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Original Article

The C-reactive Protein as an Inflammatory Marker in Meconium Aspiration Syndrome

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ABSTRACT

Objective: To assess the role of C reactive protein (CRP) as an inflammatory marker among neonates diagnosed with meconium aspiration syndrome and factors associated with abnormal C reactive protein

Study Design: Cross-sectional study

Place and Duration of Study: Combined Military Hospital Rawalpindi. Six months, Jan to June 2022

Methodology: Neonates who were diagnosed with meconium aspiration syndrome underwent all baseline investigations including C reactive protein within 24 hours of diagnosis and admission in nursing intensive care unit. Gender of neonate, preterm birth, 1- minute APGAR score and 5-minute APGAR score were correlated with presence of raised C reactive protein levels among the neonates suffering from meconium aspiration syndrome.

Results: A total of 500 neonates suffering from meconium aspiration syndrome were included in the study. Median age was 2.0 (2.0) days. 280 (56.0%) were males while 220 (44.0%) neonates were females. 211 (42.2%) had C reactive protein within range while 289 (57.8%) had raised C reactive protein levels at time of diagnosis of meconium aspiration syndrome. Our study results showed that APGAR score less than 7 at 1 and 5 minutes and pre-term birth had statistically significant relationship with raised C-reactive protein levels (p-value<0.05).

Conclusion: Raised levels of C reactive protein was found in significant number of neonates diagnosed with meconium aspiration syndrome. Low APGAR scores at 1 and 5 minutes and pre-term birth of neonates emerged as risk factors for raised C reactive protein levels among neonates suffering from meconium aspiration syndrome.

Keywords: C Reactive Protein; Meconium Aspiration Syndrome; Neonates

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INTRODUCTION

Neonatal intensive care has been an emerging specialty in our part of the world involving the individuals of most tender age group struggling for their survival. Multiple disease processes among neonates' including meconium aspiration warrant admission in neonatal intensive care unit.[1] Meconium aspiration syndrome has been one of the common presentations in which neonates require intensive care.[2] This condition among neonates has high mortality and morbidity.[3] Early diagnosis and aggressive management in a specialized care unit play a key role in reducing the mortality related to this potentially life threatening condition.[4]

Obstetrician in labor room or operation theatre is usually the first clinician to encounter meconium aspiration syndrome. In high risk cases, sometimes pediatrician or neonatologist may be on board. Diagnosis of this condition is usually clinical and straightaway requires admission to nursing intensive care unit.[5] Multiple biochemical and inflammatory markers have been studied to find their association with diagnosis and severity of meconium aspiration syndrome including proclacitonin, C-reactive protein, Interleukin-8, interleukin-8, white cell count and absolute neutrophil count.[6]

It has been interesting how clinicians have tried to look for the role of inflammatory markers in diagnosing, assessing severity and predicting prognosis of meconium aspiration syndrome. Mahendiran *et al.*, published a study in 2018 with an aim to compare serum procalcitonin levels in full-term neonates having meconium aspiration syndrome with or without bacterial infection. They concluded that mean total leukocyte count, absolute neutrophil count, immature to total leucocyte ratio, microerythrocyte sedimentation rate, and CRP were comparable in both the groups and procalcitonin levels were increased in neonates with meconium aspiration syndrome irrespective of the presence of bacterial infection.[7] Yokoi *et al.*, from Japan published an interesting study in 2019 revealing the findings that elevated acute-phase inflammatory reaction score were associated with increased incidence of meconium aspiration syndrome among neonates with meconium stained amniotic fluid.[8] Lee *et al.*, Published a similar study in 2016 with objective to look whether or not

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intraamniotic inflammation and funisitis predispose the neonates to develop meconium aspiration syndrome. They concluded that combination of intra-amniotic inflammation with fetal systemic inflammation were significantly associated with development of meconium aspiration syndrome.[9]

Burden of disease id not low with regard to meconium aspiration syndrome in our part of the world. Moeed *et al.,* published a study in 2020 highlighting the local indices for meconium aspiration syndrome. It would be interesting if we could establish any role of inflammatory markers associated with this illness. We planned this study with the rationale to assess the simple and readily available inflammatory marker i-e C reactive protein for this purpose therefore abnormal C reactive protein levels among neonates diagnosed with meconium aspiration syndrome and factors associated with abnormal C reactive protein were studied for given study duration.[10]

METHODOLOGY

This cross-sectional study was planned and conducted at pediatrics department, Combined Military Hospital Rawalpindi between January 2022 and June 2022. Sample size was calculated by using the WHO sample size calculation by using the population prevalence proportion of meconium aspiration syndrome as 3%.[11] Non probability consecutive sampling was used to gather the sample.

Inclusion Criteria: All the neonates diagnosed as meconium aspiration syndrome on the basis of clinical, laboratory and radiological findings[12] by consultant pediatrician were included in the study.

Exclusion Criteria: Neonates with diagnosis of sepsis or any other inflammatory or immunological condition at the time of birth were excluded from the study. Babies with any syndromic conditions diagnosed before the birth were also excluded from the study. Neonates whose C reactive protein test could not be performed or tracked or those whose parents did not consent to participate in the study were also part of the exclusion criteria.

Ethical approval was taken from the ethical committee of hospital via letter no 346. Neonates diagnosed with meconium aspiration syndrome and admitted in neonatal intensive care unit were included in the study after application of inclusion/exclusion criteria. They underwent all baseline blood investigations including C reactive protein within 24 hours after getting the diagnosis of meconium aspiration syndrome. C reactive protein levels were considered raised if were more than 10.0 mg/dL.[13] APGAR score was calculated for all the neonates at 1 and 5 minutes as per protocol.[14] A specialized performa was designed for the study to record all the socio-demographic variables required for this study. Pre-term birth was defined as birth of baby before 37 weeks of gestation.[15]

Statistical analysis was done by Statistical Package for the social sciences (SPSS) version 24:00. Frequency and percentage were calculated for the qualitative variables whereas mean and standard deviation was calculated for the quantitative variables. Chi-square test was used to look for the relationship of Gender of neonate, preterm birth, 1- minute APGAR score and 7-minute APGAR score with raised C reactive protein levels among the target population. The *p*-value less than or equal to 0.05 was considered significant.

RESULTS

A total of 500 neonates suffering from meconium aspiration syndrome were included in the study. Median age was 2.0 (2.0) days. Out of 500 participants, 280(56%) were males while 220(44%) neonates were females. 211(42.2%) had C reactive protein within range while 289(57.8%) had raised C reactive protein levels at time of diagnosis of meconium aspiration syndrome. Table-I summarized the general characteristics of patients included in our study.

Table-I: Characteristics of study participants (n=500)

Variables	Values
Age (days)	
Median (IQR)	2.0 (2.0)
Gender	
Male	280(56.0%)
Female	220(44.0%)
C reactive protein levels	
Within range	211(42.2%)
Raised	289(57.8%)
APGAR score <7 at 1 minute	
No	277(55.4%)
Yes	223(44.6%)
APGAR score >7 at 5 minute	
No	283(56.6%)
Yes	217(43.4%)
Preterm Birth	
No	328(65.6%)
Yes	172(34.4%)

Table-II showed the results of statistical analysis applied on data generated in this study. APGAR score

less than 7 at 1 minute and 5 minutes after the birth and pre-term birth had statistically significant relationship with raised C-reactive protein levels in our study participants (*p*-value<0.05) while gender of the neonate did not show any such association (*p*-value 0.377).

Table-II: Association of various factors with raised C reactive protein levels in neonates with meconium aspiration syndrome (n=500)

Factors studied	Normal C reactive protein levels (n=211)	Raise C reactive protein levels (n=289)	*p*-value
APGAR score<7 at 1 minute			
No	132(62.5%)	145(50.2%)	0.006
Yes	79(37.5%)	144(49.8%)	
APGAR score<7 at 5 minute			
No	185(87.7%)	98(33.9%)	<0.001
Yes	26(12.3%)	191(66.1%)	
Gender			
Male	123(58.3%)	157(54.3%)	0.377
Female	88(41.7%)	132(45.7%)	
Preterm Birth			
No	151(71.6%)	177(61.3%)	0.016
Yes	60(28.4%)	112(38.7%)	

DISCUSSION

Neonatal intensive care is a huge task which not only involves organ support for these little beings but also demands immense care and caution to save them from iatrogenic harm. Meconium aspiration syndrome is one of the common causes for admission in neonatal intensive care unit. No definitive test exists for this potentially life threatening condition and the diagnosis is usually clinical supported by laboratory and radiological findings. Role of inflammatory markers among neonatal infective conditions has been an area of interest for researchers and clinicians. Idea of having a simple blood investigation helping in diagnosis or prediction of prognosis of a patient always appeal the physicians. We therefore planned this study with the objective to assess the presence of abnormal C reactive protein and factor associated with abnormal C reactive protein among neonates diagnosed and admitted with meconium aspiration syndrome in our neonatal intensive care unit.

Romero *et al.*,[16] published an interesting analysis to look for the role of Secreted phospholipase A2 in development of meconium aspiration syndrome among neonates delivered via spontaneous labor at full term. They concluded that Secreted phospholipase A2 and interleukin-6 were found significantly more in patients suffering from meconium aspiration syndrome as compared to those who did not suffer from this condition. They clearly highlighted the involvement of these inflammatory markers in meconium aspiration syndrome. We studied a much simpler marker i-e C reactive protein but found it raised in most of the neonates suffering from meconium aspiration syndrome.

Rao *et al.*,[17] published a paper in 2001 and studied similar association in a different way by observing relationship of placental membranes inflammation with development of meconium aspiration syndrome. They concluded that incidence of meconium aspiration syndrome and neonatal morbidity was higher in the presence of acute inflammation of placental membranes. Our emphasis was same that if we could find a reliable inflammation marker which has association with meconium aspiration syndrome, it may become easy for the clinicians to diagnose and manage such cases.

A similar study was carried out in Japan by Yokoi *et al.*,[8] and published in 2019, comprised of 95 full term neonates with meconium-stained amniotic fluid, who were hospitalized at a neonatal intensive care unit. This study revealed that various inflammatory markers were statistically significantly raised in patients suffering from meconium aspiration syndrome. Our study supported their results and around 57.8% of neonates included in our study had raised C reactive protein.

Khazardoost *et al.*,[18] published a study in 200 to study the risk factors for development of meconium aspiration syndrome among neonates with meconium stained amniotic fluid. Presence of inflammation, increased heart rate and low APGAR score at 5 minutes emerged as strong risk factors for development of meconium aspiration syndrome in their target population. Low APGAR score at 1 and 5 minute and preterm birth were related to raised CRP in our study and raised CRP was found in most of patients suffering from meconium aspiration syndrome. Inflammatory markers and clinical signs have been interlinked in such a complex manner in such patients that it is very difficult to establish exact cause and effect relationship.

Our study had few limitations. Study design does not establish cause and effect relationship. Long term outcome and severity of meconium aspiration syndrome was not studied in our analysis. Patients from only one center were included in the study which also limit the generalization of results. Studies on a larger scale addressing these limitations may generate better results regarding relationship of C reactive protein and meconium aspiration syndrome.

CONCLUSION

Raised levels of C reactive protein was found in significant number of neonates diagnosed with meconium aspiration syndrome. Low APGAR scores at 1 and 5 minutes and pre-term birth of neonates emerged as risk factors for raised C reactive protein levels among neonates suffering from meconium aspiration syndrome.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MI & ZM: Data acquisition, data analysis, critical review, approval of the final version to be published.

FI & BA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RT & SAHK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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