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AN EPIDEMIOLOGICAL AND CLINICAL STUDY OF EYE INFECTIONS IN NEWBORNS IN KARACHI, SINDH, PAKISTAN

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Abstract

Introduction: Newborns can acquire potentially pathogenic microorganisms at birth which can lead to infections among neonates. This study aimed to determine the carriage of pathogenic bacteria at birth and the development of eye infections during the early neonatal period.

Methods: Women admitted to the obstetric ward of two tertiary care hospitals in Karachi were enrolled. Eye swabs of newborns were taken immediately after birth and examined for the presence of bacteria. Neonates were examined on day seven to determine the incidence of eye infections. Data were analyzed using SPSS and SAS soft wares. Risk ratios (RR) and hazard ratios (HR) with 95% confidence interval (CI) were calculated through Cox regression and Weibul regression analysis.

Results: A total of 205 women and newborns were recruited into the study. About 34% (95% CI: 27.48-40.52%) of eye swabs were positive for bacteria. Escherichia coli and Staphylococcus species were the most common bacteria. The incidence of eye infections was 20% (95% CI: 14.53-25.47%). The number of vaginal examinations during labor (HR=1.22; 95%CI: 1.02-1.46), presence of bacteria in the eye swab sample taken at birth (HR=2.89; 95% CI: 1.10-7.61), and less than four antenatal visits during pregnancy (HR=5.31 95% CI: 1.37-20.49), were associated with the development of eye infections.

Conclusion: More than one-third of newborns had positive eye swab samples and one-fifth developed eye infections during the first week. Appropriate counseling towards personal hygiene during antenatal visits may help in reducing ascending infections, thus preventing infections in neonates.

Keywords: Newborn, Eye infections, Eye swab, Pediatrics, Obstetrics, Karachi, Pakistan.

Introduction

Globally, about five million cases of neonatal eye infections occur annually.[1] Even though mild and often self-limiting, bacterial eye infections in newborns, if not diagnosed and treated properly, can lead to overwhelming consequences. Over half of the cases of blindness worldwide are still attributed to ophthalmia neonatorum, caused by Neisseria gonorrhea or Chlamydia trachomatis

which neonates acquire at birth. [2, 3] Potentially pathogenic bacteria such as Staphylococcus aureus, Staphylococcus epidermidis, Klebsiella species, Escherichia coli, enterococcus, Streptococcus species, Hemophilus influenzae, Pseudomonas species, and Corynebacterium species can be found in the eyes of a newborn. [3-5]

The occurrence of neonatal illnesses is mostly linked to maternal health and the postnatal environment. Maternal infections such as Gonorrhea and purulent endometritis are considered the chief source of infection in neonates. [3, 6, 7] Various studies have reported the association of urinary tract infections, prolonged labor, premature rupture of membranes, amnionitis, and anemia as maternal risk factors predisposing the newborn to infections such as sepsis and conjunctivitis or eye infections. [3, 8]

In many developing countries, including Pakistan, home delivery is a common practice usually conducted by a traditional or unskilled birth attendant. Unsafe birthing practices or indigenous medicines during labor can expose laboring women and their newborns to potential infections. [9, 10]

Very few studies have evaluated the occurrence of bacterial pathogens in the eye swab samples of newborns and the subsequent development of neonatal eye infections. Information on types of bacterial pathogens carriage at birth and the occurrence of neonatal eye infections during the early neonatal period is not available in Pakistan. It is important to have this information available to assess the risk of newborns developing eye infections and to facilitate prophylactic or therapeutic interventions. We hypothesized that babies born to mothers with prolonged duration of labor will have a higher incidence of positive eye swab culture at birth and a higher incidence of eye infections during the first seven days of life as compared to babies born to mothers with a normal duration of labor. This study aimed to identify the incidence and factors associated with the isolation of bacteria from eye swab samples at birth and the development of eye infections during the early neonatal period.

Methods

We have recruited women from the obstetrics wards of the Qatar Hospital and the Civil Hospital of Karachi, Sindh, Pakistan. These are two large tertiary care hospitals that predominantly serve the low and middle-class communities of Karachi. Women aged 18-49 years, who had a singleton, vaginal delivery, or emergency c-section and who gave consent to take part in the study were enrolled. Women with multiple gestations, intrauterine death, face or breech presentation, and those who do not have a resident home address in Karachi city were excluded. Labor durations of at least 18 hours in primiparas and 15 hours in multiparas were considered as prolonged labor while labor durations of less than 18 hours in primiparas, and less than 15 hours in multiparas were considered as normal duration of labor. The start of labor was defined as the onset of labor pains. Swabs were taken from one eye of the newborn, immediately after birth. These swabs were immediately placed in AMIES Transport medium (Transwab for Aerobes and Anaerobes, Medical Wire and Equipment Co. Ltd., Corsham, Wilts., UK). On swab samples, the date of sample collection and identification number of participants was mentioned. We sent the AMIES Transport media to the Dow Diagnostic Reference and Research laboratory in Karachi, for sample processing and identification of pathogens. For assessment of the development of eye infections, the newborns were followed up on day seven at home.

A research medical officer was trained by a neonatologist to diagnose neonatal eye infections at follow-up home visits. Mothers were shown pictures of the neonates with eye infections to establish the diagnosis in retrospect if they mentioned redness, eye discharge, or swelling of the eye preceding the day seven follow-up. At the seven-day visit, neonates with an eye infection were referred to consultant ophthalmologists at one of the study hospitals. Laboratory reports of the neonatal eye swabs were provided to the mothers. Randomly selected unused swabs were sent to the laboratory with hypothetical identification numbers for quality checks. All quality check reports showed no growth.

Our power calculation was based on the ability to discern a significant difference in neonatal eye infections between women with normal and long lengths of labor. With an anticipated risk ratio of

2.0, an anticipated incidence of neonatal eye infections of 23% in neonates born to women with a normal duration of labor, with a ratio of 1:1 in both groups, 80% power, and an additional sample of 20% for loss to follow-up, a total of 194 women were required in the study. Epi info version 3.3.2, 2005 was used to calculate the sample size.

Data were analyzed using SPSS and SAS computer packages to calculate the mean and standard deviation for quantitative variables. Crude risk ratios (RR), adjusted risk ratios (ARR) and rate ratios i.e., hazard ratio (HR) and adjusted hazard ratio (AHR) with 95% confidence intervals (CIs) were calculated through Cox regression and Weibul regression analysis after checking for the proportional hazard assumption for independent variables. None of the interaction terms were found significant. The final model was adjusted for covariates.

Before the start of the study, approval was obtained from the Ethics Review Committee (ERC) of Aga Khan University, Karachi, Pakistan. We obtained permission from the study hospital authorities for conducting the study and informed written consent was obtained from each study participant women.

Results

Total 851 women admitted to the obstetrics ward of Civil Hospital and Qatar Hospital in Karachi were screened and invited to participate in the study. Of these, 205 (24%) women were found eligible and enrolled in the study. One hundred and five women (51%) had prolonged labor while 100 (49%) had a normal duration of labor. Ninety (44%) women were primiparous. Descriptive characteristics of the study participants are given in Table 1.

Table: 1 Descriptive characteristic of the mothers and newborns enrolled in the study

Characteristics	Number (percentage)
***Age of mother**	24.86 ± 4.65
Parity	
Primiparous	90 (43.9)
Multiparous	115 (56.1)
Mothers' education (years)	
11 and above	24 (11.7)
9-10	62 (30.2)
1-8	64 (31.2)
No schooling	55 (26.8)
Antenatal care in pregnancy	
No	14 (6.8)
Yes	191 (93.2)
***No. of antenatal visits in days**	6.02 ± 3.18
Antenatal visits categories	
Less than 4 visits	48 (23.4)
Between 4-6 visits	91 (44.4)
More than 6 visits	66 (32.2)
Iron supplement in pregnancy	
No	40 (19.5)
Yes	165 (80.5)
***Duration of iron supplement in days**	81.13 ± 56.44
Duration of iron use	
No use	40 (19.5)
1-30 days	41 (20.0)
31-90 days	87 (42.5)
>90 days	37 (18.0)
Co-morbidity (during pregnancy)	
No	160 (78)
Yes	45 (22)

***Number of vaginal examinations during labor**	4.7 ± 2.59
Duration of Labor	
Normal	100 (48.8)
Prolonged	105 (51.2)
Person conducted delivery	
Doctor	147 (71.7)
Nurse/ Midwife	58 (28.3)
Mode of delivery	
Vaginal delivery	190 (92.7)
Caesarean Section	15(7.3)
ROM	
SROM	92 (44.9)
AROM	113 (55.1)
Sex of newborn	
Male	114 (55.6)
Female	91 (44.4)
***Birth weight in kilograms**	2.94± 0.489

* Mean ± standard deviation (SD)
Rupture of the membrane (ROM)
Spontaneous rupture of membrane (SROM)
Artificial rupture of membrane (AROM)

Eye swab culture results

Bacterial or yeast growth on culture was observed in 69 (34%) of the 205 conjunctival swabs taken from newborns at birth. Sixty samples had one bacterium grown, while more than one type of bacteria was observed in 9 (4%) samples including three different types of bacteria from a single eye swab culture. From these 69 positive cultures and 79 bacteria, gram-positive bacteria were observed in 19 (24%), gram-negative bacteria observed in 57 (72%), and yeast in 3 (4%) cultures. Gram-positive bacteria included Staphylococcus species 16 (20.3%), Corynebacterium species 2 (2.5%), and Micrococcus species 1 (1.3%). Gram-negative bacteria included Escherichia coli 20 (25.3%), Acinetobacter species 10 (12.7%), Enterobacter species 8 (10.1%), Pseudomonas stutzeri 6 (7.6%), Pseudomonas species 6 (7.6%), Pseudomonas aeruginosa 4 (5.1%) and Klebsiella species 3 (3.1%). Candida albicans was also observed in 3 (3.8%) samples. Antimicrobial resistance patterns of these bacteria are described elsewhere. [11]

Risk factors for positive eye swabs

The cumulative incidence of positive eye swab samples in newborns was 34% (95% CI: 27.48-40.52%). Parity, number of antenatal visits, duration of iron supplement received in pregnancy, and birth weight of the newborn were associated with positive conjunctival cultures on bivariate analysis. The final adjusted model indicated that multiparity (ARR=1.83; 95% CI: 1.06-3.16) and lack of antenatal visits during pregnancy (ARR=2.23; 95% CI: 0.89-5.55) were associated with positive eye swab samples in neonates at birth. The risk of positive eye swab samples in newborns of mothers with prolonged labor was greater (ARR = 1.26; 95% CI: 0.75-2.14) than the risk in newborns of mothers with normal labor, although this difference was not statistically significant. Crude risk and adjusted risk ratios are presented in Table 2.

Table 2: Crude and adjusted risk ratios for positive eye swab cultures of newborns taken at birth.

Characteristics of participant	RR (95 % CI)	p-value	ARR (95 % CI)	p-value
Age of mother	1.05 (0.99-1.09)	0.07		
Parity				
Primiparous	1		1	
Multiparous	1.91(1.14-3.22)	0.01	1.83 (1.06-3.16)	0.029

Mothers' education (years)				
11 and above	1			
9-10	0.75 (0.34-1.68)	0.74		
1-8	0.79 (0.36-1.75)			
No schooling	1.02 (0.47-2.22)			
***Antenatal care in pregnancy**				
Yes	1		1	
No	1.77 (0.85-3.70)	0.13	2.23 (0.89-5.55)	0.085
No. of antenatal visits in days	1.07 (1.00-1.14)	0.04		
Iron supplementation				
Yes	1			
No	1.44 (0.84-2.46)	0.19		
Duration of iron supplement in days	1.01 (1.00-1.00)	0.01		
Co-morbidity (during pregnancy)				
No	1			
Yes	1.37 (0.81-2.33)	0.24		
Number of vaginal examinations during labor	0.92 (0.84-1.11)	0.11		
Person conducting Delivery				
Doctor	1			
Nurse/ Midwife	1.02 (0.61-1.72)	0.94		
Mode of delivery				
Cesarean Section	1			
Vaginal delivery	1.29 (0.47-3.56)	0.61		
ROM				
AROM	1			
SROM	0.85 (0.53-1.38)	0.53		
Sex of newborn				
Male	1			
Female	0.91 (0.56-1.47)	0.70		
Birth weight of a newborn in kilograms	1.49 (1.03-2.16)	0.03		
APGAR at one minute				
7 or more	1			
Less than 7	0.66 (0.21-2.11)	0.49		
Labor duration				
Normal	1		1	
Prolonged	0.81 (0.50-1.29)	0.37	1.26 (0.75-2.14)	0.379

*ARR adjusted for covariate "number of antenatal visits in pregnancy."
Risk ratio (RR), adjusted risk ratio (ARR)
Confidence interval (CI)
Rupture of the membrane (ROM)
Spontaneous rupture of membrane (SROM)
Artificial rupture of membrane (AROM)

Neonatal eye infections

We were able to follow 192 (94 %) of the babies on day seven after delivery and found eye infections in 40 (20%; 95% CI: 14.53-25.47%) babies. Other than eye infections, jaundice, fever, difficulty in respiration, skin infections, and diarrhea were also observed in 68 (35%) of the babies.

Risk factors for neonatal eye infections

At invariable analysis, iron supplementation during pregnancy was associated with a reduced risk of development of eye infections but the duration of labor had no effect on the development of eye infections during the early neonatal period. Crude and adjusted hazard ratios are shown in Table 3. The adjusted Weibull regression model indicated that the risk of eye infection in newborns of mothers with prolonged labor was similar (HR = 0.94: 95% CI: 0.41-2.17) to the risk of infection in newborns of mothers with a normal duration of labor. The number of vaginal examinations during labor was linearly associated with the development of eye infection in babies during the first seven

days of life (AHR=1.22; 95% CI: 1.02-1.46). Positive eye swab cultures were more likely to be associated with the development of eye infections as compared to negative eye swab cultures (AHR=2.89; 95% CI: 1.10-7.61). The risk of having an eye infection in newborns of mothers who had less than four antenatal visits was greater as compared to mothers who had seven or more visits. [For 4-6 antenatal visits AHR= 4.34 (95% CI: 1.27-14.79) and for less than four antenatal visits AHR=5.31 (95% CI: 1.37-20.49)]. The final model was adjusted for the covariates; mother's education, iron supplementation in pregnancy, type of birth attendant, and Apgar score at one minute after birth.

Table: 3 Weibull Regression Model with crude and adjusted hazard ratios for the development of eye infections within the first week of life

Characteristics	HR (95%CI)	p-value	AHR (95%CI)	p-value
Age of mother	1.04 (0.95-1.14)	0.38		
Parity				
Primiparous	1			
Multiparous	1.31 (0.55-3.15)	0.54		
Mothers' education (years)				
11 and above	1			
9-10	2.95 (0.09-1.23)			
1-8	0.40 (0.11-1.41)	0.36		
No schooling	0.38 (0.09-1.46)			
***Antenatal visits categories**				
More than 6 visits	1		1	
Between 4-6 visits	2.23 (0.75-6.68)		4.34 (1.27-14.79)	
Less than 4 visits	2.5 (0.73-8.53)	0.27	5.31 (1.37-20.49)	0.035
Duration of iron use				
>90 days	1			
31-90 days	3.01 (1.09-8.26)			
1-30 days	0.45 (0.09-2.01)	0.05		
No use	1.09 (0.32-3.57)			
Co-morbidity (during pregnancy)				
No	1			
Yes	0.85 (0.31-2.38)	0.76		
***Number of vaginal examinations during labor**	1.11 (0.95-1.29)	0.19	1.22(1.02-1.46)	0.030
Person conducting delivery				
Doctor	1			
Nurse/ Midwife	1.61 (0.65-4.00)	0.31		
ROM				
AROM	1			
SROM	0.96 (0.41-2.29)	0.93		
Sex of newborn				
Male	1			
Female	0.88 (0.37-2.11)	0.78		
Birth weight of a newborn in kilograms	0.69 (0.27-1.79)	0.45		
APGAR score at one minute				
7 or more	1			
Less than 7	1.21 (0.24-6.22)	0.82		
***Culture status at birth**				
Negative	1		1	
Positive	1.66 (0.67-4.12)	0.27	2.89 (1.10-7.61)	0.031
Labor duration				
Normal	1		1	
Prolonged	1.07 (0.45-2.54)	0.86	0.94 (0.41-2.17)	0.894

*AHR Adjusted for covariates "person conducting delivery, iron supplements in pregnancy, mother's education and APGAR score at one minute".

Hazard ratio (RR), adjusted hazard ratio (ARR)

Confidence interval (CI)
Rupture of the membrane (ROM)
Spontaneous rupture of membrane (SROM)
Artificial rupture of membrane (AROM)

Discussion

High incidences of positive eye swabs in newborns have been reported in several studies. Eder et al reported 84% incidence in two hospitals in Argentina and Paraguay. Similarly, in 86% of eyes examined reported the presence of bacteria in a large study in India.[4, 12-14] In our study, a comparatively low incidence is observed because we have not used special techniques to identify Chlamydia and viruses in our samples, whereas other studies included these organisms. The microorganisms observed in conjunctival swabs such as Staphylococcus species, Escherichia coli, Enterobacter species, Klebsiella and Pseudomonas species, and Candida albicans have also been reported from other parts of the world. The prevalence of gram-negative rods was reported as 11.6 % in an Algerian population, whereas Diphtheroid was present in only 2.8% of the eyes examined in a study from Los Angeles.[15, 16] Coagulase-negative staphylococcus species (CNS) was identified as a major bacterial pathogen in 25% of the cases of eye infection in neonatal intensive care units in New York.[17] Similarly, CNS was observed in 75% of the conjunctival cultures in a NICU in Connecticut and 21% in South Korea.[16, 19] E. coli in a newborn is mostly acquired at birth from an infected mother. Staphylococcus species, E. coli, Klebsiella species, Enterobacter species, and Candida albicans are common causes of urinary tract infections in females.[20] The presence of these bacteria in the eye swab samples of newborns at birth is likely acquired from the mother. Sixty-six percent of conjunctival cultures did not reveal any growth in our sample, however, the possibility of the presence of other microorganisms such as viruses cannot be ruled out.

Limited literature is available regarding the association between the duration of labor and the acquisition of bacteria in eye swab samples taken at birth. We could only find one study where the association of prolonged labor with ocular flora in newborns and the development of eye infections was found.[21] In that study, the eye swab samples were positive in 56.8% of the newborns; with 63% of newborns in the prolonged labor group and 51% in the normal duration of labor group, but our study did not show any association of prolonged labor with the incidence of eye contamination in the newborn.

In our study, multiparty was associated with the presence of bacteria in newborns. This could be because of the increased risk of ascending infections in multiparas, leading to subsequent transmission of microorganisms to the newborn conjunctiva. It may be that antenatal care helps prevent maternal and newborn infections through maternal treatment of urinary tract infections and other infections during pregnancy, and the mother's enhanced awareness about health and hygiene.[22, 23]

Since limited resources did not allow us to do the vaginal swabs at the time of delivery and repeat eye swab samples on day seven of infected eyes, we are cautious in claiming that vaginal microorganisms were the cause of eye infections in neonates in our study. It is reported in previous studies that half of neonatal eye infections would occur within the first 48 hours of life, 57% within 48-72 hours after birth and 92% of eye infections of bacterial origin would develop within the first week after birth if newborn's eyes get contaminated at birth.[5, 13, 24] Acute cases usually last for 4-6 days; the mean duration of infection is reported as 2.4 days (SD 1.8 days).[2, 25] In eye infections of bacterial origin, the period of incubation and communicability is one to seven days and two to seven days, respectively.[1] So, we can speculate that the bacteria identified in eye swab samples taken at birth could be responsible for eye infection development in neonates in our study during the first seven days of life.

Our findings are consistent with other studies that eye infections developed more frequently in those with positive eye swab cultures.[13, 21] CNS, Klebsiella species, Pseudomonas aeruginosa, Enterococcus species, E. coli, and Yeast were identified in other studies as the organisms causing eye infections in newborns.[5, 17, 26] We also identified these microorganisms in eye swab samples, so we hypothesize that these are the same microorganisms responsible for the development of eye

infections in neonates during the first seven days of life. However, the development of eye infections depends on the pathogenicity and quantity of microorganisms as well.

We did not observe a significant association between the duration of labor with the incidence of eye infections in neonates. Our results are consistent with findings reported by Ilako et al in which eye infections developed in 31% of newborns in the prolonged labor group and 23% in the normal labor group. Repeated vaginal examinations during labor have been identified as a risk factor for introducing maternal and newborn infection.[22, 27] Our results show that increases in the number of vaginal examinations during labor are linearly associated with an increased risk of eye infections in neonates, but in contrast to our findings, Verma et al report that vaginal examinations do not increase the risk of eye infections in neonates.[24]

The use of maternal health care services reduces maternal and child mortality and improves the reproductive health of women, as identifying women at increased risk of adverse pregnancy outcomes is possible during regular antenatal care.[28, 29] According to World Health Organization (WHO) guidelines, women should have at least four antenatal care visits during their pregnancies. [30] The newborns of women attending antenatal clinics, especially in the first trimester of pregnancy, are at a lower risk of getting serious infections.[22] We also observed that the number of antenatal care visits was associated with eye infection development in newborns. The gender and weight of the newborn were not associated with developing eye infections in our study. Similar results were observed by Rao et al in Dehli India. However, Verma et al found that the incidence of eye infections was higher in male neonates as compared to females, and low birth weight was reported as a predictor of conjunctival infection.[13, 24] No differences were identified in the incidence of eye infections according to the mode of delivery in our study which is consistent with some other studies as well. [24]

The main limitation of our study is related to the assessment of the duration of labor, which was based on reporting of the commencement of labor by women themselves and is subjective. However, since in both groups, the same methodology was used, we believe that this bias is non-differential, and has not affected the results spuriously. Another limitation of our study is examining bacteria only, thereby excluding Chlamydia trachomatis and viruses. We are cautious in generalizing our study findings as we sampled neonates from two public sector hospitals in Karachi, which might not be representative of all hospitals or community settings of Karachi.

To summarize, the duration of labor had no association with positive eye swab cultures in newborns at birth and the development of eye infections in the early neonatal period. Environmental factors such as repeated vaginal examinations during delivery increased the risk of eye infections in newborns. Antenatal care during pregnancy was associated with a reduced risk of eye contamination at birth and developing eye infections during the early neonatal period.

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Ethical Approval

Approval was obtained from the ethical review committee (ERC) of Aga Khan University Hospital Karachi, Sindh, Pakistan.

Authors' contributions

Under the supervision of SS, JM conducted the study, performed the statistical analysis, and drafted

the manuscript. SIA provided technical inputs on the statistical analysis. NFZ, and MRK provided the subject knowledge of Obstetrics & Gynecology and Microbiology. SS, NFZ, MRK, SG, and SIA, contributed to the review of the report. All authors read and approved the final manuscript.

Competing Interests

The author (s) declares that they have no competing interests.

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