Incidence of Meconium Aspiration Syndrome and Associated Risk Factors in Babies Born to Mothers with Meconium Stained Amniotic Fluid

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ABSTRACT

Introduction: Meconium stained amniotic fluid has long been associated with fetal distress with possible fatal complications unless addressed. We analyzed the results from the hospital births taken place at Kamineni Institute of Medical Sciences, Narketpally between October 2010 and June 2012 to understand the risk factors and the possible treatment modalities for the same.

Material and methods: All live birth in the institution between October 2010 and June 2012 were considered and analysed for possible risk factors, clinical outcomes and treatment modalities for Meconium Aspiration Syndrome.

Results: Out of 2380 live births 160 i.e. 67 per 1000 live births had meconium stained amniotic fluid. Out of 160 cases with MSAF, 21 (6.7%) cases had MAS. Out of 21 cases with MAS, 5 (23.81%) cases needed CPAP support and 4 (19.04%) cases needed mechanical ventilation. Only one mortality was encountered in the present study.

Conclusion: Increased maternal age, term and post terms, oligohydramnios, small for gestational age, premature rupture of membranes, APGAR score <7 are some of the risk factors for developing meconium aspiration syndrome according to our study.

Keywords: Fetal Distress, Fetal Asphyxia, Meconium, Low APGAR Score, Oligohydramnios.

INTRODUCTION

According to Greek literature “mekonianarion” – “opium like” as said by Aristotle in reference to its tarry like appearance and a belief that it induces sleep in the fetus.¹ The passage of meconium into the amniotic fluid during labour (fresh meconium) is one of the traditional indicators of fetal distress, and is associated with increased perinatal morbidity and mortality.² MSAF is known to be associated with several maternal and neonatal risk factors.³ Meconium has for long been considered to be a bad predictor of fetal outcome and meconium aspiration syndrome.⁴ Thus prevention of neonatal meconium aspiration syndrome (MAS) remains a major objective for obstetricians and neonatologists.⁵ Management of MSAF has changed substantially over years with the most recent recommendations of the national resuscitation program.⁶ This study was done at Kamineni Institute of Medical Sciences, Narketpally. The objective of this study is to better understand the maternal and neonatal risk factors associated with meconium stained amniotic fluid leading to meconium aspiration syndrome and the possible management options. The main objective of this study was to evaluate the incidence of MAS in babies born with MSAF, to associate maternal risk factors with MAS, to associate neonatal risk factors with MAS.

MATERIAL AND METHODS

All Babies born to mothers with meconium stained amniotic fluid in labour room & operation theatre at KIMS, Narketpally were considered for this study. This study was a case series. Study had taken place at Kamineni Institute of Medical Sciences Narketpally. The study was done during the period starting from Oct 2010 to July 2012. Clearance from the institutional ethical committee was taken. The inclusion criteria was - All babies born to mothers with Meconium stained amniotic fluid, all babies born with Meconium staining of nails/cord/skin.

Babies with Congenital anomalies including Congenital Heart Disease and Metabolic disorders like inborn errors of metabolism were excluded from the study. The outcomes and the risk factors were assessed. All babies born to mothers with Meconium stained amniotic fluid were subjected to detailed antenatal and natal history, thorough clinical examination and investigations were done as per proforma. Babies with respiratory distress were admitted in NICU and followed up. Meconium aspiration syndrome (MAS) is said to be present when the following criteria are present:

1) History of Meconium stained amniotic fluid.
2) Evidence of respiratory distress like tachypnoea, sub costal and inter costal retractions, grunting.
3) Chest x-ray showing bilateral asymmetric patchy infiltrates.

STASTICAL ANALYSIS

Microsoft office 2007 was used for the analysis. Descriptive statistics like mean and percentages were used for the analysis.

RESULTS

All the live births recorded in the institution between 22.10.2010 and 30.6.2012 are 2380 were taken into consideration which had meconium stained amniotic fluid. Out of 2380 live births 160 i.e. 67 per 1000 live births had meconium stained amniotic fluid. Of 160 cases with MSAF, 21 (6.7%) cases had MAS. Out of 21 cases with MAS, 5 (23.81%) cases needed CPAP support and 4 (19.04%) cases needed mechanical ventilation. Only one mortality was encountered in the present study.

There was a male distribution of 92 cases and female 68 cases.

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In the present study only one mortality was encountered. This out of 21 cases with MAS 20 (95.24%) cases were discharged. Support and 4 (19.04%) cases needed mechanical ventilation. Out of 21 cases with MAS, 5 (23.81%) cases needed CPAP post term pregnancy (50%), oligohydramnios (25%). In our study the incidence of maternal risk factors with MAS are category had no cases.

The incidence is noted more in small and appropriate for gestational age (SGA), post-dates, or with fetal distress. Previous studies have shown that MAS occurs in 10-15% of all deliveries. Approximately 5% of these deliveries are complicated by MAS. The incidence of MAS in preterm infants is very low. Most babies with MAS are 37 weeks or older, and most meconium stained infants are post mature and small for gestational age. MS is associated with increased risk of respiratory disorders and approximately 50% of these infants require mechanical ventilation. MAS babies are associated with high morbidity and mortality. Approximately 5% of infants with this diagnosis in a tertiary care centre die of its complications and the same number continue to require supplemental oxygen 30 days later. A complete understanding of the epidemiology of MAS has been hampered by the lack of population based studies and by difficulties in assembling large cohorts of infants with confirmed disease. In the largest study available to date, Wiswell et al reported of 176,000 neonates born from 1973 to 1987 in military medical hospitals. During this period of 15 years, there were 4-9 per 1000 live births of MAS neonates and between 3–8% of neonates who had meconium-stained amniotic fluid. In more recent studies the overall frequency of MSAF has ranged from 5 to 25% (median 14%) of all deliveries. As it predicts adverse perinatal outcome even in relatively low risk pregnancies MAS can be treated as an independent marker of fetal distress. In neonates born with MSAF, 10.5% of them had MAS with 12% mortality rate. However, the incidence is 2-4% in infants in whom endotracheal suctioning is performed immediately. The reported mortality for MAS varies from 0 to 30%. The wide variability is related to delivery room care. Among infants born with MSAF, chances of severe mental retardation and cerebral palsy are significantly higher. Of late the attention has been on the need for improving newborn care at the primary care level. Early detection of infants at risk for meconium aspiration syndrome would help in further studyofintrapartum and postnatal therapeutic modalities. Quiet a number of intrapartum risk factors have been identified for meconium aspiration syndrome, but no specific or sensitive tool for risk prediction has been developed. There are several factors that increase the likelihood of passage of meconium in-utero. They include – hypoxia, placental insufficiency, preeclampsia, maternal hypertension, maternal diabetes mellitus, maternal smoking, post term pregnancy, oligohydramnios, intrauterine growth restriction (IUGR).

The risk of developing MAS in an infant born through MSAF increases with heavy MSAF, nulliparity, fetal heart rate abnormalities, caesarean section and low Apgar scores. Three risk factors were identified for thick MSAF by Sankhyan and colleagues:

- Smoking, post term pregnancy, oligohydramnios, intrauterine growth restriction (IUGR).
- Increased severity of MSAF (heavy versus moderate).
- Intrapartum complications as a cause of meconium passage.
1) Maternal age >30,
2) Postdated pregnancy, and
3) Fetal distress with a negative and positive predictive value of 19.5% and 94.5% respectively.

It has been concluded that the predictors of MSAF are postdated pregnancy, cord problems, fetal distress, and retarded fetal growth while postdated pregnancy, increased maternal age > 30 years and fetal distress predicts thick MSAF.

The cause of MSAF is controversial, the relationship between MSAF and fetal asphyxia is unclear. A number of studies have failed to show any consistent effects of MSAF on Apgar scores, fetal scalp pH, or incidence of fetal heart rate abnormalities (Abramovici et al., 1974; Baker et al., 1992; Miller et al., 1975). These studies led to speculation that asphyxial episodes were too brief to decrease pH or Apgar scores. These conclusions were supported by a study showing that there was no correlation between the consistency of meconium and markers of fetal asphyxia (Trimmer and Gilstrap, 1991).

Several studies have suggested that the presence of meconium, especially thick meconium (Nathan et al., Berkus et al., 1994), increases the risk of fetal acidosis and an adverse neonatal outcome. Moreover, one study found that although MSAF correlated poorly with markers of acute intrauterine asphyxia (pH, lactate, and hypoxanthine concentrations), it correlated well with blood erythropoietin concentration (a marker of chronic intrauterine asphyxia). The strong correlation between MSAF and gestational age supports two additional theories:

1) Likely cause of meconium passage is the result of transient stimulation of parasympathetic nerves due to cord compression in a neurologically mature fetus.
2) Passage of meconium in utero is a natural phenomenon that reflects the maturity of the gastrointestinal tract.

Despite these theories, most authorities agree that MSAF in connection with fetal heart rate abnormalities is a marker for fetal distress and is associated with an increased perinatal morbidity.

Meconium passage is most likely to occur in the post-term baby, the term baby after asphyxia or the baby with IUGR. It rarely happens in preterm baby of <34 weeks gestation as even with severe asphyxia the anal sphincter does not usually relax.

Anoxia is often the cause of fetal distress that results in passage of meconium. The aspiration of meconium if sufficiently massive, will result in alveolar and bronchial obstruction, with overdistention of the peripheral alveoli, secondary atelectasis, and massive arterial alveolar block in those alveoli in which meconium has passed beyond the smaller bronchioles.

MAS causes respiratory distress in the infant after delivery, by several mechanisms. The initial presentation of MAS is primarily as a result of airway obstruction by thick meconium. However there are other mechanisms of injury as well.

The surfactant deficiency seen in MAS is not from an insufficient quantity of surfactant unlike a preterm neonate, but is likely a result of inhibited surfactant function(s) or alterations in surfactant composition. There is however limited information concerning specific adverse effects of meconium on surfactant.

**Chest X-ray**

The common early changes are widespread patchy infiltration and in 20-30% of the patients, small pleural effusions. Overexpansion is also common in the early stage. In mild-moderate cases, the changes resolve within 48 hours. In severe cases, as the disease progresses, by 72 hours of age with or without ventilation the appearances are often changed to that of diffuse and homogeneous opacification of both lung fields, as a result of a pneumonitis and interstitial oedema secondary to irritant effect of the inhaled meconium. These changes gradually resolve over the next week, but in severe cases the X-ray may still be abnormal at 14 days, and may merge in to the pattern seen in BPD, although this is uncommon. Airleaks, in particular pneumothorax and pneumomediastinum, are very common in MAS.

**Management of Persistent Pulmonary Hypertension of the Newborn (PPHN)**

Management of infant with MAS is primarily supportive. Maintenance of adequate oxygenation; good systemic blood pressure; and correction of acidosis, hypoglycemia, or other metabolic disorders are the main goals of treatment. An umbilical arterial catheter or radial arterial catheter should be inserted in infants who have moderate-to-severe MAS to monitor blood gases and blood pressure without disturbing the infant. Infants who have MAS with low blood pressure may present with clinical features of PPHN. Blood transfusion is indicated to keep hematocrit greater than 40% (0.40). For infants who have intrauterine hypoxia and sustained hypotension, physiologic replacement with hydrocortisone may help overcome possible adrenal insufficiency and may stabilize the blood pressure.

Because hypoxia, acidosis, and hypercapnia may increase pulmonary vascular resistance, oxygen and ventilator therapy should be administered to maintain appropriate blood gas values and acid-base balance. Infants who have PPHN are very labile during the acute phase of the disease. Maintain the arterial PO2 near or above 100 mm Hg. Arterial blood gases should be monitored frequently and oxygen and ventilator support weaned gradually until the acute stage is over and the infant’s condition stabilizes.

Early use of high-frequency ventilation (HFV), inhaled nitric oxide (iNO), or both may be needed to maintain appropriate blood gas values and acid-base balance. This approach may prevent PPHN which may subsequently develop.

Sildenafil given intravenously is an effective and selective pulmonary vasodilator, which completely reverses the alterations in resistance of pulmonary vasculature in this model of meconium aspiration syndrome. The fall in pulmonary vascular resistance was achieved by a combination of a decrease in pulmonary artery pressure without a change in wedge pressure, and an increase in cardiac output. The pulmonary hemodynamic changes produced by sildenafil in this model were comparable to those seen with nitric oxide inhalation therapy. Neither of these had a significant effect on oxygenation of the infant.

**Surfactant replacement**

At least two different mechanisms have been proposed for surfactant inactivation after lung injuries causing respiratory distress. A first model involves blood proteins, inflammation proteins and other surface-active substances, which compete with surfactant complexes from adhering to the interface. A second mechanism hypothesizes that surfactant dysfunction results from the intrinsic impairment of complexes of surfactant by small amphiphilic molecules such as free fatty acids,
cholsterol, lysolipids, bile acids, and/or diacylglycerol. These substances, in part coming from the degradation of surfactant itself by inflammatory phospholipases, insert into the surfactant complexes rendering it dysfunctional.\textsuperscript{21}

There is a dose dependent inhibitory effect of meconium. Low concentrations of surfactant are therefore relatively more sensitive to inhibition than high concentrations.\textsuperscript{22}

Promising effects of surfactant administration have been documented in animal models of MAS. Treatment with the clinically recommended dose of Curosurf improves lung compliance, gas exchange, and alveolar expansion in newborn rabbits and adult rats with experimental meconium aspiration but does not restore normal lung physiology.\textsuperscript{23}

**Mechanical Ventilation**

Mechanical ventilator management of the neonate with MAS is challenging because of the complicated altered pulmonary physiology resulting from atelectasis and areas of hyperinflation, in association with airway compromise and ventilation perfusion mismatch. Nearly 40% of babies with MAS require mechanical ventilation and additional 10% require continuous positive airway pressure (CPAP).\textsuperscript{24}

The extent of ventilator support depends on severity of respiratory distress. Some infants only require supplemental oxygen. In newborns with MAS who have hypercarbia (PaCO\textsubscript{2} > 60mmHg), hypoxemia (PaO\textsubscript{2} < 50mmHg), or acidosis (pH less than 7.25) in an oxygen-enriched environment with an inspired oxygen fraction (FiO\textsubscript{2}) > 0.6 are often considered candidates for mechanical ventilatory support.\textsuperscript{19}

**Role of Antibiotics**

Theoretically, the presence of meconium increases the chances of positive cultures from amniotic fluid in preterm and term newborns. Significantly, studies evaluating the development of sepsis in infants with MSAF failed to demonstrate that relationship. Atleast three randomized control studies reported that routine antibiotic prophylaxis is not recommended for those without perinatal risk factors in the management of MAS. Antibiotic therapy did not affect the clinical course and outcome related to infection without perinatal risk factors in MAS. The role of antibiotics in the management of MAS may need to be re-evaluated in more extensive trials\textsuperscript{19}

Unless there is significant risk for infection, prophylactic use of antibiotics in MAS did not help reduce infection. For suspected infection if antibiotics are started due to perinatal risk factors, consider discontinuing antibiotics once the blood culture results are negative.\textsuperscript{18}

**Extracorporeal Membrane Oxygenation: (ECMO)**

Extracorporeal Membrane Oxygenation (ECMO) has been used as a final rescue therapy in infants with severe and refractory hypoxemia with MAS. Usage of ECMO has decreased significantly in developed countries with the availability of HFV and iNO. Newborns with MAS make up approximately 35% of the infant population who require ECMO. The survival rate has approached 95% of infants with MAS who were managed with ECMO. In the ECMO register, the highest survival rates (>90%) were seen in the patients with MAS who qualified for ECMO.\textsuperscript{25}

**Potential Future Therapy**

Currently MAS treatments are all supportive in nature and do not directly affect the injurious effects of meconium on the lung. There is no effective and safe treatment or prophylactic measure for MAS once the meconium has gone below the vocal cords into the lungs. It has been suggested that fetal pancreatic digestive enzymes play a vital role in the lung damage after meconium aspiration by disrupting of intercellular connections and cell detachment from the basement membrane. In the treatment or prophylaxis, a protease inhibitor cocktail prevented the cell detachment induced by meconium suggesting that it may be useful.\textsuperscript{25}

**CONCLUSION**

The presence of Meconium stained amniotic fluid (MSAF) at delivery is a potential sign of fetal compromise. MSAF is known to be associated with several maternal and neonatal risk factors like hypoxia, placental insufficiency, preeclampsia, maternal hypertension, maternal diabetes mellitus, maternal smoking, post term pregnancy, oligohydramnios, intrauterine growth restriction (IUGR).

Meconium aspiration syndrome is a serious and potentially preventable condition occurring usually in term and post-term babies. Management of MSAF has changed substantially over years with use of sildenafil, ventilators, antibiotics, Extra corporeal Membrane Oxygenation.

**REFERENCES**


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