Original Research Article



FACTORS ASSOCIATED WITH COVID-19 POSITIVITY AMONG NEWBORN BABIES BORN TO COVID-19 CONFIRMED MOTHERS AT A DEDICATED COVID TREATMENT CENTRE – A CASE CONTROL STUDY

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ABSTRACT

Background: COVID 19 infection has become a major public health problem throughout the world as a pandemic. Antenatal mothers and their babies form a vulnerable population to acquire this infection. Many maternal and neonatal factors are reported to be related with COVID positivity in the babies of COVID positive mothers and identification of these factors is essential for proper care. But studies evaluating the association of these factors with COVID positivity are limited. The objective of the present study was to determine the factors associated with COVID positivity among babies born to COVID confirmed mothers.

Materials and Methods: An unmatched case control study was conducted at a dedicated tertiary care COVID treatment hospital among babies born to mothers who were COVID positive within 14 days before delivery. The cases included COVID positive babies and the controls included COVID negative babies of these mothers. The consecutive cases and concurrent controls were chosen from same source population with control to case ratio 2:1 by retrospective chart review from August 2020 to December 2021. The COVID testing for babies was done at 24 to 48 hours after birth. The outcome variable was the COVID positivity status of babies. The maternal and neonatal factors were analysed to study the significant association with the outcome variable. Chi square test was used to study the association of categorical variables with outcome variable in Univariate analysis. Bivariate analysis and Multivariate Logistic regression were done to explore the significant risk factors associated with neonatal COVID positivity.

Results: The total study population included 261 babies (cases included 87 babies and controls included 174 babies). Prolonged Rupture of Membrane was found to be a significant maternal risk factor associated with neonatal COVID positivity(P = 0.018, OR 2.19, 95%CI 1.13 to 4.27). Meconium-Stained Amniotic Fluid was another significant risk factor observed with the outcome (P = 0.005, OR 2.48, 95%CI 1.29 to 4.77). The other maternal variables such as age of mother, parity, mode of delivery, presence of maternal co morbidity and clinical category of COVID did not show significant difference. Among the neonatal factors, Prematurity was seen significantly more in case group (P=0.01, OR 2.81, 95%CI 1.2 to 6.3). Other neonatal variables like Birth weight, gender, Small for Gestation, need of NICU admission, active resuscitation and Low APGAR score did not show significant difference between the two groups. After evaluating possible confounders, Multivariable Logistic Regression was done which showed significance of neonatal COVID positivity with Prolonged

rupture of Membrane (aOR 2.02), Meconium stained Amniotic fluid (aOR 2.4) and Preterm deliveries (aOR 2.7).

Conclusion: The significant risk factors associated with neonatal COVID positivity identified in the present study were Prolonged Rupture of Membrane during delivery, Meconium stained amniotic fluid and Preterm delivery. This highlights the importance of management in the peripartum period which will ultimately help in neonatal care during a pandemic situation.

Keywords: COVID 19 positivity, Newborn, Prolonged Rupture of Membrane, Meconium Stained Amniotic Fluid, Prematurity.

INTRODUCTION

COVID-19 infection has become a major public health problem throughout the world as a pandemic. Since its first detection in late 2019, it has spread across continents and more than 6.5 million people have died.^[1] Several studies have shown higher rates of morbidity and mortality in groups of population with high risk factors like elderly, obese, type 2 diabetes, hypertension and immunosuppression.^[2] Along with these, pregnancy remains as a vulnerable period not only for mother but also for the fetus in the midst of a pandemic.

During pregnancy, body undergoes physiologic changes which lead to altered immune functions. Therefore, pregnant women are at high risk for getting viral respiratory infections during a pandemic. The studies done in the initial period of pandemic suggested that incidence of COVID infection was more in pregnant women along with increased risk of vertical transmission to newborns.^[3] Many maternal and neonatal factors were reported to be associated with COVID positive newborns.^[4]

As per our current knowledge, research work done in a study population comprising only babies born to COVID positive mothers were very few. The studies involving maternal and neonatal factors associated with neonatal COVID positivity were also limited. The majority of available studies focused on clinical outcome of mothers when they get COVID infection during the antenatal period and majority of these studies were done during the early phase of pandemic.^[5] There was a need for research work to be done exclusive on babies of COVID positive mothers with a comparative group to get a clear understanding of factors operating in COVID positivity transmission from mother to baby.

In this back ground, this study was planned to determine the factors associated with neonatal COVID positivity in babies born of COVID positive mothers. The objective of the study was to determine the factors associated with COVID positivity among babies born to COVID-19 confirmed mothers in a tertiary care hospital.

MATERIALS AND METHODS

This hospital-based case-control study was conducted at Government Medical College Kollam, Kerala, a tertiary care hospital that served as a dedicated COVID treatment facility during the pandemic. The study included babies born to COVID-positive mothers, with cases defined as babies who tested positive for COVID within 24-48 hours of birth, and controls as babies who tested negative in the same time frame. Data was collected retrospectively from August 2020 to December 2021, and the study was carried out between February and July 2022, following ethical and administrative approvals.

The inclusion criteria required babies born to COVID-positive mothers confirmed by RTPCR or Tru Nat tests, with exclusions made for babies whose or their mothers' COVID status was not confirmed, those referred within 24 hours, or those whose mothers refused COVID testing for newborns. The study variables included maternal factors such as preterm delivery, mode of delivery, severity of COVID illness, co-morbidities during pregnancy, and prolonged rupture of membranes, while neonatal factors like gestational age, birthweight, need for active resuscitation, and NICU admission were also considered.

The sample size was calculated to be 257 babies, with a 2:1 control-to-case ratio, based on assumptions about the preterm delivery rate and odds ratio. Statistical analysis was done using SPSS v.26, with univariate and multivariable logistic regression to identify significant factors associated with neonatal COVID positivity. The study ensured strict confidentiality and data security, with all data stored in password-protected systems and paper records kept securely for a minimum of three years after data collection.

Ethical Considerations

The study was under the category of 'Less than Minimal Risk' as it involved only retrospective chat review. The data extraction sheets were filled after getting the approval from IEC on February 2nd 2022. The Participant information was kept confidential and extra vigilance was taken to ensure anonymity at each level in data collection, data analysis sheets, data storage, and research communication. As the study included retrospective chart review, administrative sanction was also obtained for data collection. The Paper forms were kept under lock and key for a minimum period of 3 years after data collection and study-related electronic data was kept password protected.

RESULTS

The association of maternal and neonatal risk factors with neonatal COVID positivity was evaluated in babies born to COVID positive mothers in this study. This was a hospital-based case control study by retrospective chart review. A total of 261 participants with 87 cases and 174 concurrent controls were studied. The Flow chart showing the study population is given in [Figure 1].

The detailed description of base line variables was given in [Table 1].



Figure 1: Flow chart showing Case and control selection

Table 1: Descriptive statistics of baseline variables for case and control group.						
Variable	Case (n=87) n (%)	Control (n=174) n(%)	Total			
Maternal Age						
- Median (yr)	25	25	25			
- IQR	5	7	6			
Maternal Age group						
-<21 year	8(9.2%)	10 (5.7%)	18			
21-29 year	69(79.3%)	124 (71.3)	193			
\geq 30 year	10(11)	40(23)	50			
Parity – Primi	40(46%)	90(51.7)	130			
Multipara	47(54%)	84 (48.3)	131			
COVID Category						
- Asymptomatic	72(82.8)	145 (83.3)	217			
- Mild	12(13.8)	18(10.3)	30			
- Moderate	2(2.3)	8(4.6)	10			
- Severe	1 (1.1)	3(1.7)	4			
Birth Weight- baby						
- Low Birth Weight (<2.5 kg)	14(16.1)	24(13.8)	38			
- Not Low Birth weight	73(83.9)	150(86.2)	223			
Gestational Age						
-Small for Gestation(SGA)	13(14.9)	21(12.1)	34			
- Appropriate for Gestation (AGA)	70(80.5)	150(86.2)	220			
-Large for Gestation (LGA)	4(4.6)	3(1.7)	7			
Gender						
- Male	35(41.2)	79(45.4)	114			
- Female	52(58.8)	95(54.6)	147			

The maternal variables like age of mother, parity, mode of delivery, presence of maternal co morbidity and clinical category of COVID did not show any statistically significant difference in COVID positive babies when compared with COVID negative babies. Among maternal co morbidities, case group had 3% more proportion of Gestational Diabetes and control group had 5% more proportion of Pregnancy induced Hypertension but the difference was not statistically significant.



Figure 2: Pie chart showing proportion of preterm and term babies in cases





Prolonged Rupture of Membrane during delivery was found to be a significant maternal risk factor associated with neonatal COVID positivity (24% in cases and 12% in controls, P= 0.018, OR 2.19 ,95% CI 1.13 to 4.27).

Meconium Stained Amniotic Fluid during delivery was another significant risk factor associated with COVID positive babies (26% in cases and 12% in controls, P = 0.005, OR 2.48 95% CI 1.29 to 4.77).

Preterm babies were 2.8 times more likely to be COVID positive when compared with COVID negative babies and the difference was statistically significant. (17.2% in cases and 6.9% in controls, P=0.01, OR 2.81 ,95% CI 1.2 to 6.3). The Pie chart showing the proportion of preterms and terms in case and control groups is given in [Figure 2 and 3].

Other neonatal variables like Birth weight, gender, Small for Gestation, need of NICU admission, active resuscitation requirement and Low APGAR score at delivery did not show significant difference between the two groups.

Bivariate Analysis with stratification was done to evaluate potential confounders and effect modifiers with the clinically significant variables. The independent risk factors identified from the study were Prolonged Rupture of Membrane during delivery, Meconium-stained amniotic fluid and Preterm delivery after evaluating the effects of confounders like maternal age, parity and mode of delivery.

Multivariate Logistic regression was also done to ascertain the independent risk factors associated with neonatal COVID positivity. A logistic regression model with Prolonged Rupture of Membrane, Meconium-stained amniotic fluid and Preterm delivery was decided to be the least biased and most parsimonious model for predicting the risk of neonatal COVID positivity among the babies of COVID positive mothers.

The variables incorporated in the model were Prolonged rupture of membrane, Meconium stained amniotic fluid and Preterm delivery. The model characteristics is given in [Table 2].

Table 2: Logistic Regression Model with clinically and statistically significant variables.						
Risk factors	Regression coefficient (β)	P value	Adjusted OR	95% CI Lower	95%CI Upper	
PROMa	.746	.033	2.109	1.061	4.195	
MSAFb	.962	.005	2.618	1.339	5.121	
Preterm(1)	1.042	.014	2.834	1.231	6.526	
Constant	-1.127	.000	.324			

aProlonged rupture of membrane bMeconium stained amniotic fluid

As per the model the -2 log likelihood ratio was 313.6, Nagelkarke R2 0.096 and Hosmer Lemeshow statistics shows a p value = 0.935 which shows model fitness. The variation of dependant variable ranges from 6.9% to 9.6%. The area under ROC curve shows 0.629. In the reduced model, there was no reduction of regression coefficient and P values are also significant. The adjusted OR also showed significance. The log likelihood showed increase and Hosmer Lemeshow showed good model fitness.

After doing logistic regression models, it the independent risk factors associated with neonatal COVID positivity in this study were Prolonged Rupture of Membrane during delivery, Meconium-Stained Amniotic Fluid during delivery and Preterm Delivery.

DISCUSSION

This retrospective case-control study investigated factors associated with neonatal COVID positivity among infants born to COVID-positive mothers. The study included 87 COVID-positive neonates as cases and 174 COVID-negative neonates as controls, maintaining a 2:1 control-to-case ratio to improve statistical power. Maternal age, parity, and symptomatic status were not found to be significant risk factors for neonatal COVID positivity, which aligns with previous research by Villar et al. and Yang et al.^[6,7] However, there were conflicting findings in studies by Wu et al,^[8] and Allotey et al,^[9] where symptomatic mothers had a higher likelihood of neonatal transmission. Additionally, maternal comorbidities such as diabetes and preeclampsia, although more frequent in mothers of COVID-

positive neonates, did not show a statistically significant association, supporting findings from studies by Daclin et al.^[2] and Jafiri et al.^[10]

Among the perinatal factors examined, Prolonged Rupture of Membranes (PROM), Meconium-Stained Amniotic Fluid (MSAF), and preterm delivery were identified as independent risk factors for neonatal COVID positivity. Preterm infants had a 2.8 times higher likelihood of testing positive, while PROM and MSAF were associated with adjusted odds ratios of 2.1 and 2.6, respectively. These findings are supported by previous studies by Panda et al., Vivanti et al., and Martinez et al,^[11–13] which emphasized the role of inflammatory mediators in increasing the risk of neonatal COVID transmission. Furthermore, histopathological studies, such as those by Romero et al,^[14] have demonstrated elevated levels of inflammatory markers like Interleukin-6 (IL-6) in preterm deliveries, reinforcing the possible biological mechanism behind these associations.

The study's findings underscore the importance of careful monitoring of COVID-positive mothers, particularly in cases of PROM, MSAF, and preterm birth, to mitigate neonatal risks. While previous research reported conflicting associations between mode of delivery and neonatal COVID positivity, this study found no significant correlation, aligning with systematic reviews by Cai et al.^[15] The use of a uniform data extraction protocol helped minimize selection and information biases, enhancing the study's reliability. Additionally, by focusing exclusively on neonatal COVID positivity rather than broader maternal and neonatal outcomes, this study fills a crucial knowledge gap and provides a strong baseline for future prospective research. Its findings

will be instrumental in guiding clinical decisionmaking regarding perinatal care in COVID-positive pregnancies, both during and after the pandemic.

Methodologic Limitations

The source population consisted of the babies born to COVID positive mothers, in which majority of antenatal mothers were referred cases. Therefore, the study findings may not reflect the whole maternal population with COVID infection. The mothers were selected towards the end of third trimester and the factors operating during the last phase of pregnancy period were evaluated in this study. So, the results cannot be generalised to the entire duration of pregnancy. Some true COVID positive mothers may be missed during delivery – the exposure might have occurred within 7 days before delivery and getting positive later- that may lead to selection bias. The RTPCR was taken as confirmatory test for selecting COVID positive mothers. But as the sensitivity was around 80% for RTPCR, some amount of misclassification would be present in the study. As chart review was done for the data collection, the impact of retrospective ascertainment bias cannot be ruled out.

CONCLUSION

The present study helped to do an exploration of maternal and neonatal risk factors associated neonatal COVID positivity. The non-modifiable risk factors like maternal age, parity and gender of baby were not associated with neonatal COVID positivity from this study. At the same time, it was reassuring to note that the mode of delivery, maternal co morbidities, need of active resuscitation and Low APGAR score were not associated with increased risk of COVID positivity in babies as reported in previous studies.

The significant risk factors independently associated with neonatal COVID positivity in this study are operating in the peripartum period which can also be modifiable to some extent. This highlights the importance of optimum clinical care for the mother baby dyad during the peripartum period which is also the most critical and precious time of their life together.

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