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Bacterial Profile and Antibiogram of Neonatal Sepsis in Nigeria: Literature Review

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ABSTRACT

Bacterial neonatal sepsis is one of the foremost causes of morbidity and mortality in the newborn period. Determining the causative organism and corresponding treatment with sensitive antibiotics remain the standard of care. However, this is not easily achievable in developing and resource-poor settings. This study explored the inter-regional spread of bacterial isolates and the antibiogram of neonatal sepsis in Nigeria to guide the recommendation of effective and empirical use of antibiotics. Review of the published studies on neonatal sepsis in Nigeria addressed between 2009 and 2019 as culled from Google Scholar, Cochrane and PubMed search. A total of eleven studies conducted between 2009 and 2019 were reviewed and sorted geographically into Northern, Western, Eastern and Southern regions of Nigeria. Generally, the isolated bacteria and antibiogram of the studies across the regions were similar. Klebsiella pneumonia (63.6%) and Staphylococcus aureus (63.6%) topped the prevalence table across the regions, followed by Escherichia coli (36.4%) and subsequently the Coagulase Negative Staphylococcus, Streptococcus pneumonia and Pseudomonas aueruginosa which had an equal prevalence of 27.3%. Ciprofloxacin 8+ and Ofloxacin 5+ had the highest sensitivity, followed by Ceftriaxone 4+, Gentamycin 4+ and Meronem 3+. All the organisms tested were resistant to ampicillin. The inter-regional similarity of the bacterial isolates and antibiogram is striking. This finding could be utilized in making an evidence-based decision on the choice of antibiotics in the treatment of neonatal sepsis where a local pattern is challenging to establish.

Keywords: Bacterial profile, Neonatal sepsis, Nigeria

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INTRODUCTION

Newborn period is the most vulnerable period in life due to the relative deficiency of both cellular and humoral immunity compared to older ages.[1] This deficiency puts the newborn at risk of succumbing to certain morbidities, including sepsis. The burden of sepsis in the newborn is high, accounting for 36% and 30-50% of neonatal deaths globally and in the developing countries, respectively.[2–4] Studies in various parts of Nigeria have documented several incidence and prevalence figures. The following figures were documented in the Eastern (29.7%), Northern (32.2%), Western (34%) and Southern (33.1%) parts of the country.[5–8] These figures, however, may represent an underestimation as the diagnosis of neonatal sepsis in these studies was based on positive blood culture isolates. The latter is not commonly

done for all suspected cases of sepsis due to cost. At most of the health care facilities in Nigeria and, indeed, throughout sub-Saharan Africa, diagnostic microbiology laboratories are not readily available, and where they are available, the service is neither free nor affordable. Thus, most septic newborns are treated empirically.[9] It has been stated that as much as one-third of survivors of neonatal sepsis develop neurological sequelae. However, where appropriate measures inclusive of adequate supportive care and rational antimicrobial therapy are applied, the associated morbidities and mortality can be largely prevented.[8] In the current era of indiscriminate use of antibiotics without prescription,[10] emerging multidrug-resistant bacteria with high risk of death from sepsis in the newborn period, it becomes imperative to administer antibiotics in a health facility, based on culture-proven isolate and antibiotic sensitivity at same health facility to achieve treatment goals. Such practice may not be entirely practicable due to the limited opportunity for blood culture in most centers. However, with the current trend of enhanced intra- and inter-regional movement and communication of people (which constitutes the carrier medium of these infective organisms), there could be the similarity of isolated organisms and antibiogram within and between regions. Thus, in centers where local isolation and antibiogram is not available, the antibiotic prescription could be guided by knowledge of the prevalent isolates and sensitivity pattern in the region where the center is located. This study, therefore, sets out to survey the bacteria profile and antibiogram of neonatal sepsis as documented from 2009-2019 at various centers/regions in Nigeria. It is hoped that if there is a similarity of isolates and antibiograms in a region, it will guide empirical treatment for centers that have challenges with pathogen identification and sensitivity tests within that region.

METHOD

This study reviewed various published studies on bacteria neonatal sepsis in Nigeria between 2009 and 2019. The studies reviewed included the studies which showed the isolated bacteria with or without antibiotic sensitivity pattern. Searches were performed using Google Scholar, Cochrane and PubMed search. We searched for manuscripts that incorporated any of the following medical subject-headings in the title or abstract: Nigeria, sepsis, septicaemia, bacteraemia, neonatal, neonate, neonates.

The findings were presented in tabular form to show the author, year of study, study center, isolated bacteria and antibiotic sensitivity and resistant pattern (Table 1). Further analysis to show a representative national prevalence of the bacteria isolates was carried out by collating the number of studies that isolated a particular organism from various regions of the country. This was done by simple additions and expressed as a percentage of the total number of reviewed studies (Table 2). Furthermore, the antibiotic sensitivity and resistance were further analyzed to show the organism-specific (Table 3) and non-organism specific patterns (Table 4). Antibiotic sensitivity per organism per study was indicated by a plus (+) signs and summed to show the number of studies in which a particular antibiotic was sensitive to a particular organism (Table 3). For studies that did not specify antibiotics sensitivity and resistance pattern per organism, the number of reviewed studies which demonstrated sensitivity or resistance to a particular antibiotics were indicated by a plus (+) sign (Table 4).

RESULTS

Of the 11 studies reviewed, 5 (45.4%) were from the Northern, 3 (27.3%) from the West, 2 from the East (18.2%) and only 1 (9.1%) study was accessed from the Southern part of the country. All the studies reviewed were conducted in a teaching hospital. Klebsiella pneumonia (63.6%) and Staphylococcus auerus (63.6%) topped the prevalence table (Table 2), followed by Escherichia coli (36.4%). Coagulase Negative Staphylococcus, Streptococcus pneumonia and Pseudomonas aueruginosa each had an equal prevalence of 27.3% to rank the third most prevalent group. Proteus Spp (18.1%) was the fourth while the least prevalent bacteria were Streptococcus pyogenes, Alpha Haemolytic Streptococcus, Coliforms and Citrobacter, which had an equal prevalence of 9.1% (Tables 1, 2). For studies that specified the antibiotics sensitivity and resistance pattern per organism, Ciprofloxacin 8+ and Ofloxacin 5+ had the highest sensitivity followed by Ceftriaxone 4+, Gentamycin 4+ and Meronem 3+ (Table 3).[12,14,15,17] All the organisms tested were resistant to ampicillin. It is also of interest to note that a particular organism Klebsiella quasipneumoniae subsp. Simili pneumoniae. Strain G4582, G4584, G4593, G4601, and G4612 isolated at the University of Abuja Teaching Hospital, Gwagwalada, central Nigeria was resistant to all the tested antibiotics, including the Carbapenems, Impenems, Meropenem and Ertapenems.[11] For studies that did not specify antibioitics sensitivity and resistance pattern per organism, Ciprofloxacin 4+ was still among the most sensitive drug followed by Ceftriaxone 2+, Chloramphenicol 2+ and Cefuroxime 2+ (Table 4).[11,13,16,18]

DISCUSSION

The similarity of bacterial isolates across all the studies harvested from different regions of the country is striking. Klebsiella and Staphylococcus species were isolated in more than 60% of the studies involving five of the six geo-

Table 1. Regional distribution of the bacterial neonatal sepsis and antibiogram in Nigeria

Region (number of studies)	Author (s)/year	Study center (s)	Isolated bacteria	Sensitive antibiotics	Resistant antibiotics
NORTH (5)	Brinkac et al.,[9] 2016	University of Abuja Teaching Hospital, Gwagwalada, Central Nigeria	Klebsiellaquasipneumoniae subsp. Similipneumoniae. Strain G4582, G4584, G4593, G4601, and G4612	None	Carbapenems Imipenem, Meropenem, and Ertapenem
	Medugu et al.[12] 2014	National Hospital Abuja, Kubwa General Hospital, Garki General Hospital and Wuse General Hospital in Abuja, Nigeria	Group B Streptococcus (GBS)	Penicillin, Ceftriaxone and Vancomycin	Clindamycin, Erythromycin and Ofloxacin was observed in 24 (25.3%), 13 (13.7%) and 6 (6.3%)of the colonized neonates
	Onyedibe et al.[15] 2011	Jos University Teaching Hospital	Klebsiella pneumoniae Staphylococcus aureus Escherichia coli Coagulase Negative Staphylococci Citrobacter spp	Klebsiella pneumonia sensitive to meropenem 83%, Ciprofloxacin 67%, Chloramphenicol 54%. Staphylococcus aureus sensitive to Cefotaxime 94%, Cefepine and Gentamycin 87%, Ceftriaxone and Ciprofloxacin 83% Escherichia coli sensitive to Meropenem 100%, Ciprofloxacin and Gentamycin 75%, Cefepime and Augumentin 50%	Klebsiella pneumonia resistant to; Ampicillin 96%, Augumentin 87%, ceftriaxone 79%. Staphylococcus aureus resistant to ampicillin 61%, oxacillin 55%, penicillin 65%. Escherichia coli resisitant to Ampicillin and Oxacillin 75%, Ceftriaxone and Cefoxitin 63%, Cefotaxime 57%
	Okon et al.[16] 2009	University of Maiduguri Teaching Hospital	Staphylococcus aureus (39%), klebsiella spp (15%), Escherichia coli 6%	Ofloxacin Ciprofloxacin Chloramphenicol	Ampicillin –Cloxacillin, Cotrimoxazole Augumentin
	Medugu and Iregbu[17] 2013	National Hospital Abuja	Staphylococcus aureus (59.3%)' klebsiella pneumonia (11.1%), Pseudomonas aeruginosa (8.6%)	Staphylococcus aureus (Amoxicillin Clavulanate 76%, Cefuroxime 0%, Ciprofloxacin 67%, Erythromycin 30%, Gentamycin 29%, Ceftriaxone 27%). Klebsiella pneumonia (Imipenem 75%, Ceftazidime 0%, Floroquinolones 63%, Ceftriaxone 66%	Staphylococcus (Cefuroxime), Klebsiella pneumonia (ceftazidime)
WEST (3)	Shobowale et al.[11] 2014	Babcock University Teaching Hospital, Ilishan-Remo, Ogun	Coagulase-negative staphylococci, Staphylococcus aureus,	Meropenem (94.1%); Ciprofloxacin (77.4), Clindamycin (73.3%) Amikacin (68.9%).	

Table 1. CONT.

Region (number of studies)	Author (s)/year	Study center (s)	Isolated bacteria	Sensitive antibiotics	Resistant antibiotics
		State, Nigeria	and Klebsiella pneumoniae	Piperacillin-Tazobactam and Cefepime (66.7%) co-Amoxiclav (53.9%) Cefuroxime (58.3%), Ceftazidime (50%), Ampicillin-sulbactam (12.5%)	
	Olatunde et al.[13] 2009	Wesley Guild Hospital (WGH), Ilesa, Osun State, Southwest Nigeria. The WGH is a unit of the Obafemi Awolowo University Teaching Hospital, Ile Ife, located in Ilesa, the largest town in Ijesaland	The most prevalent organism was staphylococcus aureus (70.7%).Klebsiellaspp, alpha haemolytic streptococci and pseudomonas were isolated in 11.1%, 8.3% and 6.9%, respectively. E.coli was isolated in 2.8% while proteusspp was isolated in	Ciprofloxacin (86.7%), Cefuroxime (82.7%) and Ceftriaxone (81.3%) were the antibiotics with the highest sensitivity	Cloxacillin (80%) and Ampicillin (77.3%).
	Shobowale et al.[7] 2016	Lagos University Teaching Hospital Idiaraba	1.4% Klebsiella pneumonia, Staphylococcus aerus, Coagulase negative staphylococci	-	-
EAST (2)	Ekwochi et al.[5] 2012	Special Care Baby Unit ESUTH, Enugu	Staphylococcus aureus (53%) out Streptococcus pneumonia, 18%), Escherichia coli18%)	-	-
	Ekwochi et al.[18] 2016	Special Care Baby Unit ESUTH, Enugu	Coliforms 63.2%, staphylococcus spp 24.6% Streptococcus spp 0.1%	Floroquinolones Ceftriaxone Chloramphenicol Gentamycin	Amoxicillin, Clindamycin Cefixime
SOUTH (1)	Peterside et al.[14] 2013	Niger Delta University Teaching Hospital Bayelsa State	Staphylococcus aureus (51.5) Escherichia coli 16.5 Klebsiella pneumonia 14.1 Proteus mirabilis 8.2 Pseudomonas aeruginosa (7.2)	Escherichia coli demonstrated the highest sensitivity to both gatifloxacin and ofloxacin followed by pefloxacin and ciprofloxacin. Klebsiellapnuemoniae	

Table 1. CONT.

Region (number of studies)	Author (s)/year	Study center (s)	Isolated bacteria	Sensitive antibiotics	Resistant antibiotics
			Streptococcus pyogenes (2.1)	demonstrated the highest sensitivity to ofloxacin followed by ciprofloxacin and both gatifloxacin and pefloxacin. It was highly resistant to cefixime. Proteus mirabilis demonstrated the highest sensitivity to ciprofloxacin followed by ofloxacin. Pseudomonas aeruginosa also demonstrated the highest sensitivity to ciprofloxacin (100.0%) followed by ofloxacin. Klebsiella pneumoniae and Pseudomonas aeruginosa showed poor sensitivity to gentamici.	

Table 2. Prevalence of the isolated bacteria

Region (Total number of studies)	# of studies isolating the organisms	Kleb.	Staph.	CONS	E. coli	GBS	Strep. pn	Pseud	Proteus spp	Strep pyo	AHS	Coliforms	Citrobacter
Northern region (5)		3	1	1	1	1	1	1	-	-	-	-	1
Southern region (1)		1	1	-	1	-	-	1	1	1	-	-	-
Western region (3)		3	3	2	1	-	-	1	1	-	1	-	-
Eastern region (2)		-	2	-	1	-	2	-	-	-	-	1	-
Nigeria (11), n (%)	Total studies	7 (63.6)	7 (63.6)	3 (27.3)	4 (36.4)	1 (9.1)	3 (27.3)	3 (27.3)	2 (18.1)	1 (9.1)	1 (9.1)	1 (9.1)	1 (9.1)

Kleb: Klebsiella pneumonia; Staph: Staphylococcus auerus; CONS: Coagulase Negative Staphylococci; E.coli: Escherichia coli; GBS: Group B Streptococcus; Strep. pn: Streptococcus pneumonia; Pseud: Pseudomonas aeruginosa; Proteus spp: Proteus mirabilis; Strep pyo: Streptococcus pyogenes; AHS: Alpha Haemolytic Streptococcus.

Table 3. The antibiotics sensitivity and resistance pattern (organism-specific)

Bacteria	Antibiotic sensitivity and resistance pattern														
	Cefix	Ceftaz	Cefox	Agum	Genta	Cefepin	Van	Chlr	Mero	Cefo	Ceftri	Cipro	Clind	Oflox	Eryth	Ampi
Kleb		-		-	-			+	++		-+	+++		++		-
Staph				+	++	+				+	++	++		-	+	-
CONS																
E.Coli			-	+	+	+			+			++		+-		-
Strep. Pn																
GBS					+		+						-	-	-	
KlebQuassi	-		-		-	-	-	-	-	-	-	-	-	-	-	-
Proteus		-		-							+			+		
Pseud.												+		+		
Aggregate.					4+				3+		4+	8+		5+		

Kleb: Klebsiella pneumonia; Staph: Staphylococcus auerus; CONS: Coagulase Negative Staphylococci; E.coli: Escherichia coli; GBS: Group B Streptococcus; KlebQuassi: Klebsiella quasip neumoniae subsp. Similipneumoniae. Strain G4582, G4584, Strep. Pn: Streptococcus pneumonia; Pseud: Pseudomonas aeruginosa; Proteus: Proteus mirabilis; (Sensitivity +, resistance -)

Table 4. The antibiotics sensitivity and resistance pattern (non-organism specific)

Antibiotics	Sensitivity	Resistance
Ofloxacin	+	
Ciprofloxacin	++++	
Chloramphenicol	++	
Meronem	+	
Clindamycin	+	+
Amikacin	+	
Cefixime	+	+
Piperacillin-Tozabactam	+	
Cefepine	+	
Amoxiclav	+	
Cefuroxime	++	
Ampicillin- sulbactam	+	+
Ceftriaxone	++	
Gentamycin	+	
Ampicillin-Cloxacillin		+
Amoxicillin		+

Number of +, connotes the number of studies that documented Sensitivity or Resistance.

political zones of Nigeria. The finding is similar to what was obtained in a review in South Africa in 2017.[19]

The high prevalence of these organisms is not unexpected given the ubiquitous nature of those bacterial organisms and their common occurrence in women's reproductive tracts from which the neonates could have been infected. Noteworthy is the changing pattern of bacterial isolates responsible for neonatal sepsis over time. Some decades ago, gram-negative organisms closely trailed by group B Streptococcus (which is a gram positive coccus) was the predominant pathogen.[20,21] However, this work has shown a shift towards Staphylococcus aureus, which is a gram positive organism. The reason might be related to improved hygiene and toilet practices, which now limit ascending infection from mothers' anus to the vaginal tract. Most of the gram-negative coliforms are part of the flora in the colon of humans, and therefore, almost always present in the stool. With improved health education and genital hygiene, the impact of these stool pathogens may be waned. Staphylococcus aureus is usually not part of the normal colon flora and therefore is not affected by this practice hence the possible shift in observed neonatal sepsis etiopathogen. However, this unfavourable skew to staphylococcal organism calls for a review and improvement of certain practices in nurseries that are known to enhance the dissemination of this organism. Such practices include hand washing, use of separate nursery wears (scrubs) and adequate skin care. It

could also call for the need to improve the general hygiene practices in the nurseries, such as cleaning of surfaces, instruments and appliances, including a general need to provide efficient running water in the nurseries.

The changing pattern of antibiotic sensitivity is equally unsurprisingly similar across the regions. Unlike what obtained decades back, ciprofloxacin, a fluoroquinolone, has demonstrated the greatest sensitivity to the cultured organisms. Earlier first-line drugs like the penicillin are becoming increasingly less effective and efficacious in treating neonatal sepsis nowadays. Again, this is unsurprising given that most of the penicillin is now over the counter medications which have been considerably abused by mothers for treating even unrelated ailments in their newborns. Ciprofloxacin, even though equally an over the counter antibiotic in Nigeria has relatively been spared of that level of abuse because of the longstanding but largely unfounded fear that it was unsafe for neonates. The organisms equally showed substantial sensitivity to meropenems, which is not unexpected owing to its hitherto low use and abuse as a result of its relative scarcity and high cost in the Nigerian environment. The relative efficacy of the fluoroquinolones shown in these studies may, however, the pave way to overuse and abuse of this class of drug, which is largely reserved as second-line anti-tuberculosis drug. Therefore, newborn health practitioners should be mindful of this and resort to its use only in cases where there is no available efficacious substitute.

The emergence of resistant organisms, including organisms that cause neonatal sepsis, is now a global challenge.[19] It is both instructive and unsettling that this review showed evidence of increasing resistance to what used to be the antibiogram staples. It is, therefore, very important that we keep tracking these changes in neonatal sepsis pathogen and their corresponding sensitivity spectrum in other to stay ahead one of the greatest killers of our neonates.

CONCLUSION

There is observed remarkable interregional similarity of the bacterial isolates and antibiogram. This finding could be utilized in making an evidence-based decision on the choice of antibiotics in the treatment of neonatal sepsis where a local pattern could not be established. We, however, recommend further studies and reviews in this crucial field in view of the current global challenge of emerging resistant bacterial strains.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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