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Ophthalmia Neonatorum Hospitalizations: Clinical Evaluation and Etiological Factors

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Summary

Ophthalmia neonatorum is one the common neonatal infection, it remains a significant cause of ocular morbidity, blindness and even death in some countries. The organisms causing ophthalmia neonatorum are acquired mainly from the mother's birth canal during delivery and a small percentage of cases are acquired by other ways. it can lead to childhood blindness through corneal ulceration & scarification or can lead to extra ocular site involvement (meningitis, pneumonia, arthritis sepsis). The aim of the study was to assess the clinical profile , risk factors and the bacterial causes of ophthalmia neonatorum among Iraqi neonates in AlNajaf, Iraq. Therefore, we conducted a prospective clinical study on neonates visited our hospital, pediatric department outpatient-Clinic and followed up to assess the management outcome and complications during 2017-2018. We included 100 cases admitted to the neonatal ward after proved diagnosed as having conjunctivitis based on the clinical evaluation. Eye swabs were obtained and cultures were performed. Our findings revealed , 57 positive growth and five group of microorganisms were identified using standard techniques. Klebsiella sp. was the more frequent contributed for (23%), Enterobacter (12%), Staphylococcus aureus (9%), Escherichia coli (7%) and Pseudomonas aeruginosa in (6%) Susceptibility patterns of bacterial isolates to antibiotics were determined. Male sex, normal vaginal delivery, prolong rupture of membrane & age less than one week were identified as risk factors.

Keywords*: Ophthalmia Neonatorum, pathogenesis, bacterial causes, Risk factors*

1 INTRODUCTION

The ophthalmia neonatorum is defined as the conjunctival inflammation that occurs within the first days after birth. This inflammation can present in an acute and purulent form and in a subacute form with mucopurulent discharge and few manifestations. The name ophthalmia neonatorum refers to an entity formerly considered classic in the newborn, who acquired it through the birth canal of mothers infected with gonorrhea. The appearance of the prophylactic method, antibiotic therapy, the lower incidence of venereal diseases and the better knowledge of the entities capable of producing these conditions make it necessary to consider conjunctivitis of the newborn within a broader concept in which they should be included oculogenital diseases, chemical conjunctivitis, bacterial conjunctivitis and herpes simplex of other causes (1–10). Ophthalmia neonatorum also called neonatal conjunctivitis, conjunctivitis of newborn , is the most common neonatal disease worldwide and the main reason for frequent consultation with a variable incidence from 1.6% to 23% of newborns. Its etiology can be chemical or infectious. chemical ophthalmia neonatorum manifests itself in the first 24 to 48 hours of life and is linked to prophylaxis with instillation into the conjunctival sacs of silver nitrate by 1% or other drugs to prevent gonococcal ophthalmia (6,11–15) Silver nitrate used as prophylactic agent since 1880s, and despite the reduction in the concentration of silver nitrate since and saline flushing, 5-10% of neonates will develop chemical conjunctivitis (7,8,11) For many years, infectious ophthalmia neonatorum has been considered a major problem of health due to the serious consequences that can determine with variable compromise of vision, including blindness(10,16). This can be of bacterial or viral etiology. The bacteria are closely related to the frequency of sexually transmitted infections in adults. In recent years, there has been a change in the epidemiological profile, in the pre-prophylaxis era, Neisseria gonorrhoeae was the commonest causative agent, currently, the prevalence of ophthalmia neonatorum for this agent is less than 1% in developed countries and Chlamydia trachomatis is the most frequent agent. However, Neisseria gonorrhoeae continues to be the leading cause of childhood blindness in developing countries In the absence of transmissible infections in pregnant women, the more frequent infectious agents isolated

are Staphylococcus aureus, Haemophilus influenzae, Streptococcus pneumoniae and Streptococcus viridans (2,3,17–19). Viral ophthalmia neonatorum due to adenovirus and especially herpes viruses are rare. Various health policies such as improvements in health gynecological-obstetric controls, control of sexually transmitted infection, routine nitrate prophylaxis 1% silver and improvements in neonatal checkups are determinants of changes in the epidemiological profile of ophthalmia neonatorum(9,20). However, it is possible that the heterogeneous implementation of these actions has not allowed the reduction with the same impact of the prevalence of all ophthalmia neonatorum agents, especially Chlamydia trachomatis infections (8,21). Although the ophthalmia neonatorum by this agent in most cases produces mild and self-limited clinical manifestations, subclinical infection or moderate can persist for years, generating complications and sequelae in untreated neonates (22,23). Since 2016, prophylaxis of ophthalmia neonatorum with 1% silver nitrate in drops. Later the withdrawal from the market of this drug began to recommend erythromycin 0.5% (7,24). As ophthalmia neonatorum can be caused by different agents, therefore, have a variety of clinical manifestations, it must also be recognized that the concept encompasses different means of contamination, ranging from infection through the birth canal to direct contamination by any other way.

Etiology

The newborn is sensitive to different routes of contamination. Of these, probably the most important is the birth canal, where the microorganisms present in the vagina and cervix have easy access to the ocular surface and more significantly and prolonged if it coexists with a premature rupture of the membranes or a prolonged labor and hard.

Epidemiological studies show that in asymptomatic women without a history of vaginal infections, up to five different species of bacteria may exist in the cervix at the time of delivery. It has also been shown that 12% of pregnant women in the first trimester present chlamydia in the endocervix and up to 44% of those infected can give newborn with ocular infection.

Although herpes simplex infections of the cervix are relatively rare when compared with other microorganisms, infection with this virus in the gestation product can lead to a number of important complications, such as severe keratitis, meningitis, and even systemic

viremia Therefore, given the history of a woman with herpetic infection and the risk of infection in the product, cervical herpetic infection is currently accepted as an indication for cesarean section.

The maternal anogenital area is frequently contaminated with gram-negative organisms such as Proteus , Klebsiella , Pseudomonas, and Escherichia coli , which can lead to conjunctival infections in the newborn(15,19,23).

In Iraq, there are no previous national studies that describe the frequency of hospitalizations for ophthalmia neonatorum of infectious cause; Knowing and characterizing this problem, clinical profile, risk factors , causative agents and management options makes it possible to analyze care practices and indirectly the impact of the change incorporated in the prophylaxis of ophthalmia neonatorum. Therefore, we aimed to the clinical profile , risk factors and the bacterial causes of ophthalmia neonatorum among Iraqi neonates in AlNajaf, Iraq

2 | PATIENTS AND METHODS

This study was conducted at AlHakeem General Hospital in Najaf city for 12 months in 2019 included 100 cases who were admitted to the neonatal ward diagnosed as having conjunctivitis based on the presence of purulent discharge from the eyes associated with edema of the conjunctiva, marked hyperemia & lid edema . Previously treated patients or using of antibiotics were excluded from the study. Parents of the neonates gave their consents to participate their neonates in the study and agreed the treatment options.

The fallowing neonatal and maternal data were reported :

Age, sex, residence, date of onset of conjunctivitis , gestational age at delivery (term or preterm), mode of delivery (Normal vaginal delivery or Cesarean section), status of ruptured membrane (Prolonged rupture of membrane (more than 12 hours) or premature), the use of antibiotics within 3days, laboratory findings and culture results of eye swabs.

Samples were collected by swabbing the lower conjunctival surface (with sterile swab), the swab in the container were labeled for the required tests & then transported to the microbiology laboratory of the hospital within less than one hour of collection, on arrival at

laboratory the specimens were registered & then cultured on to pre-labeled oven dried agar plate at 37 C for 24 hours the chocolate plates were incubated under microaerophilic condition or anaerobic environment using CO2 jar after overnight in incubation

Using standard techniques, which included cultural, colonial morphology & biochemical characteristics of these isolates on the media (by using many biochemical reagent such as kliglar iron test, mannitol, indol, ureas) identified the isolates obtained. The antibiotics susceptibility patteren were determined by using disc diffusion test with microorganism cultured onto neutrant media for 24 hours. After completion of all clinical data , laboratory investigations data were entered in a computerized database as a reference and then analyzed using the statistical package for social sciences version 26 where appropriate statistical tests applied according to the type of variables under the assumption of two tailed P. value of 0.05 to be significant. Possible risk factors assessed with odds ratio compared to reference categories. The higher odds ratio value indicated the higher risk (25).

3 | RESULTS

A total of 100 neonates were enrolled in this study, of them 68% age < 8 days, 73% were males, (Table 1). Normal vaginal delivery (NVD) was the more frequent mode of delivery , contributed for 77% compared to 23% cesarean sections . Prolonged rupture of membrane reported in 36%, premature rupture of membrane in 12% (Table 2). Clinical manifestations of neonates with ophthalmia neonatorum are shown in (Table 3); all cases had ophthalmic manifestations, 13 had accompanying respiratory symptoms and 9 had fever, on the other hand, findings of ophthalmological examination revealed purulent eye discharge bilateral in 55 cases and unilateral in 27 cases, Blepharitis in 32 cases (19 bilateral and 13 unilateral) , and conjunctival hyperemia in 11 cases (5 bilateral and 6 unilateral), (Table 4).

The possible risk factors of ophthalmia neonatorum were (in sequence) , vaginal delivery, younger age neonates (< 8 days), male gender neonate, and prolonged/premature rupture of membrane, odds ratio was 2.79, 2.60, 1.42 and 1.23, respectively, (P. value was significant in all these factors <0.05).

Culture of eye swabs yielded growth in 57 (57%) swabs. the identification of isolates is presented in (Table 6). The more frequent microorganism was Klebsiella in 23 cases, followed by 12 Enterobacter, 9 Staph. Aureus , 7 E. coli, 6 Pseudomonas. Furthermore, sensitivity of these microorganisms to antibiotics varied according to their types, results of sensitivity of these microorganisms to different antibiotics are demonstrated in (Figures 1 – 5).

Table 1. Age and sex distribution of neonates with conjunctivitis

Variable		No.	%
Age (days)	< 8	68	68.0
	8 - 28	32	32.0
Sex	Male	73	73.0
	Female	27	27.0

Table 2. Obstetrical profile of mothers of the studied neonates

Variable		No.	%
Mode of delivery	NVD	77	77.0
	Cesarean section	23	23.0
rupture of membrane	Prolong	36	36.0
	Premature	12	12.0
	Normal	52	52.0

NVD: Normal vaginal delivery

Table 3. Clinical manifestations of neonates with Ophthalmia Neonatorum

Manifestation	No.	%
Accompanying Respiratory symptoms	13	13
Fever	9	9
Ophthalmic manifestations	100	100.0

Table 4. Findings of ophthalmological examination

Finding	Bilateral		Unilateral		Total
	No.	%	No.	%	
Purulent eye discharge	55	55.0	27	27.0	82
Blepharitis	19	19.0	13	13.0	32
Conjunctival hyperemia	5	5.0	6	6.0	11

Table 5. Odds ratio estimates for significant risk factors of Ophthalmia Neonatorum

Risk factor	Odds ratio (OR)	95% C.I. for OR	P. value*
NVD	2.79	1.62 – 6.55	0.001
Age < 8 days	2.60	1.39 – 4.52	0.002
Male gender	1.42	1.24 – 1.63	0.018
Prolonged/Premature rupture of membrane	1.23	1.11 – 2.24	0.031

P. value is significant in all factors

Table 6. Isolated etiological microorganism

Microorganism	No.	%
Klebsiella	23	23.0
Enterobacter	12	12.0
Staph. Aureus	9	9.0
E. coli	7	7.0
Pseudomonas	6	6.0
No growth	43	43.0
Total	100	100.0

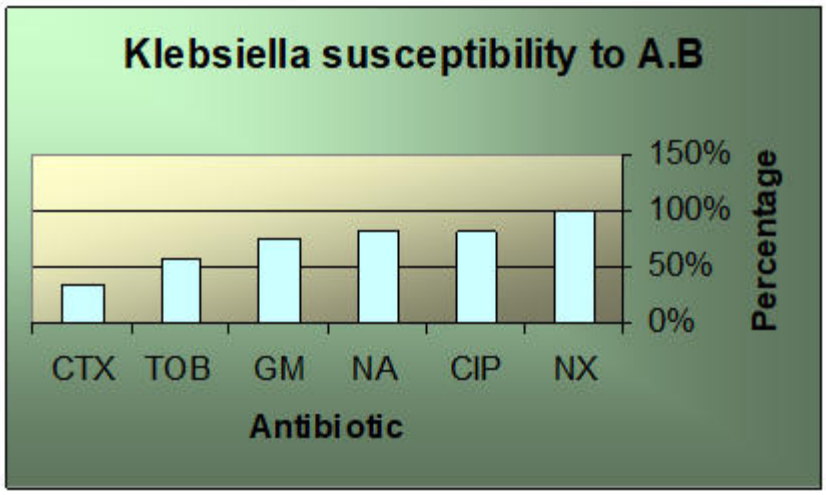

Figure 1. Susceptibility of Klebsiella to antibiotics

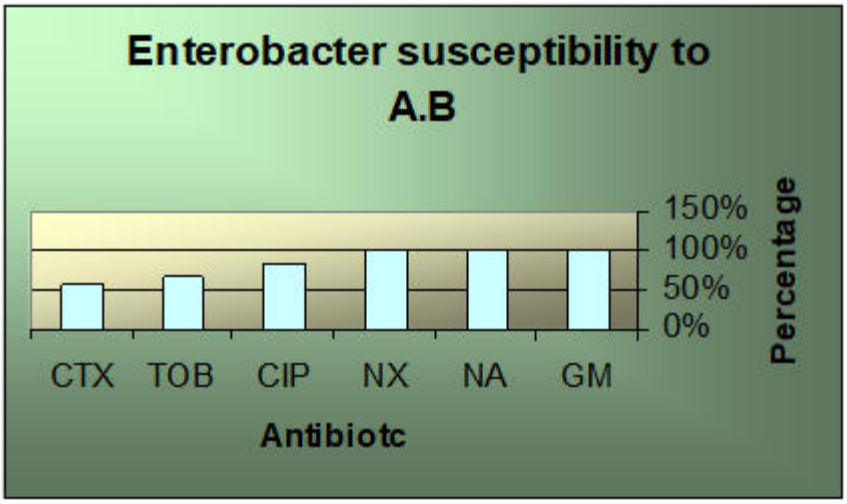

Figure 2. Susceptibility of Enterobacter to antibiotics

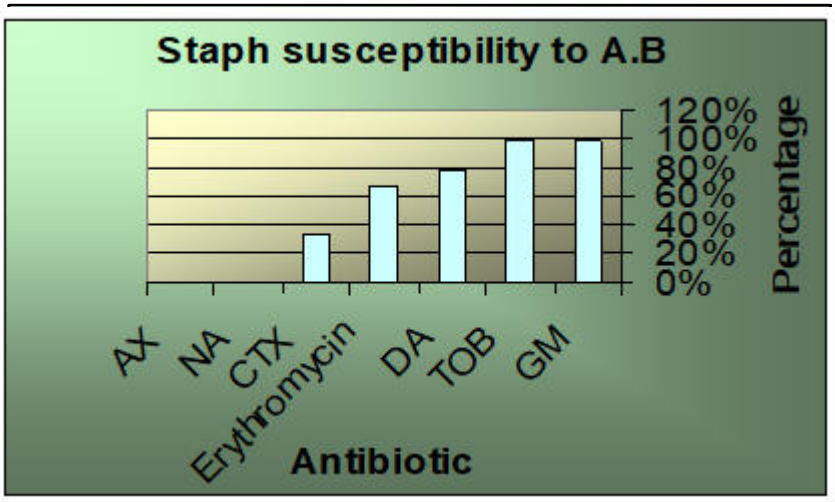

Figure 3. Susceptibility of Staphylococcus aureus to antibiotics

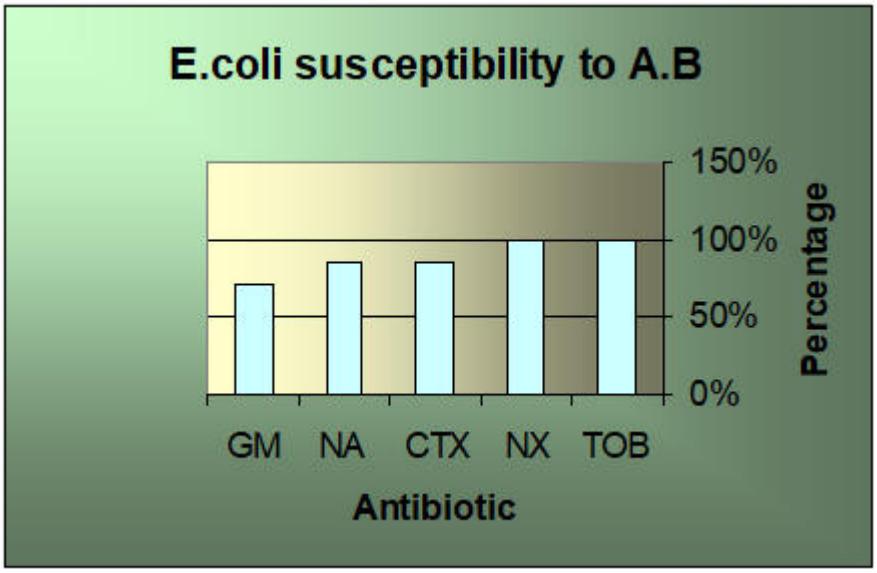

Figure 4. Susceptibility of E. coli to antibiotics

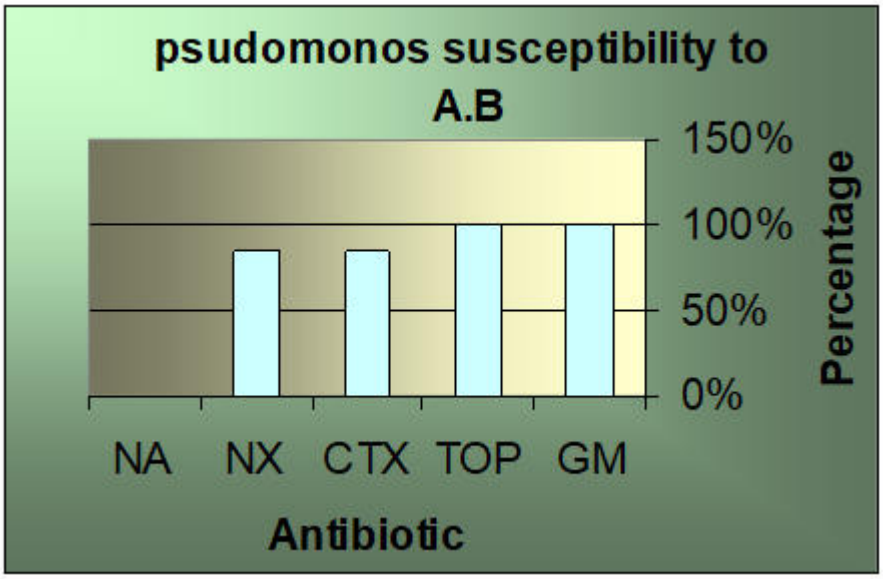

Figure 5. Susceptibility of Psudomonos to antibiotics

4 DISCUSSION

Most newborns began with symptoms of conjunctivitis in the second week of life. The predominant clinical manifestations were exclusive ocular involvement with bilateral involvement, motivating early consultation. Similar data were previously reported in the international literature. Other risk factors for ophthalmia neonatorum are postulated, in addition to prematurity and low birth weight, such as maternal vaginal sepsis, premature and prolonged rupture of ovular membranes, culmination of vaginal delivery. In this series, due to the retrospective design and the lack of data in the clinical records, it was not possible to obtain reliable data on all these variables. It is important to design prospective studies where these risk factors are investigated (2,4,26).

The cornea is generally not involved. Occasionally, observe pseudo membrane formation. With treatment adequate, healing usually occurs without sequelae, Untreated or improperly treated infection can persist for two to 12 months, and some cases fit asymptomatic Persistent infection can lead to formation of conjunctival scars and corneal abscesses. The bibliography refers to this complication as late in cases without treatment or inadequate treatment (27).

Many developed countries have abandoned ocular prophylaxis and have focused actions on prevention, detection and timely treatment of transmitted infections sexual intercourse in pregnant women and their partners (7,8,11,24).

We observed that normal vaginal delivery was the higher risk factor (OR; 2.7) indicated that neonates delivered by NVD were about 2.7 folds more likely to have conjunctivitis compared to those delivered by cesarean sections, these findings agreed that reported in 2011 by Wadhwani et al. (28) and in 2016 by Pak et al. (29). We also found that neonates aged < 8 days, male sex, , prolong or premature rupture of membrane, are risk factors. Our findings supported by the findings of other studies, however, some variation in the sequences of these risk factors are widely postulated in different studies (1,2,4,5,12,15,30,31). Moreover, earlier study conducted by Yetman et al. (32) found that premature rupture of membranes, documented or suspected sexually transmitted disease and local eye injury during delivery were identified as risk factors for ophthalmia neonatorum to occur. Most ophthalmic infections in the neonatal period are acquired during vaginal delivery and reflect the sexually transmitted diseases prevalent in the

community

Regarding the male to female ratio which is about 3:1, this finding go with theory that said male sex is more liable for infection (33). A neonate of age less than one week is more prone to infection, not only because there are low level of antibacterial agent & protein like lysozyme & immunoglobulin A&G but because the tear film and flow are only just beginning to develop Ascending infection play important role in prolonged rupture of membrane (12,15,34)

Our study showed that several organisms were isolated from the eye swabs of neonates with conjunctivitis. Klebsiella sp. predominated as a cause of ophthalmia neonatorum. Enterobacter, Staphylococcus aureus, E. coli & Pseudomonas aeruginosa, followed this. Chlamydia trachomatis, Neisseria gonorrhoeae was not isolated because of some tachnical difficulties . This finding is differed from the results of Nsanze et al. (35) who reported that Staphylococcus aureus was the commonest causative agent of ophthalmia neonatorum followed by Escherichia coli, Pseudomonas aeruginosa, while Chlamydia trachomatis and Neisseria gonorrhoeae were responsible for less than 5% of all cases. This study also differed from that of Yetman et al. (32) who found Chlamydia trachomatis most prevalent. In Mani et al. study (36) Haemophilus influenzae, Streptococcus pneumoniae and Pseudomonas aeruginosa were at one point or the other found as the prevalent bacterial pathogens in ophthalmia neonatorum. This discrepancy may be explained by different endemicity of our country to different types of infectious bacteria, also to nosocomial infection with high resistant bacteria especially klebsilla .

However, futures studies will be necessary to evaluate the impact of said modification. Changes in the epidemiology of infectious ophthalmia neonatorum have led to its approach and treatment not currently represent an urgency, since it is about usually mild clinical manifestations without complications. When suspicion of infection, without treatment serious complications can occur and sequelae such as perforation of the cornea and blindness. There are some clinical manifestations that can contribute to the etiological diagnostic orientation. Anyway, since in most cases symptoms and signs are nonspecific, it is necessary in patients with symptoms suggestive of ophthalmia neonatorum request bacteriological study.

5 CONCLUSIONS

Ophthalmia neonatorum still common neonatal problem in our population, with no specific clinical manifestations that confirm the causative agent, Vaginal delivery, younger neonatal age, male sex and prolonged or premature ruptured membrane are significant risk factors for development of disease. Kebsilla sp. microorganism was the more frequent isolated microorganism causing ophthalmia neonatorum and it may be as nosocomial infection with high resistance to antibiotic. Other bacterial causes cannot be isolated in our lab because of technical difficulties in addition to nonbacterial causes like viral & chemical. Further studies are required for further assessment and evaluation

Ethical Issue:

All ethical issues were approved by the author, in accordance with Ethical Principles of Declaration of Helsinki of the world Medical Association, 2013, for research involving human subjects

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