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Meconium aspiration syndrome and associated risk factors: An original research article

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Abstract

Introduction: Meconium Aspiration syndrome forms one of the common causes of respiratory distress in the newborn presenting with complications ranging from mild transient tachypnea to respiratory failure. This study analyzed newborns delivered in Nalanda Medical College and Hospital, Patna over the period of 3 months.

Objective: To know the incidence, clinical profile and associated risk factors of developing meconium aspiration syndrome in neonate delivered through meconium stained amniotic fluid (MSAF).

Material and Methods: 1196 live newborn babies delivered during the study period from July 2019 to September 2019 were enrolled in this study and assessed accordingly.

Result: During the present study, out of 1196 deliveries, 176 (14.7%) neonates were found to be born through MSAF. 76% of the babies born out of MSAF in our study had birth weight between 2.5 – 3.5 kg. Incidence of perinatal asphyxia among MSAF cases was 70.4%. It our study, 15.3% cases of MSAF developed MAS. Incidence of MAS was 2.2% out of total delivery in our hospital. Tachypnea and grunting were present in all cases of MAS. Out of 27 cases of MAS, 7 improved with CPAP, whereas 6 needed mechanical ventilation. Mortality among MAS was 14.8% in present study.

Conclusion: Meconium Aspiration Syndrome was the common cause of respiratory distress in neonate. Term and post terms, birth weight >2.5 kg, appropriate and large for gestational age, APGAR score <7, Oligohydramnios are some of the risk factors for developing meconium aspiration syndrome according to our study. It is concluded that good perinatal management can reduce the incidence of perinatal asphyxia and thus the complications of meconium aspiration syndrome to a great extent.

Keywords: meconium aspiration syndrome, meconium stained amniotic fluid, respiratory distress, perinatal asphyxia

Introduction

Meconium, the faecal material that accumulates in the fetal colon throughout gestation, is a term derived from the Greek *mekoni*, meaning poppy juice or opium; it was so named by Aristotle (350 B.C.) [1]. Meconium is sterile, thick, black-green, odourless material first observed in the fetal intestine during 3rd month of gestation. Meconium results from the accumulation of debris, including desquamated cells from the intestine and skin, gastrointestinal mucin, lanugo hair, fatty material from vernix caseosa, amniotic fluid and intestinal secretions. When aspirated into lung, either in the fetus or newly born infant, meconium may stimulate the release of cytokines and other vasoactive substances that lead to cardiovascular and inflammatory response. In the fetus, passage of meconium occurs physiologically early in gestation, when it contributes to alkaline phosphatase in amniotic fluid. Fetal defecation diminishes after 16 weeks and ceases by 20 weeks, concurrent with innervations of anal sphincter [2]. At that time, the rectum appears to be filled with meconium. From approximately 20 to 34 weeks, fetal passage of meconium becomes infrequent [3]. Most newborn infants who pass meconium are mature (term). Many are post-mature and the babies may exhibit peeling skin, long fingernails and decreased vernix. The vernix, umbilical cord and nails may be meconium stained, depending upon how long the infant has been exposed *in utero.* In general, nails become stained after 6 hours and vernix after 12 to 14 hours of exposure.

The passage of meconium normally occurs within the first 24 to 48h after birth. However, passage of fetal meconium resulting in MSAF, occurs in 8–20% of all deliveries [4, 7], increasing to 23–52% after 42 weeks of gestation [8, 9]. Meconium aspiration may occur before birth, or during the birth process. About 2–9% of infants born through MSAF develop MAS [5, 10, 11]. About one third of infants with MAS require intubation and mechanical ventilation [11]. Death occurs in 4.9% to 37% (median 12%) of infants with MAS [5].

The risk of meconium stained amniotic fluid is strongly correlated with gestational age. Meconium stained fluid is rarely seen prior to 37 weeks gestation but may occur in more than 30% of pregnancies that continue past 42 weeks gestation.

Meconium aspiration syndrome (MAS) is defined as respiratory distress in an infant born through meconium stained amniotic fluid (MSAF) with characteristic radiological changes and whose symptoms cannot be otherwise explained [4]. Cleary and Wiswell (1998) had proposed a severity criteria to define MAS: (a) mild MAS is a disease that requires less than 40% oxygen for less than 48 hours, (b) moderate MAS is a disease that requires more than 40% oxygen for more than 48 hours with no air leak, and (c) severe MAS is a disease that requires assisted ventilation for more than 48 hours and is often associated

with PPHN.

Traditionally the passage of meconium has been thought to be a sign fetal distress from hypoxia. The hypothesis is that in utero hypoxia results in diving reflex causing preferential shunt of blood to vital organs and ischemia to gut. The ischemia or mesenteric vasoconstriction results in transient period of hyperperistalsis and relaxation of anal sphincter due to vagal stimulation causing passage of meconium [12]. Vagal stimulation of a mature gastrointestinal tract either due to compression of fetal head of umbilical cord may cause passage of meconium. Aspiration of meconium into the lungs may occur from both in utero gasping and post Partum imbibitions during the initial breaths of the neonate.

Hypoxia could be the cause or effect or both of meconium aspiration, favours the view that intrauterine asphyxia is the cause which later on perpetuates and contributes to further hypoxia [13, 14]. Factors that promote the passage of meconium in utero include placental insufficiency, maternal hypertension, preeclampsia, oligohydramnios, and maternal drug abuse, especially of tobacco and cocaine. Factors associated with the development of MAS among infants with MSAF include thicker consistency of meconium, nonreassuring fetal heart tracing, fetal acidosis, caesarean delivery, meconium below the cords, infants who needed intubation at birth, and a low Apgar score [11, 15]. MAS remains a serious problem in developing and newly industrialized countries, and MAS accounts for about 10% of all cases of respiratory failure with 39% mortality rate [16].

The present study was undertaken with a view to:

- To calculate the incidence of MSAF and MAS in newborn delivered in tertiary level hospital in North India
- Observe clinical parameters, risk factors and outcome in neonates born out of MSAF deliveries.

Material and Methods

1196 live newborns delivered in Nalanda Medical College and Hospital, Patna, during the study period from July 2019 to September 2019 were included in this study and assessed accordingly.

The inclusion criterion was all babies delivered during study period. Newborns with Congenital anomalies including congenital heart disease and metabolic disorders like inborn errors of metabolism were excluded from the study. Incidence of MSAF, MAS along with the risk factors and final outcomes 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. Maternal data regarding age, parity antenatal care, presence of risk factors e.g. eclampsia, pregnancy induced hypertension etc. were noted as per the Performa. Babies with respiratory distress were admitted in NICU and managed as per unit protocol.

In neonates born out of MSAF deliveries, consistency of meconium, presence of meconium above or below the vocal card and Apgar score at 1 and 5 minutes were documented.

Definitions

Criteria for Meconium Aspiration: The baby was labeled to have meconium aspiration when, in meconium stained delivery, meconium was visualized below the vocal cord or some meconium could be sucked out during tracheal suctioning.

Criteria for Meconium Aspiration Syndrome:

1. Meconium staining of amniotic fluid and/or nails/umbilical cord/skin.
2. Development of respiratory distress soon after birth.
3. Radiological evidence of aspiration pneumonitis with areas of atelectasis and hyperinflation.

Criteria for severity of MAS:

It is based on the severity criteria proposed by Cleary G M & Wiswell TE [5] to define MAS:

1. Mild MAS is disease that requires less than 40% oxygen for less than 48 hrs.
2. Moderate MAS is disease that requires more than 40% oxygen for more than 48 hrs with no air leak, and
3. Severe MAS is a disease that requires assisted ventilation for more than 48 hrs and is often associated with persistent pulmonary hypertension.

Criteria for Birth Asphyxia

The baby was labelled to have suffered from birth asphyxia if his Apgar score was $\leq$ 6 at 1 minute.

(Severe birth asphyxia when Apgar at 1 min. $\leq$ 3, moderate birth asphyxia when apgar at 1 min 4-6).

All MSAF cases with respiratory distress were admitted in NICU had undergone septic work up consisting of total WBC count, differential count, mature to band cell ratio, CRP, micro-ESR and Hb%. A chest x-ray was done in all the cases.

Statistics

Quantitative data were presented as a mean and standard deviation (SD), and compared by one-way analysis of variance or Mann-Whitney *U*-test. Qualitative data were presented as percentages and compared using Pearson Chi Square or, in the case of very rare conditions, Fisher's exact test. A conditional logistic regression was used to determine significant independent variables associated with an increased risk of severe MAS. Adjusted odds ratio (OR) and their 95% confidence intervals (CI) were calculated. Level of significance assumed in all tests was 5%. Statistical analysis was done using SPSS 22.0 version.

Result

During the present study, out of 1196 deliveries, 176 neonates were found to be born through meconium stained amniotic fluid (MSAF), making the incidence of MSAF to be 14.7%. Out of these 176 newborns delivered through MSAF, 27(15.3%) developed MAS. Overall incidence of MAS among all delivered babies was 2.2%.

There was male preponderance in incidence of both MSAF and MAS, with 55.1% of MSAF contributed by male newborns. 17.5% of Male and 12.6% of female MSAF respectively went on to develop MAS (Table1). However, this difference was not statistically significant.

Table 1: Neonatal Risk Factors for MASF and MAS

		MSAF(n=176)	MAS (n=27)	P value
Gender	Male	97 (55.1%)	17 (63%)	0.4075
	Female	79 (44.9%)	10 (37%)	
Gestation Age	< 37 week	55 (31.3%)	3 (11.1%)	0.1120
	37- 42 weeks	109 (61.9%)	21 (77.8)	
	>42 weeks	12 (6.8%)	3 (11.1%)	
Birth Weight	<2.5 Kg	10 (5.7%)	1 (3.7%)	0.6818
	2.5 – 3.0 Kg	66 (37.5%)	9 (33.3%)	
	3.0 – 3.5 Kg	68 (38.6%)	11 (40.7%)	
	3.5 – 4.0 Kg	30 (17.1%)	5 (18.5%)	
	>4.0 kg	2 (1.1%)	1 (3.7%)	
Status At Birth	SAG	42 (23.9%)	2 (7.4%)	0.0875
	AGA	104 (59.1%)	20 (74.1%)	
	LGA	30 (17%)	5 (18.5%)	
APGAR	<3	68 (38.6%)	15 (55.6%)	0.0190
	3 -6	56 (31.8%)	10 (37%)	
	≥ 7	52 (29.6%)	2 (7.4%)	

Only 3 cases of MAS occurred in Post-term babies. However, incidence of MAS was significantly (p=0.0133) higher in newborns delivered beyond 37 weeks of gestation (Term + Post-term). It was observed that newborn weighing less than 2.5 kg contributed for only 5.6% case of MSAF and 3.7% of MAS. Maximum cases of both MSAF (76.1%) and MAS (74%) were observed among babies weighing between 2.5 kg and 3.5 kg. AGA babies contributed for 59.1% cases of MSAF and 74.1% cases of MAS. Incidence of MAS was significantly (p=0.0284) higher in AGA+LGA group, in comparison to SGA neonates. MAS occurred significantly higher in children having 1 min APGAR of less than 7. Incidence of both MASF and MAS was higher in Primipara (53.4% MASF; 59.3% MAS) and mothers having age more than 30 years (58% MSAF; 66.7% MAS) (Table 2). Newborns born through caesarean section had higher incidence of both MASF (60.8%) and MAS (66.7%).

Table 2: Maternal Risk Factors for MASF and MAS

		MSAF (n=176)	MAS (n=27)	P value
Parity	Primipara	94 (53.4%)	16 (59.3%)	0.5369
	Multipara	82 (46.6%)	11 (40.7%)	
Maternal Age	<30 years	74 (42%)	9 (33.3%)	0.3986
	≥30 years	102 (58%)	18 (66.7%)	
Mode of delivery	Caesarean Section	107 (60.8%)	18 (66.7%)	0.7020
	Normal Vaginal	51 (29%)	6 (22.2%)	
	Assisted	18 (10.2%)	3 (11.1%)	
Antenatal Care	Booked	78 (44.3%)	10 (37%)	0.5284
	Unbooked	98 (55.7%)	17 (63%)	

In our study the incidences of Antenatal risk factors with MAS were Oligohydramnios (37%), maternal anemia (33.3%), PIH (11.1%), Eclampsia (11.1%) and 7.4% each for PROM and Chorioamnionitis (Table 3).

Table 3: Incidence of Antenatal risk factors

	Maternal Anemia	PIH	PROM	Oligohydramnios	Eclampsia	Chorioamnionitis
MASF (n=176)	58 (32.9%)	28 (15.9%)	21 (11.9%)	28 (15.9%)	17 (9.6%)	12 (6.8%)
MAS (n=27)	9 (33.3%)	3 (11.1%)	2 (7.4%)	10 (37%)	3 (11.1%)	2 (7.4%)

All the neonates with mass had complaints of tachypnea and retractions. 81.5% had grunting and only 22.2% over distended chest (Table 4).

Table 4: Clinical Feature of MAS

Symptom and Sign	No. of cases (n=27)	Percentage
Tachypnea	27	100
Retraction	27	100
Grunting	22	81.5
Cyanosis	8	29.6
Over distended chest	6	22.2
Abnormal breath sound	6	22.2

Table 5: Severity Grade wise incidence of MAS

Severity Grade of MAS	No. Of Cases (n=27)	Percentage
Mild	13	48.1
Moderate	6	22.2
Severe	8	29.6

Incidences of mild, moderate and severe MAS in this study were 48.1%, 22.2% and 29.6% respectively (Table 5).
Out of 27 cases with MAS, 14 (51.8%) cases improved with oxygen therapy (nasal prongs, masks, HFNC), whereas, 7 (25.9%) cases needed CPAP support and 6 (22.2%) cases needed mechanical ventilation. 4 patients with MAS died, giving mortality of 14.8%.

Discussion

In this study, Meconium stained amniotic fluid (MSAF) cases were 14.7% out of total deliveries in our institute during study period. 27(15.3%) of MSAF cases went on to develop Meconium Aspiration Syndrome (MAS), overall incidence of MAS being 2.2% of all live births. These findings were similar to that observed by various authors, who described incidence of MSAF varying between 9 to 22% [17]. MAS have been reported to occur in between 8.4-25% cases of MASF [18, 19]. Incidence of MAS among MASF babies was found to be 10.5% in a study done by Narang *et al* [20], with the reported incidence of MAS out of total deliveries being 0.6%. Wiswell TE reported that MAS develops in 1.7% to 35.8% of infants born through MSAF [5]. Difference in incidence of MASF progressing to MAS in different studies can be attributed to associated co-morbid factors and interventions performed.
In the present study majority of MAS babies had gestational age between 37- 42 (77.7%), with 11.11% each contributed by preterm and post-term babies. This correlates with findings of study by Errkola *et al* [21], who found 95% cases of MAS in babies with gestation age of more than 36 weeks. In one another study, the incidence of MSAF increased with increasing gestational age of fetus i.e. 7% before 38 weeks, 78% between 38-42 weeks and 35% or more in pregnancies lasting longer than 42 weeks [22]. Katz and Bowes, (1992) observed that meconium passage was rare before 38 weeks of gestational age(GA) and increased after 40 weeks of gestational age [35]. Ostrea & Naqvi (1982), found that meconium passage occurs in 4% in gestation age < 38 weeks, in 6% between 39-42 weeks & in 52% in more than 42 weeks [36]. Our results also correlated with studies of Usher *et al*, who observed MSAF in 15.3% in 89-40 weeks 27 in 42 weeks and 31.5% in more than 42 weeks [37]. M Santomi *et al* (2011) found MSAF in 9.1 % in 22-36 weeks

GA, 11 % in 37-40 weeks GA and 22% in 41-43% of GA [38]. Fischer *et al* observed incidence of MSAF to be 3.52% in 37-38 weeks GA, 9.07 % in 39-41 week GA and 14.37% in 42-43 weeks GA [33]. These studies further confirm the increasing incidence of MSAF with advancing age found in our study.

These observations can be explained by the fact that the gastrointestinal tract of the preterm baby is relatively immature than term and post term babies. The relative deficiency of Motilin, an intestinal peptidase responsible for peristalsis, and relative immaturity and non-myelination of neural plexuses of gastrointestinal tract are responsible for less incidence of meconium passage in preterm babies.

We found maximum incidence (40.7%) of MAS among children weighing 3-3.5 kg. Various studies [19, 23] have previously similarly found higher incidence among children weighing 2.5-3.8 kg. Fischer *et al* (2011) found mean birth weight in MSAF to be 3388 $\pm$ 549 gms [33].

In our study, APGAR Score was >7 (7.4%), 3-6 (47%) and < 3 (55.5%), which is comparable with Gregory *et al* [24] who found APGAR > 7 (4.5%), 4-7 (49%) and < 3 (36.5%). It shows an important relation between APGAR Score and MAS babies. MAS babies with 1 min Apgar < 3 failed to show any improvement. In 1988 Falciglia *et al*[39], reported that 60% cases of MAS had Apgar score < 6 at 1 min and after resuscitation the number reduced to 3% at 5 min. Usta (1995) [40] showed 13% of MAS cases having Apgar < 4 at 1 min and 6% having Apgar < 7 at 5 min.

Pushpa Bhatia *et al* (2007) observed that Apgar score in 1 min was $\leq$ 3 in 51.7% of MAS and at 5 min $\leq$ 5 in 32.5% of MAS [41]. Uzma Firdaus *et al* (2010) showed that Apgar score in 1 min was $\leq$ 5 in 96.7% of MAS, after 5 minutes of resuscitation it was $\leq$5 in only 48.4% of MAS [42]. Fischer *et al* (2011) found apgar score to be $\leq$ 3 at 1 min in 51.7% MAS and $\leq$ 5 at 5 min, after resuscitation to be 32.5% [33].

From our study it was clear that babies who were severely depresses at birth did not improve event after doing active resuscitation. This was thought to be due to intrauterine asphyxia causing in utero passage of meconium and in utero gasping causing aspiration of meconium & subsequent MAS.

In our study 2 cases that had Apgar score > 6 at 1 minute developed MAS; leading to conclusion that MAS can develop even in babies with normal Apgar score.

Asphyxia could be the cause or effect or both of meconium aspiration and current understanding of in-utero meconium aspiration favors the view that intrauterine asphyxia is the cause which later on perpetuates and contributes to further hypoxia.

The present study revealed that incidence of MSAF was higher in primiparous mothers as compared to multipara. Various previous studies [31, 32, 33] have had similar observations.

The increase in incidence of meconium staining with advancing gestational age in present study was in agreement with findings of most other workers [33, 34].

In this study, antenatal risk factors for MAS were Oligohydramnios (37%), maternal anemia (33.3%), PIH (11.1%), Eclampsia (11.1%) and 7.4% each for PROM and Chorioamnionitis.

Pregnancy induced hypertension (PIH) has been found to be associated with 8.20 % to 23.58 % of case in various previous studies [23, 25, 26]. Premature rupture of membranes (PROM) has been reported in 3.10- 6.60% [25, 27], anemia in 22.2% [23] and Oligohydramnios in 4% [28] cases in various previous studies.

While studying the clinical profile of MAS cases tachypnea and retraction was observed in all the 27 cases. 81.5% had grunting, 29.6% patients developed cyanosis & 22.2% had over-distended chest and abnormal breath sounds. Wiswell *et al* [5] and many others had similar observations.

In the present study, it was found that out of 27 cases of MAS, 13(48.1%) presented as mild MAS, 6 (22.2%) as moderate & 8 (29.6%) as severe MAS. The finding were consistent with those of Carson *et al*, (1976) who reported 50% cases of mild, 16.6% cases of moderate & 33.3% cases of severe MAS out of total 18 cases [43].

Out of 27 cases with MAS, 14 (51.8%) cases improved with oxygen therapy (nasal prongs, masks, HFNC), whereas, 7 (25.9%) cases needed CPAP support and 6 (22.2%) cases needed mechanical ventilation. 4 patients with MAS died, giving mortality of 14.8%.

Mortality of MAS cases in our study was 14.8% with 22.2% needing mechanical ventilation during their NICU stay. Previous studies had stated need for mechanical ventilation ranging from 29.7 – 44% cases of MAS [29, 30].

Conclusion

Meconium Aspiration Syndrome is one of the common clinical conditions observed during neonatal period and is one of the important causes of respiratory distress in newborns, contributing significantly to the neonatal morbidity and mortality. The presence of Meconium stained amniotic fluid (MSAF) at delivery is an indicator of probable fetal compromise. MSAF is usually associated with several maternal and neonatal risk factors like hypoxia, placental insufficiency, preeclampsia, maternal hypertension, post-term pregnancy, Oligohydramnios. It is concluded that good antenatal and intrapartum care and management can significantly reduce the incidence of meconium aspiration syndrome.

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