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Severity, complications and outcome of meconium aspiration syndrome in neonates.

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ABSTRACT... Objective: To determine the severity, complications, and outcomes of meconium aspiration syndrome (MAS) in neonates. **Study Design:** Cross-sectional study. **Setting:** Neonatal Intensive Care Unit (NICU) of the National Institute of Child Health, Karachi, Pakistan. **Period:** January 2024 to June 2024. **Methods:** Neonates aged 1-28 days of either gender, and having MAS were analyzed. Vital signs were noted and necessary laboratory investigations were done. Presenting clinical features and associated complications of MAS were noted. Outcome was noted in the form of discharged, admitted to pediatric unit, or mortality. **Results:** In a total of 92 neonates, 66 (71.7%) were male. The mean age was 12.47±6.55 days. Evaluation of MAS severity revealed mild, moderate, and severe cases among 2 (2.2%), 16 (17.4%), and 74 (80.4%) neonates, respectively. The most frequently noted complications were sepsis 65 (70.7%), hyperinflated lungs 55 (59.8%), respiratory distress 34 (37.0%), and pulmonary hypertension 31 (33.7%), were the most commonly associated complications of MAS. Two neonates left against medical advice so those were excluded from the final outcome analysis. In the remaining 90 neonates, mortality was reported in 6 (6.7%). Mortality had significant association with bluish skin at presentation (p=0.044), severe MAS (p=0.001), and pulmonary hypertension (p=0.001). **Conclusion:** Vast majority of the neonates (80.4%) presented with severe MAS which should raise alarm about the time identification of these high risk neonates. The most frequently noted MAS associated complications were sepsis, hyperinflated lungs, respiratory distress, and pulmonary hypertension. At presentation, bluish skin, pulmonary hypertension, and severe MAS were significantly associated with mortality.

Key words: Cyanosis, Meconium Aspiration Syndrome, Pneumonitis, Respiratory Distress, Sepsis.

INTRODUCTION

Meconium, the gastrointestinal excreta of the fetus, originates from the Greek word "mekonion," meaning "from poppy" or "like opium." It is a thick, sticky, odorless, dark green substance composed of intestinal epithelial cells, lanugo, mucus, amniotic fluid, bile, and water.[1] Typically, meconium remains in the infant's bowel until after birth, but occasionally it is expelled into the amniotic fluid.[2] Meconium staining of amniotic fluid (MSAF) is a relatively common issue, occurring in 7-22% of all term deliveries.[3] Meconium aspiration syndrome (MAS) develops in approximately 5% of MSAF cases and contributes to neonatal death in up to 0.05% (1 in 2000) of all pregnancies.[4] Unfortunately, Pakistan ranks third among the ten countries contributing to two-thirds of the world's neonatal deaths, with an estimated neonatal mortality rate of 42 per 1000 live births.[5]

Risk factors for the passage of meconium in utero include placental insufficiency, maternal hypertension, preeclampsia, oligohydramnios, and maternal drug abuse.[6,7] Neonatal Intensive Care Unit (NICU) admissions and complications such as MAS, perinatal asphyxia, neonatal sepsis, cerebral palsy, and seizures are more commonly observed in these cases.[8] MAS is categorized as mild, moderate, or severe based on the oxygen required, the duration of oxygen therapy, and radiological findings, which range from normal appearance to diffuse patchy infiltrates and consolidation.[9]

A study by Kumar A, et al., evaluated 205 neonates, finding mild MAS in 50.7%, moderate MAS in 23.9%, and severe MAS in 25.4%.[10] The most commonly reported complication was hypoxic ischemic encephalopathy (HIE) in 22.9%,

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followed by neonatal sepsis (18.5%), persistent pulmonary hypertension of the newborn (PPHN) (9.3%), and death (8.3%). A local study reported that among neonates with MAS, 11.1% required mechanical ventilation.[11] Local data on the severity and complications of MAS in neonates is scarce, necessitating this study to generate valuable local data. This research aimed to identify the issues associated with MAS in our setting, ultimately improving the outcomes for affected babies. This study aimed to determine the severity, complications, and outcomes of MAS in neonates.

METHODS

This cross-sectional study was conducted at the NICU of the National Institute of Child Health, Karachi, Pakistan from January 2024 to June 2024 following the approval from institutional ethical review board (letter number: IERB-10/2023, dated: 18-12-2023). The sample size was calculated using the WHO software for "Sample size calculation," based on a study by Mohammad N, et al., which reported that 11.1% of neonates with MAS required mechanical ventilation.[11] With a confidence interval of 95% and a margin of error of 6.5%, the required minimum sample size was 90. A non-probability consecutive sampling technique will be employed. The inclusion criteria for this study were neonates aged 1-28 days of either gender, and having MAS. Neonates with congenital anomalies, those who required CPR at birth, and those whose parents are unwilling to participate were excluded.

Data collection commenced after obtaining written and informed consents from the parents/caregivers of the neonates. Vital signs, including respiratory rate, blood pressure, pulse, oxygen saturation, and temperature, were recorded. Signs and symptoms of MAS were evaluated, and a chest x-ray were performed to confirm MAS. Blood samples were collected for a complete blood count (CBC) and random blood sugar evaluation. The presence of complications and the final outcome (discharge or mortality) were recorded until the child was discharged from the hospital. Neonate were labeled to have MAS if they presented with one or more of the following symptoms: tachypnea (rapid breathing > 60 breaths per minute), retractions (difficulty in breathing), grunting sounds with breathing, and cyanosis (bluish or purple skin color), confirmed by chest x-ray showing hyperinflation and patchy opacities.[9] MAS severity is categorized as mild (requiring < 40% oxygen for < 48 hours), moderate (requiring > 40% oxygen for > 48 hours), and severe (requiring assisted ventilation for > 48 hours). Complications to be monitored included pneumothorax (diagnosed clinically and confirmed on chest x-ray), pulmonary hypertension of the newborn (PHN) (defined by pre- and post-ductal oxygen saturation difference of >10% or echocardiographic evidence), respiratory distress (respiratory rate > 60 breaths per minute), and neonatal sepsis (diagnosed by a combination of clinical symptoms and positive blood culture report). Data was recorded on a structured proforma.

For statistical analysis, IBM-SPSS Statistics, version 27 was used. Mean and standard deviation were calculated for quantitative variables such as age (days), gestational age (weeks), maternal age (years), weight at admission (kg), weight at birth (kg), length of hospital stay (days), respiratory rate (breaths/min), blood pressure (mmHg), pulse (per minute), oxygen saturation (%), temperature (°C), total leukocyte count (cells/mm^3), absolute neutrophil count (cells/mm^3), platelet count (cells/mm^3), and random blood sugar (mg/dl). Frequencies and percentages were calculated for categorical variables such as gender, age, tachypnea, retractions, grunting sounds with breathing, cyanosis, severity of MAS (mild, moderate, severe), MAS complications (mechanical ventilation, pneumothorax, pulmonary hypertension (PHN), respiratory distress), and outcome (discharge or mortality). Effect modifiers like gender, age, gestational age, maternal age, weight at birth, length of hospital stay, severity of MAS, and complications were controlled through stratification. The chi-square test was applied to compare categorical data while independent sample t-test was used to compare quantitative data. P value below 0.05 was considered significant.

RESULTS

For this study, a total of 92 neonates were enrolled as per inclusion and exclusion criteria. Among these 92 neonates, 66 (71.7%) were male. The mean age was 12.47±6.55 days. The most frequent clinical presentations were tachypnea, nasal flaring, retractions, grunting sounds, cyanosis, and bluish skin, noted in 92 (100%), 92 (100%), 86 (93.5%), 86 (93.5%), 57 (62.0%), and 14 (15.2%), respectively. The most frequently noted complications were sepsis 65 (70.7%), hyperinflated lungs 55 (59.8%), Respiratory distress 34 (37.0%), pulmonary hypertension 31 (33.7%), HIE 30 (32.6%), chemical pneumonitis 20 (21.7%), flattened hemidiaphragm 18 (19.6%), and gas taping 8 (8.7%).

Retractions were significantly more common in males (97.0% vs. 84.6%, p=0.031), and in neonates aged 8-28 days (97.2% vs. 80.0%, p=0.006). Grunting sounds were more prevalent in males (97.0% vs. 84.6%, p=0.031). Cyanosis was significantly higher in males (69.7% vs. 42.3%, p=0.015), and more common in older neonates (70.8% vs. 30.0%, p=0.001). The severity of MAS showed that severe MAS was more frequent in males (84.8% vs. 69.2%, and was significantly higher in neonates aged 8-28 days (83.3% vs. 70.0%, p=0.022). Mild MAS was only noted in males (3.0%) and younger neonates (10.0%). In terms of complications, sepsis was more common in males (75.8% vs. 57.7%), and significantly higher in older neonates (76.4% vs. 50.0%, p=0.022). Hyperinflated lungs were significantly more frequent in males (p=0.035). Pulmonary hypertension was significantly higher in neonates aged ≤7 days (70.0% vs. 23.6%, p<0.001). HIE was significantly more common in relatively older neonates (38.9% vs. 10.0%, p=0.015). Chemical pneumonitis was significantly more prevalent in females (100% vs. 69.7%, p=0.002), and was also higher in younger neonates (100% vs. 72.0%, p=0.008). Table-I presents the association of gender, and age with clinical presentation, severity, and associated complications of MAS in neonates.

Two neonates left against medical advice so those were excluded from the final outcome analysis. In the remaining 90 neonates, mortality was reported in 6 (6.7%). Mortality had significant association with bluish skin at presentation (p=0.044), severity of MAS (p=0.001), respiratory distress (p=0.028), pulmonary hypertension (p=0.001), and chemical pneumonitis (p=0.029). Table-II presents association of final outcome with respect to demographics, clinical presentation, severity and complications of MAS in neonates.

Baseline diastolic blood pressure was significantly less among neonates who died (p<0.001). Platelet count was significantly high among neonates who died (p<0.001). Table-III is showing association of baseline vital, biochemical and laboratory parameters with final outcome.

DISCUSSION

In the present study, evaluation of MAS severity revealed mild, moderate, and severe cases among 2.2%, 17.4%, 80.4% neonates, respectively. The literature has indicated that severe MAS has a unique pathophysiology distinct from mild or moderate MAS. There seems no observed correlation between the duration and amount of meconium exposure and the severity of MAS.[12,13] Tthe clinical progression of MAS cannot be accurately predicted from the severity of radiologic findings on neonatal chest x-rays. The pathological changes in the alveoli of neonates with pulmonary hypertension, commonly linked with severe MAS, seem to be chronic rather than acute, likely due to meconium aspiration occurring during the peripartum period.[14]

In the present study, the most frequently noted MAS associated complications were sepsis (70.7%), hyperinflated lungs (59.8%), respiratory distress (37.0%), pulmonary hypertension (33.7%), HIE (32.6%), chemical pneumonitis (21.7%), flattened hemidiaphragm (19.6%), and gas taping (8.7%). A local study by Shaikh M, et al, evaluated 72 neonates with MAS and found that chemical pneumonitis was present in 23.6% neonates while pulmonary hypertension was found in 20.8%.[15] A recent study from China documented that neurological injury were the most frequent MAS associated complications among early term newborns.[16]

Characteristics		Gender		P-Value	Age (days)		P-Value
		Male (n=66)	Female (n=26)		≤7 (n=20)	8-28 (n=72)	
Frequency of clinical presentation	Tachypnea	66 (100%)	26 (100%)	1	20 (100%)	72 (100%)	1
	Nasal flaring	66 (100%)	26 (100%)	1	20 (100%)	72 (100%)	1
	Retractions	64 (97.0%)	22 (84.6%)	0.031	16 (80.0%)	70 (97.2%)	0.006
	Grunting sounds	64 (97.0%)	22 (84.6%)	0.031	18 (90.0%)	68 (94.0%)	0.476
	Cyanosis	46 (69.7%)	11 (42.3%)	0.015	6 (30.0%)	51 (70.8%)	0.001
	Bluish skin	11 (16.7%)	3 (11.5%)	0.537	2 (10.0%)	12 (16.7%)	0.463
Meconium aspiration syndrome severity	Mild	2 (3.0%)	-	0.079	2 (10.0%)	-	0.022
	Moderate	8 (12.1%)	8 (30.8%)		4 (20.0%)	12 (16.7%)	
	Severe	56 (84.8%)	18 (69.2%)		14 (70.0%)	60 (83.3%)	
Frequency of complications	Sepsis	50 (75.8%)	15 (57.7%)	0.087	10 (50.0%)	55 (76.4%)	0.022
	Hyperinflated lungs	31 (47.0%)	6 (23.1%)	0.035	8 (40.0%)	29 (40.3%)	0.982
	Respiratory distress	28 (42.4%)	6 (23.1%)	0.083	10 (50.0%)	24 (33.3%)	0.172
	Pulmonary hypertension	22 (33.3%)	9 (34.6%)	0.907	14 (70.0%)	17 (23.6%)	<0.001
	Hypoxic ischemic encephalopathy	21 (31.8%)	9 (34.6%)	0.797	2 (10.0%)	28 (38.9%)	0.015
	Chemical pneumonitis	46 (69.7%)	26 (100%)	0.002	20 (100%)	52 (72.0%)	0.008
	Flattened hemidiaphragm	53 (80.3%)	21 (80.8%)	0.960	16 (80.0%)	58 (80.6%)	0.956
	Gas taping	60 (90.9%)	24 (92.3%)	0.830	20 (100%)	64 (88.9%)	0.119

Table-I. Association of gender and age with clinical presentation, severity, and complications of meconium aspiration syndrome in neonates (n=92)

Characteristics		Outcome			P-Value
		Discharged (n=39)	Admitted (n=45)	Mortality (n=6)	
Gender	Male	28 (71.8%)	33 (73.3%)	3 (50.0%)	0.492
	Female	11 (28.2%)	12 (26.7%)	3 (50.0%)	
Age (days)	≤7	8 (20.5%)	10 (22.2%)	-	0.439
	8-28	31 (79.5%)	35 977.8%)	6 9100%)	
Frequency of clinical presentation	Tachypnea	39 (100%)	45 (100%)	6 (100%)	1
	Nasal flaring	39 (100%)	45 (100%)	6 (100%)	1
	Retractions	38 (97.4%)	40 (88.9%)	6 (100%)	0.233
	Grunting sounds	37 (94.9%)	41 (91.1%)	6 9100%)	0.627
	Cyanosis	24 (61.5%)	27 (60.0%)	6 (100%)	0.154
	Bluish skin	4 (10.3%)	7 (15.6%)	3 (50.0%)	0.044
Meconium aspiration syndrome severity	Mild	2 (5.1%)	-	-	0.001
	Moderate	14 (35.9%)	2 (4.4%)	-	
	Severe	23 (59.0%)	43 (95.6%)	6 (100%)	
Frequency of complications	Sepsis	28 (71.8%)	32 (71.1%)	3 (50.0%)	0.541
	Hyperinflated lungs	13 (33.3%)	19 (42.2%)	3 (50.0%)	0.598
	Respiratory distress	19 (48.7%)	13 (28.9%)	-	0.028
	Pulmonary hypertension	12 (30.8%)	11 (24.4%)	6 (100%)	0.001
	Hypoxic ischemic encephalopathy	11 (28.2)	16 (35.5%)	3 (50.0%)	0.519
	Chemical pneumonitis	35 (89.7%)	32 (71.1%)	3 (50.0%)	0.029
	Flattened hemidiaphragm	30 (76.9%)	41 (91.1%)	3 (50.0%)	0.024
	Gas taping	38 (97.4%)	38 (84.4%)	6 (100%)	0.083

Table-II. Association of demographics, clinical presentation, severity and complications of MAS with final outcome (N=90)

Vital, Biochemical and Laboratory Parameters	Outcome			P-Value
	Discharged (n=39)	Admitted (n=45)	Mortality (n=6)	
Respiratory rate (respirations/min)	55.54±8.47	52.80±10.45	56.00±15.34	0.416
Systolic blood pressure (mm Hg)	79.09±12.24	82.15±9.19	73.00±9.86	0.112
Diastolic blood pressure (mm Hg)	36.83±8.91	43.37±8.48	28.00±4.38	<0.001
Pulse (beats/min)	141.77±20.72	141.82±23.85	167.00±6.08	0.161
Oxygen saturation (%)	93.21±2.56	93.53±3.53	91.00±1.09	0.165
Temperature (^{0}F)	98.26±1.32	98.42±1.81	99.82±2.15	0.682
Leukocyte count	15.25±7.82	15.62±8.98	14.95±6.74	0.971
Neutrophil (%)	47.99±15.39	51.39±19.86	46.50±0.55	0.620
Platelet count	190.51±103.69	103.22±103.22	366.50±148.53	<0.001
Random blood sugar	89.45±22.65	85.68±23.84	84.50±4.93	0.748

Table-III. Association of baseline vital, biochemical and laboratory parameters with final outcome (N=90)

In this study, the mortality was observed in 6.7% neonates with MAS. Local data has reported relatively higher mortality rate of 19.4% in MAS.[15]

Our findings correlate well with a recent study by Luo et al who reported mortality rate of 7.8% in a cohort of neonates with MAS.[16] Regional data from India has shown mortality in 13.3% neonates with MAS.[17] The literature reports mortality rates ranging between 3.7-15% in neonates with MAS and there could be various factors that may affect outcomes in these neonates.[18-21] MAS has high neonatal mortality rates so there is a need to monitor the high risk newborns during pregnancy and labour so that timely identification of newborns on high risk of adverse outcomes can be made.[18] Prospective data has also revealed that infants who have MAS may go on to exhibit neurodevelopmental delays in the later years of childhood even if they show good response to initial treatment.[22]

The present stud had some limitations as well. Being a single center study and conducted on a relativley modest sample size, our findings cannot be generalized. This warrants further large scale multicentric trials analyzing MAS neonates. We only noted relatively short outcomes so there is a need to prospectively follow these infants for monitoring of long term outcomes.

CONCLUSION

Vast majority of the neonates (80.4%) presented with severe MAS which should raise alarm about the time identification of these high risk neonates. The most frequently noted MAS associated complications were sepsis, hyperinflated lungs, respiratory distress, pulmonary hypertension, HIE, and chemical pneumonitis. Overall outcome were good among neonates with MAS. At presentation, bluish skin, pulmonary hypertension, and severe MAS were significantly associated with mortality.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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1	Afifa Sohail	Methodology, Data collection, Data analysis.	
2	Mashal Khan	Literature review, Proof reading, Supervision.	