

Relation Between Inflammatory Indices and The Outcome of Meconium Aspiration Syndrome

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Abstract:

Background: Meconium aspiration syndrome (MAS) is linked to inflammation, but data on the patterns of hematological indices and C-reactive protein (CRP) in MAS are lacking. The aim of the study was to evaluate CRP, white blood cell count (WBC), absolute neutrophil count (ANC), and procalcitonin in MAS and to assess their association with disease severity.

Methods: a prospective hospital based study including 200 babies admitted in this period with MSAF, among those 50 babies have meconium aspiration syndrome (25 males). Recruited neonates were 1-7 days old with range of weight from 2 to 3.9kg

Results: all the inflammatory indices were markedly elevated in cases of MAS with septicemia in comparison with cases of MAS without septicemia, maximum CRP, and maximum PCT values were higher in neonates with very severe and severe MAS compared to non severe MAS. PCT and CRP correlated with duration of mechanical ventilation, duration of any respiratory support and length of hospital stay. PCT more sensitive rather than other inflammatory indices.

Keywords: :white blood cell count; absolute neutrophil count; procalcitonin and CRP.

Introduction:

Meconium aspiration syndrome (MAS) is a common cause of severe respiratory distress in term infants, with an associated highly variable morbidity and mortality. MAS results from aspiration of meconium during intrauterine gasping or during the first few breaths. Meconium aspiration into the lungs induces intense inflammatory response with polymorphonuclear cells infiltration diffusely throughout the lungs. Signs include tachypnea, nasal flaring, retractions, cyanosis, greenish yellow staining of umbilical cord, nail beds, or skin, underlying physiologic stressors also may contribute. If complete bronchial obstruction occurs, atelectasis results, partial blockage leads to air trapping on expiration, resulting in hyper

expansion of lungs and possibly pulmonary air leak with pneumomediastinum or pneumothorax. Persistent pulmonary hypertension can be associated with meconium aspiration as a comorbid condition or because continuing hypoxia. (Singh BS, 2009).

Meconium stores various substances including cytokines such as interleukin (IL)-1B, IL-6, IL-8, tumor necrosis factor, and thus constitutes a potent inducer of chemical pneumonitis. While previous studies have connected increased cytokine levels to MAS in vivo and in vitro, data on the most commonly used inflammatory indices in clinical practices namely hematological parameters and

C- reactive protein (CRP) are sparse. (De Beaufort AJ,2003).

Procalcitonin concentrations increase within 2 hours of an infectious episode, peak at 12 hours, and normalize within 2 to 3 days in healthy adult volunteers. A physiologic increase in procalcitonin concentration occurs within the first 24 hours of birth, and an increase in serum concentrations can occur with noninfectious conditions (eg, respiratory distress syndrome). (Chiesa C, 2003).

The aim of the present study is;

(I) Characterize patterns of CRP, CBC (white blood cell count) (WBC), absolute neutrophil ratio (ANC), (ESR), procalcitonin in neonates with meconium aspiration syndrome during the first week of life,

And,

(II) To analyze the relationship between inflammatory indices and illness severity.

Material and methods:

This was a prospective hospital based study taking place at Sohag university hospital. All full term and post term neonates admitted to neonatal unit of Sohag university hospital with meconium aspiration syndrome in period from October 2016 to September 2017 were included to the study. Preterm neonates, neonatal TTN and with hyaline membrane disease were excluded.

A total of 200 babies admitted in this period with MSAF, among those 50 babies have meconium aspiration syndrome (25 males). Recruited neonates were 1-7 days old with range of weight from 2 to 3.9kg.

Results:

This study was carried out in neonatal unit of Sohag university hospital in period from October 2016 to September 2017 and included 200 babies admitted in this period with MSAF, among those 50 babies have meconium aspiration syndrome (25 males). Recruited neonates were 1-7 days old with range of weight from 2 to 3.9kg.

Blood samples were collected into sterile Vacutainer plastic tube (BD, Becton Dickinson, USA) and divided as follow:

1-3ml Blood in K3 EDTA (Tri-Potassium EDTA) for Complete Blood Count (CBC), total (WBCs) and absolute neutrophil count.

2-2ml Serum for CRP by Red Cap Tubes.

3-3ml blood in K3 EDTA in Westergren tube for ESR.

4- 2ml Serum sample for PCT by Vidas.

Statistical Analysis:

Data was analyzed using STATA intercooled version 12.1. Quantitative data was represented as median and range. Test for trend was used to compare qualitative data. Qualitative data was presented as number and percentage. Correlation analysis was done using spearman correlation test. Roc curve analysis was used to detect best cutoff of different inflammatory indices that predict very severe MAS. Sensitivity, specificity, positive predicted value and negative predictive value were also calculated. Odds ratios were obtained from logistic regression analysis. Graphs were produced by using Excel or STATA program. P value was considered significant if it was less than 0.05.

Ethics of research:The aim of the study will be explained to each participant before collection of the data. Verbal consent will be obtained from those who welcome to participate in the study. Privacy of all the data will be assured.

(Table 1) Outcome of studied populations

Variable	Summary statistics
Duration in NICU Mean ± SD Median (range)	12.62 ± 10.74 8 (3-45)
Duration on mechanical ventilation Mean ± SD Median (range)	8.48 ± 11.79 4 (0-45)
Duration on oxygen Mean ± SD Median (range)	2.92 ± 1.50 3 (0-7)

This table demonstrates the outcome of neonates with MAS and duration of admission in NICU , The median range of admission at NICU was 8 days, median range of mechanical ventilator was 4 days and median duration of oxygen therapy was 3 days.

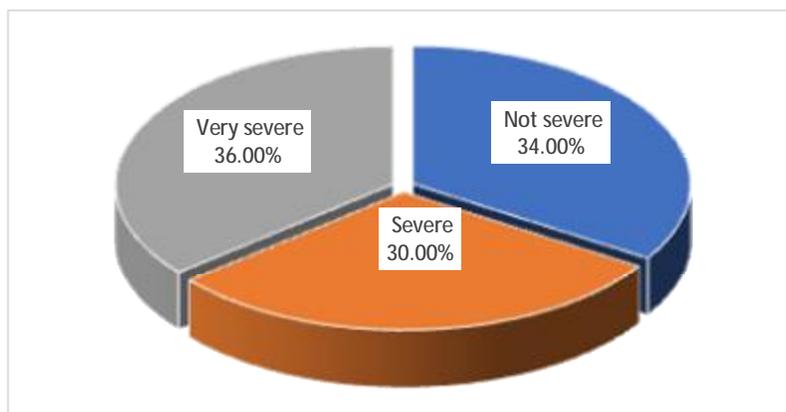
Neonates were grouped according to severity of MAF into:

Neonates with not sever MAS who didn't need respiratory support, or only need non invasive respiratory support.

Neonates with sever MAS who needed invasive mechanical ventilation for less than 7 days without the need for HFO.

Neonates with very sever MAS who needed invasive mechanical ventilation for more than 7 days with the need for HFO.

(Figure 1) Distribution of severity of MAS among studied populations



This figure demonstrates distribution of severity of MAS , very sever 36%, sever 30% and not sever 34%.

(Table 2) Relation between MAS with and without sepsis and inflammatory indices

Variable	No sepsis	Sepsis	P value
CRP	24 (6-48)	48 (12-96)	<0.0001
PCT	10 (0.9-60.4)	25 (1.8-60)	0.001
ESR	7 (2-15)	15 (5-89)	<0.0001
WBCs	8000 (4000-18000)	19000 (10000-41000)	<0.0001
Neutrophilia (%)	39.3 (22.4-79.4)	73.8 (55-89)	<0.0001

Data was represented as median (range)

As shown in the previous table, All the inflammatory indices were markedly elevated in cases of MAS with septicemia in comparison with cases of MAS without septicemia.

(Table 3) Prediction of Very Severe MAS with Inflammatory Indices

Variables	AUC	Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	OR (95% CI)	P value
CRP	0.87 (0.74-0.95)	>24	83.3 (58.6–96.4)	78.12 (60.0–90.7)	68.2 (51.9–81.0)	89.3 (74.5–96.0)	17.9 (3.99–79.74)	<0.0001
PCT	0.91 (0.73-0.97)	>15	94.4 (72.7–99.9)	81.2 (63.6–92.8)	73.9 (57.7–85.5)	96.3 (79.3–99.4)	73.67 (8.13–667.2)	<0.0001
ESR	0.87 (0.75-0.95)	>8	88.9 (65.3–98.6)	68.7 (50.0–83.9)	61.5 (48.3–73.3)	91.7 (74.5–97.6)	17.6 (3.38–91.56)	0.001
WBCs	0.88 (0.75-0.95)	>1300	88.9 (65.3–98.6)	78.1 (60.0–90.7)	69.6 (53.8–81.8)	92.6 (77.0–97.9)	28.57 (5.26–155.17)	<0.0001
Neutrophilia (%)	0.86 (0.73-0.94)	>55	94.4 (72.7–99.9)	71.9 (53.3–86.3)	65.4 (51.8–76.9)	65.4 (51.8–76.9)	43.4 (5.0–376.3)	0.001
Any marker indicate MAS			100 (81.5–100)	43.75 (26.4–62.3)	50 (32.9–67)	100 (76.8–100)	Can't calculated	
All marker in indicate MAS			72.2 (46.5–90.3)	96.9 (84.8–99.9)	92.9 (66.1–99.8)	86.1 (70.5–95.3)	80.6 (8.6–759)	<0.0001

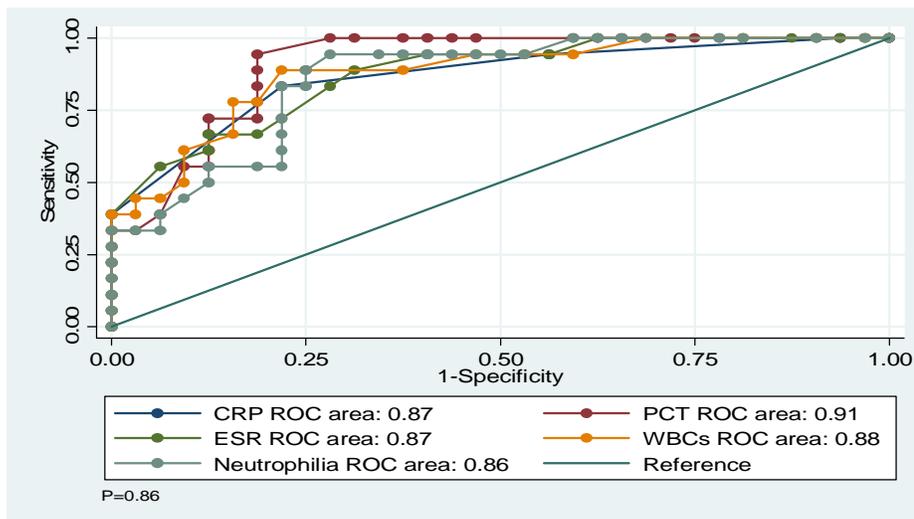
CI=confidence intervals. OR indicates the odds of very severe MAS comparing predictor values above and below the indicated cut-off

By analysis of values obtained during first 7 days of life, maximum CRP, and maximum PCT values were higher in neonates with very severe and severe MAS compared to non severe MAS. PCT and CRP correlated with duration of mechanical ventilation, duration of any respiratory support and length of hospital stay. PCT more sensitive rather than other inflammatory indices.

Roc curve comparing different indices for prediction of Very Severe MAS

(Figure 2)

This figure demonstrates that different inflammatory indices affect outcome of cases of MAS and PCT was more sensitive than others with Roc area 0.91.



Discussion

Many studies were conducted in an attempt to correlate between the severity of neonatal sepsis and/ or respiratory distress disorders in neonates in one hand and many

inflammatory indices such as ANA, WBCs, CRP, ESR, in the other hand. (Hofer N, Jank K, 2016).

Meconium aspiration is still a problem for significant neonatal morbidity

despite great advances in neonatal medicine. It is very common problem in Egypt. Unfortunately, there is no reliable source of information providing national annual estimate. Therefore neonatal MAS deserves more research. Recent studies suggest that avoidance of post-term delivery may reduce the risk of intrauterine hypoxia and the incidence of MAS.

The aim of the present study is to characterize patterns of CRP, CBC (white blood cell count) (WBC), absolute neutrophil ratio (ANC), (ESR), procalcitonin in neonates with meconium aspiration syndrome during the first week of life and to analyze the relationship between inflammatory indices and illness severity.

our study revealed that WBCs, neutrophil count and ESR were more increased in cases with MAS and with sepsis rather than cases with MAS without sepsis as **(table 2)**.

In this study, non severe MAS resemble 34% of cases, Sever MAS resemble 30% of cases and Very sever MAS resemble 36% of cases as **(Figure 1)**.

The outcome of neonates with MAS and duration of admission in NICU, The median range of admission at NICU was 8 days, median range of mechanical ventilator was 4 days and median duration of oxygen therapy was 3 days as **(table 1)**.

Diagnostic accuracy of the inflammatory indices to discriminate between

Very severe and non-severe MAS within the first 7 days of life is shown in **table (3) and figure (2)**.

All indices being above or below the cut-off values obtained by ROC analysis, CRP roc area (0.87), ESR

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roc area (0.87), Neutrophilia roc area (0.86), WBCs roc area (0.88) and PCT roc area (0.91).

The same results were documented in the study of **(Tripathi S, Saili A, Dutta R, 2007)**, in which there was relation between increase different inflammatory markers indices as WBCs, ANC and ESR and increase severity of MAS. PCT was more sensitive than other inflammatory markers.

Similar result was that of **(Simon L and Gauvin F, 2004)**,

they observed that serum PCT rapidly normalized after effective treatment. Thus, so PCT sampling helps to detect disease more quickly and is more sensitive than CRP level.

conclusion:

High CRP and PCT, ESR, WBC and ANC values were closely linked to disease severity in MAS. Though the inflammatory indices were able to predict illness severity during very early phases of the disease, the usefulness of this finding has still to be proven in clinical practice. However, results highlight the role of inflammation in the pathogenesis of MAS and its association with disease severity. Presence of sepsis increase severity of MAS and lead to more complications.

Our study revealed that cases of MAS with sepsis need more duration in NICU, more on MV and more O2 support due to increase severity of MAS than cases without sepsis.

Also this study revealed that PCT sampling helps to detect disease more quickly and is more sensitive than other inflammatory markers.

parents of neonates who participated in this study.

Authors contribution: All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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