Original article:

Clinical profile and outcome of meconium aspiration syndrome in a rural based tertiary care centre of Maharashtra

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ABSTRACT

Objectives – Our objective was to study clinical profile and outcome of meconium aspiration syndrome in a rural based tertiary care centre of Maharashtra

Methodology –All intramural neonates born through meconium stained amniotic fluid formed the population of our study .They were classified inmild, moderate and severe MASand their epidemiological profile and outcome were studied.

Results –Out of total 14,856 deliveries during the study period, 13818 were live births,2432 delivered with meconium stained amniotic fluid of which 211 (8.29%)developed MAS. Applying exclusion criteria, 205 formed the group. Mean gestational age was 39 weeks (32-44 weeks). Mean birth weight was 2625 grams (1078-3975 grams). Male: female ratio was 1.63:1 of 205 MAS cases, 104 were mild,49 moderate and 52 severe. Thick meconium and foetal distress were more frequently associated with severe than moderate or mild MAS. HIE (22.92%) was the most common complication followed by sepsis (18.53%) and PPHN (9.27 %).

Mortality was 0 in mild, 1 in moderate and 16 in severe MAS. Commonest cause of mortality was acute respiratory failure (70.58 %)followed by HIE (47.05 %).

Conclusion-Meconium aspiration syndrome is a serious neonatal emergency. Early anticipation and preparedness, thorough suctioning, close monitoring and early interventions are the keys for a good outcome.

Keywords – Meconium aspiration syndrome, Complications.

INTRODUCTION

Meconium Aspiration Syndrome (MAS) remains one of the most common causes of neonatal respiratory distress.[1]The overall frequency of meconium stained amniotic fluid varies between 5 to 25% (median 14%). Meconium aspiration syndrome occurs in 10% of infants born through meconium stained amniotic fluid (MSAF).[2] Meconium aspiration syndrome is a disease with complex pathophysiology and a potential for mortality and considerable morbidity. Traditionally meconium has been viewed as a harbinger of impending or ongoingfoetal compromise: however some investigators believe that it is not associated with foetal hypoxia, acidosis or foetal distress. Others found lower APGAR scores in meconium stained neonates. The predictive value of meconium was better when it occurred in high risk patients and was thick,dark and tenacious. Lightly stained meconium had a poor correlation with foetal hypoxia. The moderate and thick meconium group has significantly greater risk of an

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abnormal FHR tracing, a 1 and 5 minute APGAR scores less than 7, a cord PH less than 7.2,sepsis, need for oxygen requirement and level 3 NICU admission for babies. Various risk factorsare associated with increased mortality and morbidity in MAS like post-term babies,primipara and grand multipara,unbooked mothers,mothers with toxaemia of pregnancy or prolonged rupture of membranes, infants with moderate or severe birth asphyxia and operative deliveries.[3] Thick MSAF is more likely with increased maternal age, postdated pregnancy and foetal distress. In the last decades, the incidence of MAS has been decreasing which has been attributed to- 1) improved obstetrics practices, including avoidance of post term pregnancy and caesarean deliveries prior to evidence of foetal distress.[4] 2) The use of adjunct respiratory therapies such as exogenous surfactant, nitric oxide and high frequency oscillatory ventilation in the management of neonates with MAS.[5] However, MAS is still a major cause of morbidity and mortality in the neonatal period (the mortality rate of newborns with MAS was close to 50% in 1970's but currently ranges between 5% and 37%).[6] Only a few studies from developing countries have looked at the clinical profile.[7,8,9]Aim of this study is to study clinical profile and outcome of Meconium aspiration syndrome.

MATERIALS AND METHODS

STUDY DESIGN: Prospective Observational hospital based Study.

PERIOD OF STUDY: 2 years and 2 months (September 2012 to October 2014).This study was carried out in Neonatal Intensive Care Unit of Rural Medical College, Pravara Institute of Medical Sciences, Loni, District Ahmednagar, Maharashtra.

Singleton inborn neonates with meconium aspiration syndrome delivered during above mentioned period were included in the study.

EXCLUSION CRITERIA:

1. Neonates with life threatening congenital anomalies like open neural tube defects, diaphragmatic hernia etc.
2. Babies who are extremely low birth weight (<1000 grams).
3. Babies of extreme prematurity (<28 weeks of gestation).
4. Babies born to mothers positive for VDRL, HBsAg, HIV.
5. Neonates of multiple gestations.

Those who were born through meconium stained amniotic fluid but did not develop distress and chest X-Ray was normal, were not included in the study. The study was started after obtaining approval from the institutional ethics committee and written consent was taken from parents of neonates, to include them in the study.

The criteria used for diagnosing meconium aspiration syndrome were:[10]

- Presence of meconium below the vocal cords.
- Clinical respiratory distress in the first 24 hrs of life.
- Abnormal CXR consistent with aspiration pneumonitis.

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METHODOLOGY:

A detailed maternal history was elicited to find out the etiology of passage of meconium into the amniotic fluid, maternal risk factors like Ante partum hemorrhage, placenta previa, pregnancy induced hypertension, eclampsia, smoking, gestational diabetes, oligohydramnios etc. and history of premature rupture of membranes, maternal VDRL, HBsAg, HIV status was taken. Natal history was taken to find out the mode of delivery and indications for interventions, if any. Complications during and prior to labor (obstructed or prolonged labor, fetal distress) were noted. Gestational age in completed weeks was assessed on basis of mother's last menstrual period and confirmed where ever necessary by routine early antenatal ultra sonography (USG) examination. In some cases where ever last menstrual period (LMP) was not available and antenatal USG was not done, then gestational age was assessed by New Ballard's scoring system.[11] Postnatalhistory was obtained regarding birth asphyxia, cyanosis or any other complications and for details of resuscitation measures done at birth. APGAR score at 1 min. and 5 min. was assessed. Babies born through MSL were managed as per Neonatal resuscitation program of American Academy of Pediatrics 2010.[12] Babies born through MSL were managed as per NRP guidelines as modified from time to time.[13] A detail clinical examination was done; Respiratory distress was monitored throughout the hospital stay by using Downe's scoring system in term babies and by Silverman Anderson scoring in preterm. SpO_2 was constantly measured by pulse oxymetry. Onset of distress (in hours of life) and Downe's score (maximum during hospital stay) were noted and correlated with outcome of the baby. Along with routine investigations, Radiological assessment was undertaken with serial X-Rays as directed by the condition, 2 D-ECHO was done for confirmation of diagnosis of PPHN. Transient metabolic disturbances with blood glucose, serum calcium, electrolytes and arterial blood gases (ABG) were done and interpreted whenever required. All infants with the diagnosis of meconium aspiration syndrome were treated in NICU with oxygen, restricted intravenous fluids, antibiotics, inotrope support and ventilator support as and when required. Surfactant was advised to all cases of severe MAS and moderate MAS but because of its high cost and unaffordablity of parents, it was given to some patients whose parents were willing. Surfactant was given with all aseptic precaution by INSURE technique in small aliquots.

STATISTICAL ANALYSIS-

Data analysis was done by descriptive statistics as mean, SD, median, range and percentage. Comparison was done by applying Chi-square test, Chi- square test with Yates correction, paired 't' test, unpaired 't' test, Mann-Whitney test, Kruskal-Wallis test (Non parametric ANOVA), Dunn's multiple comparison test. Significance was assessed at 5% level of significance ($p < 0.05$). GraphPadInstat version 3.10 software was used for statistical analysis. Microsoft word and excel was used to generate graphs, tables and master chart. When data was qualitative and all variables were more than 5 then Chi-square test was used, when data was qualitative and one of the variables was less than 5, then Chi-square test with Yates correction was used. When data was quantitative then tests used were as follows- Dunn's multiple comparison test, a non parametric test, was used when data was quantitative and number of comparison groups were more than 2 and normality test was not passed. This test is quite similar to Kruskal-Wallis test except that we can make out difference between any two individual groups when there are more than 2 groups.

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RESULTS AND SUMMARY:

Out of total 14,856 deliveries during the period of September 2012 to October 2014. 13,818 were live births, out of which 2,432 were delivered through MSAF. Out of 2,432 MSAF cases, 211 (8.68%) developed MAS. Overall incidence of MAS was 15.27 per thousand live births. Overall study population was 205 cases, 6 cases were excluded based on our exclusion criteria. Male: Female' ratio was 1.63: 1. Primigravida mothers were 60%. Mean gestational age was found to be 39.08 ± 2.19 weeks, Median of gestational age was 39 weeks with majority of the cases between 37-39 weeks (54.15%). Total term babies were 83.41%, preterm were 8.30% and post term were also 8.30%. Minimum age of gestation was 32 weeks and maximum was 44 weeks. Mean birth weight was 2529 ± 574 grams, median of birth weight was 2625 grams, minimum birth weight observed was 1078 grams and maximum was 3975 grams. Most common birth weight category was 2501-3500 grams: 55.61%.

Most commonly associated maternal risk factor was foetal distress (44.39%), moderate to severe anemia was found in 21.95%. Only 23.86% mothers were not having any associated risk factors. Other associated risk factors were anemia, PIH, pre-eclampsia, eclampsia, oligohydramnios, premature rupture of membranes. In our study, total number of babies born through thick MSAF was 160 (78.04%) and that through thin MSAF were 45 (21.96%). 'Thick meconium: Thin meconium' ratio = 3.55:1. Foetal distress was found to be more common with thick meconium. We observed that thick meconium was more associated with severe MAS followed by moderate MAS. LSCS (n=95, 46.34%) and vertex vaginal route (n=94, 45.85%) were commonest mode of delivery. Instrumental deliveries were more common in severe MAS followed by moderate.

It was observed that among the total 205 MAS cases, majority belonged to the category of mild MAS (n=104, 50.73%), followed by severe MAS (n=52, 25.37%) and moderate MAS (n=49, 23.90%). There was no significant difference in gravida, birth weight, sex and gestational age between mild, moderate and severe MAS.

'Vigorous: Non-vigorous' ratio: 1.4:1. Number of non-vigorous babies was highest in severe MAS followed by moderate MAS. There was statistically significant association between thick meconium with non-vigorous babies and thin meconium with vigorous babies.

In our present study, APGAR score at 1 minute was between 0-3 in 38 (18.53%), 4-6 in 96 (46.83%) and ≥7 in 71 (34.64%) babies. Mean APGAR score at 1 minute was 5.34 ± 2.05 and median score was 6, ranging between 1-9. APGAR score at 5 minute was 0-3 in 5 (2.43%), between 4-6 in 50 (24.39%) and >7 in 150 (73.18%) patients. Mean APGAR score at 5 minute was 7.42 ± 2.05, Median score was 8, ranging between 3-10.By applying Chi-square test, there was statistically significant difference in APGAR score at 1 minute and 5 minute. Chi-square value, $\chi 2 = 68.059$, d.f = 2. p value <0.0001 (extremely significant).

We also found that in mild MAS (n=104), mean APGAR score at 1 minute was 6.63±1.30 and at 5 minute was 8.33±0.84. Median at 1 minute was 7, ranging between 3-9. Median at 5 minute was 8, ranging between 6-10. In moderate MAS (n=49), mean APGAR score at 1 minute was 4.95±1.35 and at 5 minute was 7.34±1.09. Median at 1 minute was 4, ranging between 3-9. Median at 5 minute was 7, ranging between 6-10. In severe MAS (n=52), mean APGAR score at 1 minute was 3.13±1.76 and at 5 minute was 5.67±1.57. Median at 1 minute was 3, ranging between 1-9. Median at 5 minute was 6, ranging between 3-10.By applying Kruskal-Wallis test (non-parametric ANOVA) it was

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found that difference in APGAR score of all categories was statistically significant. p value is <0.0001, considered extremely significant.By applying Dunn's multiple comparison test, it was found that there was statistically significant difference in APGAR score at 1 minute between mild and moderate MAS, mean rank difference was 52.947 and p value <0.001 (highly significant), between mild and severe MAS, mean rank difference was 97.736 and p value <0.001 (highly significant) and between moderate and severe MAS, mean rank difference was 44.788 and p value <0.001 (highly significant).

Among the patients who survived (n=188), mean APGAR score at 1 minute was 5.62±1.87 and at 5 minute was 7.65±1.34. Median at 1 minute was 6, ranging between 1-9. Median at 5 minute was 8, ranging between 3-10. Among the patients who expired (n=17), mean APGAR score at 1 minute was 2.35±1.42 and at 5 minute was 4.82±1.55. Median at 1 minute was 2, ranging between 1-6. Median at 5 minute was 5, ranging between 3-8.By applying Mann-Whitney test, it was found that the difference in APGAR score between the patients who survived and who expired was statistically significant. Two tailed p value is <0.0001, considered extremely significant. Mann-Whitney U-statistic = 300.00. U' =2896.0.

Out of total 205 cases of MAS, 120(58.54%) cases were vigorous at birth, of which 71 (34.63%) required Oro-nasal suction (ONS) and 49 (23.90%) required Oro-nasal suction along with oxygen (ONS+0_2). 85(41.46%) cases were non vigorous at birth and required resuscitation, of which 56 (27.31%) required Endo tracheal suctioning (ETS) along with oxygen, 21 (10.24%) required ET suctioning with bag and tube ventilation (ETS+BT) and 8 (3.90%) cases required ET suction with bag and tube ventilation with cardio-pulmonary resuscitation (ETS+BT+CPR).

Onset of respiratory distress was observed at birth in majority of the cases (n=118, 57.56%) and 59 (28.78%) developed distress within 6 hours of life. Mean duration of onset of respiratory distress was 2.21±3.73 hours with median at 0 hour of life (since birth). By applying Kruskal-Wallis test (non-parametric ANOVA), it was found that difference in onset of distress among all categories was statistically significant. pvalue <0.0001, considered extremely significant. Kruskal-Wallis statistic, KW = 59.841.

By applying Dunn's multiple comparison test, it was found that there was statistically significant difference in onset of distress between mild and moderate MAS, mean rank difference was 48.604 and p value <0.001 (highly significant), between mild and severe MAS, mean rank difference was 64.111 and p value <0.001 (highly significant) but between moderate and severe MAS mean rank difference was 15.506 and p value >0.05 (NOT significant). There was no significant difference in onset of distress between moderate and severe MAS.

Among the patients who survived (n=188) mean duration of onset of distress was 2.42 ± 3.83 hours with median at 0 hours ranging between 0-16 hours. Among the patients who expired (n=17) it was observed that distress started since birth in all patients, hence mean and median was at 0 hours.It was not possible to analyze this data statistically as in the group of dead patients mean and standard deviation was 0, but it was clearly observed that there was a difference in the onset of distress between the patients who survived and those who expired.

In our study, it was observed that out of 205 cases of MAS, 104 (50.73%) had Downe's score between 0-3 (mild respiratory distress), 58 (28.29%) had score between 4-6 (moderate respiratory distress) and remaining 43 (20.98%) had score between 7-10

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(severe respiratory distress). Mean Downe's score in all patients was 4.64±2.29, median was 3, range between 2-10. It was observed that, majority of the cases had mild respiratory distress which corresponds to the number of mild MAS cases but few cases (n=9) had moderate respiratory distress according to Downe's score but they were categorized in severe MAS as they required assisted ventilation for maintaining saturation within normal range or were having air leaks with moderate respiratory distress.

In our study, we also found that in mild MAS (n=104), mean Downe's score was 2.88±0.35 hours with median of 3, rangebetween 2-4. In moderate MAS (n=49), mean Downe's score was 4.80±0.45 with median at 3, range between 3-5. In severe MAS (n=52), mean Downe's score was 8.09±1.39 with median at 8, range between 5-10.By applying Kruskal-Wallis test (non-parametric ANOVA) it was found that difference in Downe's score among all categories was statistically significant. P value is <0.0001, considered extremely significant. Kruskal-Wallis statistic, KW = 186.52.

Among the patients who survived (n=188), mean Downe's score was 4.28±1.93 with median of 3 ranging between 2-10. Among the patients who expired (n=17) mean Downe's score was 8.94±1.39 with median of 9 ranging between 5-10.By applying Mann-Whitney test, it was found that difference in Downe's score between the patients who survived and patients who expired was statistically significant. Two tailed p value is <0.0001 (considered extremely significant) Mann-Whitney U-statistic = 148.50, U' =3047.5.

It was observed that most common complication associated with MAS was hypoxic ischemic encephalopathy 22.92% followed by sepsis 18.53%. Persistent pulmonary hypertension was third most common 9.27%. Other complications like hypotensive shock, acute respiratory failure were also present in significant number of cases. Complications like air leaks, NEC, IVH, PH, meningitis were seen in few cases. Total 122 (59.51%) patients were not associated with any major complication.

In our present study, out of the total 205 MAS cases, 17 expired (8.29%). Among 104 mild MAS cases all survived, among 49 moderate MAS cases 1 expired (2.04%) and 16 (30.76%) expired among 52 severe MAS cases. Of the total 17 deaths, it was found that most common cause of mortality was acute respiratory failure (n=12, 70.58%), followed by HIE (n=8, 47.05%) and sepsis (n=8, 47.05%).

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TABLE 2: DESCRIPTIVE PARAMETERS OF CATEGORIES OF MAS

CATEGORY	MILD		MODERATE		SEVERE		TOTAL	
	n=104	%	n=49	%	n=52	%	n=205	%
MALE	67	64.42%	24	48.97%	36	69.23%	127	61.95%
FEMALE	37	35.58%	25	51.03%	16	30.77%	78	38.055
MEAN GESTATION (weeks)	39.43	_	39.14	_	38.32	_	39.08	_
MEAN BIRTH WEIGHT (grams)	2602	_	2558	_	2357	_	2529	_
PRIMIGRAVIDA	61	58.65%	29	59.18%	33	63.46%	123	60%
MULTIGRAVIDA	43	41.35%	20	40.82%	19	36.54%	82	40%
THICK MSL	69	66.34%	40	81.63%	51	**98.07%**	160	78.04%
THIN MSL	35	33.66%	9	18.37%	1	1.93%	45	21.96%
VIGOROUS	90	86.53%	23	46.94%	6	11.53%	119	58.05%
NON VIGOROUS	14	13.47%	26	53.06%	46	**88.47%**	86	41.95%
LSCS	50	48.07%	23	46.94%	22	42.30%	95	46.34%
VAGINAL	54	51.93%	22	44.89%	20	38.46%	96	46.83%
INSTRUMENTAL DELIVERY	0	0%	4	8.16%	10	**19.23%**	14	6.83%
DEATH	0	0%	1	2.04%	16	**30.76%**	17	8.29%

TABLE 1: COMPLICATIONS ASSOCIATED WITH MAS

Complications	No. of patients	Percent (%)
HIE	**47**	**22.92%**
ARF	18	8.78%
Sepsis	**38**	**18.53%**
Shock	18	8.78%
PT	4	1.95%
PPHN	19	9.27%
Meningitis	14	6.83%
NEC	9	4.39%
Other (DIC, IVH, PH)	10	4.88%

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GRAPH 1: BAR DIAGRAM: COMPLICATIONS ASSOCIATED

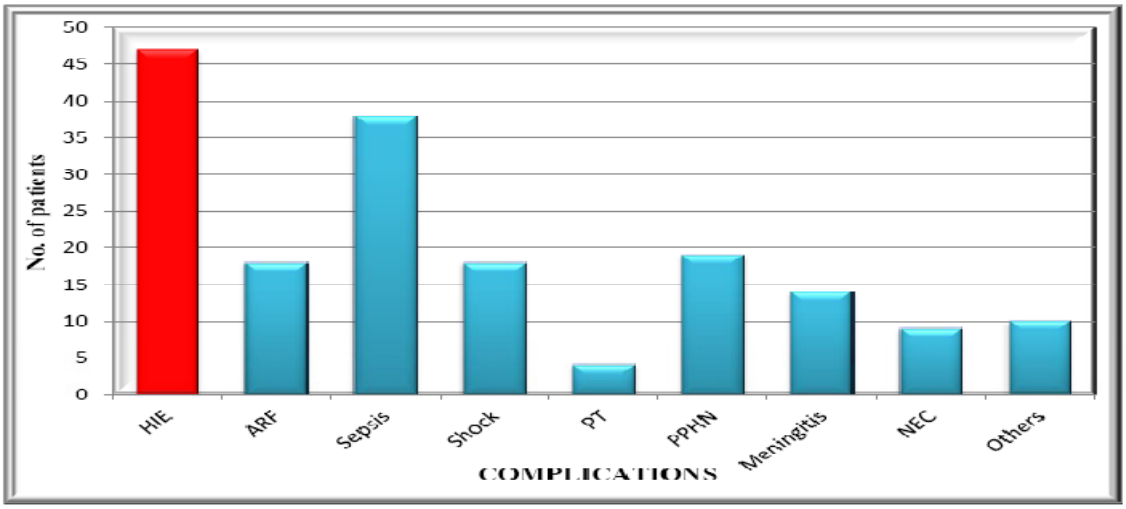

TABLE 3: CAUSE OF DEATH IN MAS

Death no.	CAUSE OF DEATH							
	HIE	ARF	PPHN	PT	PH	DIC	SEPSIS	IVH
1	+	+						
2		+	+					
3		+				+	+	
4		+		+				
5	+						+	+
6		+	+					
7	+	+						
8	+	+						
9		+						
10						+	+	
11	+	+						
12	+				+	+	+	
13	+						+	
14		+			+			
15	+					+	+	
16		+		+			+	
17		+				+	+	
TOTAL	8	12	2	2	2	5	8	1

CONCLUSION:

MAS is a serious disorder of the newborn. Our study confirms the high prevalence of MSAF after 37 weeks, but the incidence of MAS in neonates does not depend on gestational age[14]. Our study also indicates that moderate or thick amniotic fluid and foetal distress may help to anticipate the need for neonatal resuscitation in delivery room whatever gestational age is. It was also concluded that inutero passage of meconium in premature infants is uncommon (8.3%). We observed thatthick meconium was more associated with severe MAS followed by moderate MAS. The term vigorous baby, delivered through thin meconium, who is pink on oxygen (FiO_2 <40%) also needs close vigilant monitoring for sudden detoriation to moderate or severe MAS, with or without air leaks. In the end it is concluded that the knowledge of antenatal and intrapartum factors associated with MSAF provides easy prediction of adverse outcomes in neonates who can be managed by optimal timely intervention in order to avoid severe asphyxia and meconium aspiration and its complications.

Contributors:

AK planned the study,collected data, conducted analysis and drafted manuscript. RC planned the study, prepared the protocol, guided the study and drafted manuscript. ND searched literature and conducted analysis. RB searched literature and helped in retrieving the articles, VB conducted analysis and drafted manuscript. AK and RC will act as guarantors.

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