample size with newer antibiotics are recommended.

Conclusion

The prevalence of neonatal sepsis in clinically suspected cases was found to be 22.7%. Among cases of neonatal sepsis, prevalence of early onset type was 73.5% whereas the prevalence of late onset type was 26.5%. *K. pneumoniae* (n=32; 31.4%) among Gram negative and *Grp.B streptococcus* (n=15; 14.7%) among Gram positive were most common in both early and late onset groups. *Staphylococccus aureus*, *Grp.B streptococcus* and *Enterococcus spp.* were completely resistant against Ampicillin whereas *Enterococus spp* showed absolute sensitivity against Linezolid, Cefoxitin, Vancomycin, and Netilmicin. Prevalence of MDR was maximum in *P. mirabalis* (50%). None of the cases of *S.aureus, Enterococcus spp., Grp.B streptococcus, C. freuendii, Citrobacter spp., Enterobacter spp., K. oxytoca and K. pneumoniae* were MDR. One out of 6 *P. aeruginosa*, 1 out of 10 *Acinetobacter* and 2 out of 11 *E. coli* were multidrug resistant. A total of 17 cases were ESBL positive, maximum ESBL positivity was observed for *K. pneumoniae* (37.5%). A total of 5 (4.9%) mortalities took place. There were 3 (4%) early onset cases who expired whereas a total of 2 (7.4%) late onset patients also expired. None of the MRSA positive neonates expired. 3 out of 5 MDR neonates expired while 1 out of 17 ESBL positive neonates expired.

References

1. Saving Newborn Lives, The state of the world's newborns: a report from saving Newborn Lives, Washington DC, Save the Children, (2001).
2. Hyder AA, Wali SA, McGuckin J. The burden of disease from neonatal mortality: a review of South Asia and Sub-Saharan Africa, *BJOG*. 2003;110:894-901.
3. Mother-baby package: a road map for implementation in countries, Geneva, World Health Organization (1993).
4. Stoll BJ. Neonatal infections: a global perspective. In: Remington J.S., Klein J.O., eds, Infectious diseases of the fetus and newborn infant, 5th ed. Philadelphia, WB Saunders, 2001;139–68.
5. Stoll BJ. Infections of the neonatal infant. In: Nelson Textbook of Pediatrics, Behrman E.d., Kleigman R.E., RM, Jenson HB. Philadelphia: W.B. Saunders, 17th ed, 2004;623-39.

6. Agnihotri N, Kaistha N, Gupta V. Antimicrobial susceptibility of Isolates from Neonatal sapticemia. *Jpn J Infect Dis*. 2004;57:273-5.
7. Paul VK and Singh MB. Neonatal sepsis. In: Medical emergencies in children. Meharban Singh, 3rd ed, *Sagar publications, New Delhi*. 2000;117-35.
8. Koksal N, Hacimustafaoglu M, Bagci S, Celebi S. Meropenem in neonatal severe infections due to multiresistant gram-negative bacteria, *Indian J Pediatr*. 2001;68(1):15-9.
9. Litzow JM, Gill CJ, Mantaring JB, Fox MP, MacLeod WB, Mendoza M, Mendoza S et al. High Frequency of Multidrug-Resistant Gram-Negative Rods in 2 Neonatal Intensive Care Units in the Philippines. *Infect Control Hosp Epidemiol.* 2009;30:543-9.
10. May M, Daley AJ, Donath S. Early onset of meningitis in Australia and New Zealand 1992-2002. *Arch. Dis. Child. Fetal Neonatal*. 2005;90:324-7.
11. Zaidi AK, Huskins WC, Thaver D. Hospital-acquired neonatal infections in developing countries. *Lancet.* 2005;365:1175-88.
12. Mahbobeh NNF, Ahmadshah T, Parasto S, Setareh S, Mehvar A. Study of the bacterial agents in nosocomial and acquired infections based on the blood culture in neonatal intensive care unit of a hospital, northeast of Iran. *Saudi Med J*. 2007;28(5):723-6.
13. Vaidya U, Bhave S, Hegde V, Pandit AN. Neonatal septicemia: A reappraisal with special reference to the use of Cefotaxime. *Indian Pediatrics.* 1991;28:1265-70.
14. Kaistha N, Mehta M, Singla N, Garg R, Chander J. Neonatal septicemia isolates and resistance patterns in a tertiary care hospital of North India. *J Infect Dev Ctries.* 2010;4(1):055-7.
15. Tallur SS, Kasturi AV, Nadgir SD, et al. Clinico-bacteriological study of neonatal septicemia in Hubli. *Indian J Pediatr*. 2000;67:169–74.
16. Karunasekera KA, Pathirana D. A preliminary study on neonatal septicaemia in a tertiary referral hospital paediatric unit. *Ceylon Med J*. 1999;44:81–6.
17. Moreno MT, Vargas S, Poveda R, et al. Neonatal sepsis and meningitis in a developing Latin American country. *Pediatr Infect Dis J.* 1994;13:516–20.
18. Karthikeyan G, Premkumar K. Neonatal sepsis: Staphylococcus aureus as the predominant pathogen. *Indian J Pediatr*. 2001;68:715–7.
19. Lim CT, Thong MK, Parasakthi N, et al. Group B streptococcus: maternal carriage rate and early neonatal septicaemia. *Ann Acad Med Singapore*. 1997;26:421–5.
20. Maramba-Lazarte CC, Bunyi MAC, Gallardo EE, Lim JG, Lobo JY, Aguilar CY. Etiology of neonatal sepsis in five urban hospitals in The Philippines. *PIDSP Journal.* 2011;12(2): 75-21.
21. Aletayeb SMH, Khosravi AD, Dehdashtian B, Kompani F, Mortazavi1 SM, Aramesh MR. Identification of bacterial agents and antimicrobial susceptibility of neonatal sepsis: A 54-month study in a tertiary hospital. *African Journal of Microbiology Research*. 2011;5(5):528-31.
22. Kolár M, Látal T, Cermák P, Bartoníková N, Chmelarová E, Sauer P, et al. Prevalence of ESBL-positive strains of Klebsiella pneumoniae in the Czech Republic and their molecular biology analysis. *Klin Mikrobiol Infekc Lek.* 2005;11(3):92-9.
23. Shayanfar N, Rezaei M, Ahmadi M, Ehsanipour F. Evaluation of Extended Spectrum Betalactamase (ESBL) Positive Strains of Klebsiella pneumoniae and Escherichia coli in Bacterial Cultures. *Iranian Journal of Pathology* 2010;5(1):34-9.

How to cite this article: Haider F, Dar ZP, Gupta A, Yaqoob S, Singh M. Multidrug resistance pattern in bacteriological isolates of neonatal septicemia in NICU of a tertiary care center. Indian J Microbiol Res. 2018;5(3):307-312.