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ORIGINAL RESEARCH

Conjunctival bacterial infection among hospitalized neonates

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Abstract

Background: Conjunctivitis is a common infection among neonates and it is a known cause of preventable childhood blindness. There is geographical variation in the distribution of aetiological agents.

Objective: To assess the prevalence of conjunctivitis among hospitalized neonates receiving care in a tertiary health care centre in South-west Nigeria, and describe its clinical and bacteriological correlates.

Methods: The hospital records of neonates diagnosed with conjunctivitis at the Olabisi Onabanjo University Teaching Hospital, Sagamu between January 2015 and December 2019 were reviewed. Their bio-data, perinatal history, laboratory results and treatment received were extracted for analysis.

Results: One hundred and twenty-two neonates had conjunctivitis out of a total number of 2,286 admissions, giving a prevalence rate of 5.3%. Male infants had almost double the risk of developing the disease compared to female infants (OR = 1.6; 95% CI: 1.09-2.35). Eighty-six (70.5%) babies were term, while 21 (17.2%) and 15 (12.3%) were preterm and small-for-gestational-age respectively. Most cases of neonatal conjunctivitis (82.0%) occurred in the first week of life while the mean $\pm$ SD age of onset was 5.3 ± 4.5 days. *Staphylococcus aureus* and *Klebsiella* species were the commonest bacterial isolates affecting 57.1% and 23.0% neonates respectively. Moderately-high rates of resistance to erythromycin and gentamicin were observed among the bacterial isolates.

Conclusion: Neonatal conjunctivitis is commonly due to *Staphylococcus aureus* and *Klebsiella* species in this setting. It is commoner among male infants. Most cases run a mild course with good response to topical antimicrobial therapy.

Keywords: Conjunctivitis, Eye discharge, Neonates, Ophthalmia neonatorum.

Introduction

Neonatal conjunctivitis, also known as ophthalmia neonatorum, is the most common ocular disease in the first month of life. [1] It is characterized by mucopurulent eye discharge with or without conjunctival redness and eyelid oedema. Its incidence

ranges widely across the world, from 0.9% to 33%. [2] In Nigeria, there appears to be a paucity of information on the burden of the disease. However, incidence rates of 1.1% among hospitalized neonates and 4.7/1000 live births have been reported. [3, 4] Depending on the severity, the infection is potentially hazardous as it can lead to varying degrees of ocular and systemic

complications such as dacryocystitis, orbital abscess, corneal ulceration and corneal scarring with attendant visual impairment as well as neonatal sepsis. [1,5-7] Indeed, neonatal conjunctivitis has been identified as a major cause of preventable childhood blindness in developing countries of Asia and Africa. [8, 9]

The causative organisms are usually acquired from the genital tract of mothers. [1] Others are postnatally acquired from the hospital or the community. [10] Among the most frequently reported causative pathogens are coagulase-negative *Staphylococcus*, coliforms, pneumococcus, *Staphylococcus aureus* and enterococci which tend to cause mild to moderate disease. [5, 10-12] Apart from bacterial pathogens, respiratory viruses such as rhinovirus, adenovirus and bocavirus have also been implicated as causative agents of mild conjunctivitis among neonates. [13] Furthermore, no potential pathogens were isolated in some cases. [14] *Pseudomonas aeruginosa*, *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are associated with more severe conjunctival infections. [6, 7, 15] Whereas chlamydial and gonococcal conjunctivitis has become a rarity in the developed countries of Europe and North America, both are still common in many countries of the developing world. [7, 12-14, 16]

One of the targets of the VISION 2020 program of the World Health Organization for the control of blindness is to eliminate corneal scarring caused by ophthalmia neonatorum and other preventable childhood diseases such as vitamin A deficiency and measles. [17] Towards this end, there must be a prompt and effective treatment of these conditions to prevent complications and optimize visual development. To be able to do this, causative organisms of conjunctival infection among neonates in each region must be mapped out from time to time. Secondly, in this era of increasing bacterial resistance to common antibiotics, there should be regular

surveillance of the sensitivity pattern of offending microorganisms. Furthermore, the paucity of information on various aspects of the condition in our environment needs to be addressed. In the light of these conditions, this study was embarked upon to determine the prevalence of the infection in a tertiary health care facility in South-west Nigeria, identifying the causative organisms and determining the best form of antimicrobial treatment for the infection.

Methods

This retrospective descriptive study covered five years from January 2015 to December 2019. It was conducted at a tertiary care centre in Sagamu, a semi-urban town in the south-western part of Nigeria. The Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu provides tertiary health care services to the people of Ogun State and some parts of neighbouring states of Lagos, Oyo and Ondo. The hospital has a neonatal ward (NNW) where all sick infants in their first month of life are admitted for level II specialized neonatal care and management. There were no protocols in place for the prevention of ophthalmia in the hospital during the period of the study.

In the NNW, babies with eye discharge would normally have their eyes examined and eye swabs were taken for Gram staining, bacterial culture and sensitivity test at the Microbiology Laboratory. Such specimens were processed at the laboratory using standard bacteriological procedures and results obtained after 48 hours. The initial treatment would consist of saline irrigation and instillation of chloramphenicol eye drops at 4-6 hourly intervals for between five and seven days. Treatment would be reviewed after 48 hours based on the result of eye swab microscopy, culture and sensitivity. The duration of treatment was guided by a

complete clinical resolution of all ocular symptoms.

All babies within the first 28 days of life with documented eye discharges while on admission in NNW during the study period, irrespective of their primary diagnosis, were included in the study. The hospital records of the selected babies were reviewed and their bio-data, type of eye involvement (unilateral or bilateral), primary diagnosis, perinatal history, treatment given as well as the results of laboratory studies were extracted and analyzed. Similarly, the results of eye swab microscopy, bacterial culture and sensitivity were collated and analyzed. Ethical approval for the study was obtained from the Health Research Ethics Committee of the Olabisi Onabanjo University Teaching Hospital, Sagamu.

Data analysis was conducted with the aid of SPSS version 24 software using descriptive statistics such as mean, standard deviation, frequencies and percentages. The differences between proportions were compared using Chi-Square test, contingency tables and Odd ratio (OR) with 95% Confidence Interval (95%CI). *P* values less than 0.05 and CI excluding unity were considered to be statistically significant.

Results

During the period of study, the total number of admissions into the Neonatal Ward of the hospital was 2,286 with 1,277 males and 1,009 females giving a male-to-female ratio of 1: 0.8. Eighty-one males (6.3%) and 41 females (4.1%) had conjunctivitis amounting to a male-to-female ratio of 1: 0.5. This constitutes an overall prevalence rate of 5.3% for neonatal conjunctivitis among the hospitalized neonates. The difference

between the proportions of affected males and females was statistically significant (81/1277 vs 41/1009; OR = 1.6, 95% CI: 1.09 - 2.35).

The mean $\pm$ SD weight of the neonates was 2.8 ± 0.7 kg. There were 58 (47.5%) in-born and 64 (52.5%) out-born babies. Table I presents other socio-demographic and clinical characteristics of affected babies. Out of a total number of 122, 86 (70.5%) babies were term (gestational age greater than 37 completed weeks), while 21 (17.2%) and 15 (12.3%) were preterm (gestational age less than 37 weeks) and small-for-gestational-age (term babies with birth weight less than 2.5kg) respectively. None of the babies was post-term (gestational age greater than 42 weeks).

Eye involvement was unilateral in 54 (44.3%) babies and bilateral in 68 (55.7%) babies. The mode of delivery was documented in 64 cases; the majority of the neonates (62.5%) were products of spontaneous vaginal delivery. Most cases of neonatal conjunctivitis (82.0%) occurred in the first week of life while 23 (18.9%) presented within 24 hours of life. The mean age of onset was 5.3 ± 4.5 days.

In terms of their primary diagnoses, 47 (38.5%), 39 (32.0%), 18 (14.8%) and 6 (4.9%) of the neonates were admitted on account of neonatal jaundice, perinatal asphyxia, neonatal sepsis and hypoglycaemia respectively. The remaining 12 (9.8%) babies had miscellaneous diagnoses including congenital malformations, birth trauma, and anaemia. A positive history of prolonged rupture of foetal membranes (> 18 hours) was documented in 16 (13.1%) babies.

Table I: Socio-demographic and clinical characteristics of affected neonates

Parameter		Frequency	Percentage
Gender	Male	81	66.4
	Female	41	33.6
Mode of delivery*	SVD	40	62.5
	Caesarean section	23	35.9
	Vacuum	1	1.6
Gestational category	Preterm	21	17.2
	Term	86	70.5
	Post-term	0	0.0
Onset of conjunctivitis	SGA	15	12.3
	First week	100	82.0
	Second week	12	9.8
	Third week	6	4.9
	Fourth week	4	3.3

*Total number of documented modes of deliveries= 64;

SVD - Spontaneous Vaginal Delivery; SGA - Small for Gestational Age

Staphylococcus aureus was the commonest bacterial isolate (72; 57.1%), followed distantly by *Klebsiella* species (29; 23.0%). Four patients (3.2%), all female, had a mixed growth of *Staphylococcus aureus* and *Klebsiella* species while there was no growth in 16 (12.7%) cases. *Escherichia coli* was detected in 4% of the cases. Other bacterial isolates are as shown in Table II. Three (18.8%) of the 16

neonates with no bacterial growth in the eye swabs presented within the first 24 hours of life. There were no statistically significant differences in the distribution of bacterial isolates on the basis of gender ($\chi^2 = 4.808$; $p = 0.569$), mode of delivery ($\chi^2 = 3.866$; $p = 0.566$) and time of onset of the condition ($\chi^2 = 20.195$; $p = 0.322$).

Table II: Distribution of bacterial isolates

Isolate	Frequency	Percentage
<i>Staphylococcus aureus</i>	72	57.1
<i>Klebsiella</i>	29	23.0
<i>Escherichia coli</i>	5	4.0
<i>Pseudomonas</i>	2	1.6
<i>Proteus</i>	1	0.8
α -Haemolytic <i>Streptococcus</i>	1	0.8
No growth	16	12.7
Total*	126	100

*4 neonates had mixed growth of *Staphylococcus aureus* and *Klebsiella* species.

The antimicrobial sensitivity pattern of the two leading bacterial isolates is presented in Table III. *Staphylococcus aureus* was most sensitive to imipenem, augmentin and cefuroxime at 92.2%, 72.9% and 67.9% respectively. Erythromycin (56.6%) was only moderately active against the organism while 43.1% of the isolated *Staphylococcus aureus* were considered to be methicillin-resistant

strains having shown in-vitro resistance to cefoxitin. Even though gentamicin appeared to have good activity against the isolated species of *Staphylococcus aureus* at 60%, the actual number of cases tested was rather too small and may not be representative.

On the other hand, ceftazidime showed the highest in-vitro activity against the isolated

Klebsiella species, having been active against 88.0% of cases, followed by meropenem, augmentin and ceftriaxone with 68.4%, 52.2% and 50.0% sensitivity rates respectively. Although cefoxitin appeared to have very strong activity against the *Klebsiella* species at 100%, the number of isolates tested was too small. All cases of neonatal conjunctivitis resolved without any sequelae following treatment with topical antimicrobials.

Ninety-eight (80.3%) cases responded to chloramphenicol eye drops while 16 (13.1%) and 8 (6.6%) responded to gentamicin and tobramycin eye drops respectively. The mean duration of treatment was 5.5 ± 3.1 days. Additionally, the 18 (14.6%) neonates with underlying neonatal sepsis were treated with parenteral antibiotics for 10 to 14 days following microbiological guidance.

Table III: Antimicrobial susceptibility of the two major isolates

Antimicrobial	Staphylococcus aureus			Klebsiella		
	Sensitive (n)	Resistant (n)	% Sensitivity	Sensitive (n)	Resistant (n)	% Sensitivity
Augmentin	43	23	72.9	12	11	52.2
Imipenem	47	4	92.2	1	1	50.0
Cefuroxime	36	17	67.9	1	1	50.0
Erythromycin	30	23	56.6	2	3	40.0
Ceftazidime	4	5	44.4	22	3	88.0
Amoxycillin	14	23	37.8	0	11	0
Gentamicin	3	2	60.0	11	14	44.0
Ceftriaxone	3	3	50.0	9	9	50.0
Meropenem	2	2	50.0	13	6	68.4

Discussion

The present study observed a prevalence rate of 5.3% of conjunctivitis among hospitalized neonates. This is higher than 1.1% and 4.1% reported by Ochigbo *et al.* from Nigeria and Goel *et al.* from India respectively [3, 18], but lower than the 7.2%, 8.0% and 8.2% observed by other researchers from India, Togo and the United Kingdom respectively. [10, 14, 19] However, it has been pointed out that the incidence of neonatal conjunctivitis tends to vary widely from region to region. [2] This may be attributed to differences in socio-economic development, the geographical distribution of causative pathogens and standard of obstetric and perinatal care.

The observation of a significantly higher prevalence of conjunctivitis among male neonates in the present study is in agreement with earlier reports, [8, 11] thereby suggesting a sex-linked factor in host susceptibility to

infections. [20] In this respect, numerous experimental and clinical studies indicate sex-specific differences in infectious diseases and sepsis. [21-22] Additionally, studies among adults have shown male sex hormones to have a suppressive effect on both humoral and cell-mediated immune responses whereas female sex hormones tend to exhibit protective effects and this may contribute to the natural advantages of females under septic conditions. [22-23] These factors may, however, not apply to the neonate since sex hormones are not known to be active in the newborn period. In the same vein, a male disadvantage hypothesis has been proposed which suggests that male neonates are more sensitive to adverse perinatal and postnatal environmental conditions. [24-26] Further research is required to identify other contributory factors for this phenomenon.

It was also observed in the present study that an overwhelming majority of the cases occurred in the first week of life, the mean

age of onset being five days. This is in agreement with the observation of Verma and co-workers who reported that 91.6% of babies in their series developed conjunctivitis within the first week of life. [10] Similarly, Olatunji and Mohammed *et al.* reported a mean age of onset of neonatal conjunctivitis of 3.9 days and 5.7 days respectively. [8, 27] On the other hand, a Finish study reported a mean age at onset of 20 days which is at variance with the findings in the present study. [13] This discrepancy might have been because the latter study was conducted at children welfare clinics, in which case many neonates with the early-onset disease would have been missed. Nonetheless, the observation suggests the first week of life as the most vulnerable period for conjunctival infection in infants. Therefore, it behoves caregivers and health workers alike, to carefully watch out for the infection to ensure early recognition and prompt treatment.

Concerning bacterial causes of neonatal conjunctivitis, the present study observed that *Staphylococcus aureus* was the leading isolate, lending credence to earlier reports from other parts of Nigeria. Ibhanesebhor and Otobo from Benin, southern Nigeria and Olatunji from Kaduna, northern Nigeria, reported that *Staphylococcus aureus* accounted for 59% and 69.7% of cases in their series respectively. [27-28] Similarly, many studies from other parts of the world, including South Korea, Sweden, United Kingdom, Hong Kong, Togo and India reported *Staphylococcus aureus* as the leading bacterial cause of neonatal conjunctivitis. [5, 10, 14, 16, 19, 29] In contrast, Coagulase-negative *Staphylococcus*, Coliforms, Enterococci and α -haemolytic *Streptococcus* have been reported by other workers as the leading causative agents in neonatal conjunctivitis. [2, 11, 12, 18] These differences in the pattern of isolated organisms from different centres may be a reflection of the socio-economic status, hygiene practices of individuals, and predominant organisms in the newborn

environment, which usually vary from centre to centre. [8]

Two organisms namely, *Neisseria gonorrhoea* and *Chlamydia trachomatis* have been known to cause severe conjunctivitis with associated complications such as panophthalmitis and keratitis leading eventually to poor vision and blindness among neonates in many parts of the world. [7, 12, 16, 30, 31] This prompted the widespread use of Crede's eye prophylaxis with silver nitrate drops but this practice has since become obsolete because of concerns about chemical conjunctivitis and its ineffectiveness against chlamydia. [7] However, the present study did not observe any case of conjunctival infection caused by either of the two organisms among the patients studied. Other studies in recent times have also reported the similar finding of zero or minimal cases of gonococcal and chlamydial conjunctivitis in their respective series. [13-14, 31-32] These observations may suggest reducing the importance of these organisms as causes of neonatal conjunctivitis probably as a result of increased awareness and actual improvement in case management among adults. [8] Another explanation for this may lie in the fact that preventive measures are becoming very effective. These measures involve screening and treating expectant mothers for genital tract colonization by these two organisms as part of comprehensive antenatal care. [30] The use of erythromycin eye ointment, in place of silver nitrate drops, immediately after birth as a means of providing further prophylaxis against the two organisms has also been adopted as part of Essential Newborn Care. [33] It could not be ascertained, however, whether the patients in the present study received any eye prophylaxis at birth as there was no documentation to that effect.

Another finding worthy of note in the present study is the observation that no bacterial growth was identified in about 13%

of cases, in keeping with some earlier observations. [8, 14] Some of these cases might have been due to other micro-organisms like respiratory viruses, particularly rhinovirus and adenovirus, which have been identified in other studies as causative agents of neonatal conjunctivitis. [13] Increasing resistance of *Staphylococcus aureus* to methicillin, macrolides and aminoglycosides has been reported. [27, 29] In this regard, the present study observed 43.1%, 43.4% and 40% resistance of the isolated *Staphylococcus aureus* to cefoxitin, erythromycin and gentamicin respectively. Nevertheless, the organism showed good sensitivity to other common antibiotics such as co-amoxiclav and ceftazidime. In the same vein, the isolated *Klebsiella* species in our series showed high in-vitro resistance to gentamicin, cefuroxime and ceftriaxone in the range of 56%, 50% and 50% respectively. Therefore, there is a need for clinicians to ensure appropriate and judicious use of antibiotics to stem the tide of increasing bacterial resistance.

The present study also observed that systemic antibiotics were not required in the treatment of neonatal conjunctivitis as all the neonates responded to topical antibiotics in the form of chloramphenicol, gentamicin or tobramycin eye drops and ointment. This observation is in agreement with that of Verma and co-workers. [10] Lid hygiene has also been reported to be effective for a clinical cure in some cases. [5] However, chlamydial and gonococcal conjunctivitis must be treated with systemic antibiotics in the form of oral erythromycin for 14 days and single-dose of intramuscular ceftriaxone respectively. [20]

The fact that no attempt was made to use specialized laboratory techniques for the isolation of fastidious organisms like *Chlamydia trachomatis* is a limitation to the present study. Some cases of neonatal conjunctivitis due to these organisms might

have been missed. Secondly, the clinical observation of the efficacy of topical chloramphenicol and tobramycin in the treatment of neonatal conjunctivitis had no laboratory backing. Further research with the use of improved laboratory techniques will help to elucidate these points.

Conclusion

Neonatal conjunctivitis is commonly caused by *Staphylococcus aureus* and *Klebsiella* species. It occurs more commonly among male infants. Even though most cases run a mild course with good response to topical antimicrobial treatment, there is a need to ensure that measures are put in place to prevent severe infections which can lead to complications of visual impairment in affected children.

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Authors' Contributions: OOB conceived and designed the study. OOB, AJO, and AHA collated and analyzed the data. OOB and AHA conducted a literature search and review. OOB drafted the manuscript. All the authors participated in manuscript revision and approved the final version.

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