# ORIGINAL ARTICLE DETRIMENTAL COMPLICATIONS OF MECONIUM ASPIRATION SYNDROME AND THEIR IMPACT ON OUTCOME

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Background: Meconium aspiration syndrome (MAS) is respiratory distress in an infant born through meconium stained amniotic fluid (MSAF) whose signs cannot be otherwise explained. MAS is associated with different complications. Many studies have been conducted in developed world to find the outcome associated with MAS but data from developing countries is lacking. Present study was conducted to determine the impact of chemical pneumonitis, pulmonary hypertension (PHN) and air leak on outcome of new-borns with MAS. Methods: This cross sectional descriptive study was conducted in a tertiary care Neonatology unit. The babies diagnosed with MAS were included in the study. All patients were monitored for development of complications. Outcome in terms of mortality was recorded. Outcome was compared by chisquare test and p-value <0.05 is considered significant. **Results:** Seventy two babies were included in the study. Mean gestation was 37±0.56 weeks and birth weight was 2.87±0.49 kg. Male to female ratio was 1.57:1 and mean age of admission was 9.59±5.27 hours. Chemical pneumonitis, PHN and chemical pneumonitis with PHN were observed in 23.6%, 20.8% and 26.4% neonates respectively. Mortality rate was 19.44%. The mortality was highest in babies having chemical pneumonitis with PHN (p-value=0.013) followed by chemical pneumonitis group (p-value=0.02) and PHN group (p-value=0.032). Conclusion: About three fourth babies with MAS developed one or more complications. Mortality is significantly increases with the development of complications so as more the complications more is the mortality.

Keywords: Meconium Aspiration Syndrome; Chemical Pneumonitis; Persistent Pulmonary Hypertension.

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### **INTRODUCTION**

Meconium aspiration syndrome (MAS) is described as respiratory distress in an infant born through meconium stained amniotic fluid (MSAF) whose signs cannot be otherwise explained.<sup>1</sup> MSAF signifies underlying foetal hypoxia and is found in 10–15% of live births.<sup>2,3</sup>About 2–9% of infants born through MSAF develop MAS.<sup>4</sup>

Globally, every year 2.6 million neonates die and three-fourths of these deaths occur in the first week of life.<sup>5</sup> Pakistan has one of the highest neonatal mortality rate in the world, i.e., 55/1000 live births.<sup>6,7</sup> MAS is one of the leading cause of perinatal mortality.<sup>8</sup> According to a study, 27.3% of neonatal deaths had a history or evidence of meconium passage during delivery.<sup>9</sup>

Meconium aspiration syndrome is a frequent cause of admission in neonatal departments. Neonates with MAS present at or just after delivery with marked respiratory distress and hypoxemia with X-Ray chest showing hyperinflation, patchy infiltrates and occasional air leaks.<sup>10</sup>

Meconium aspiration syndrome is associated with multiple life threatening complications including hypoxic ischemic encephalopathy (HIE) (46%), hypotensive shock (22%), pneumothorax (11.4%), myocardial dysfunction (22%) and pulmonary hypertension (PHN) (17%).<sup>11,12</sup>

Many studies have been conducted in developed world to find the outcome associated with MAS but data from developing countries like Pakistan is lacking. This study has been designed to fill in this gap. This study shall help in anticipating the problems associated with MAS in our set-up that shall ultimately lead to improved outcome of such babies.

### **MATERIAL AND METHODS**

This was a cross sectional descriptive study conducted at Neonatology Department, The Children's Hospital and The Institute of Child Health, Lahore, for a period of 6 months from March to August 2015. The study was initiated after approval from the Institutional Review Board and obtaining informed consent from the All the parents/guardian. new-borns having meconium staining of skin and respiratory distress in the presence of MSAF with onset within first 24<sup>th</sup> of life were labelled as meconium aspiration syndrome (MAS) and were included in the study by consecutive

non-probability sampling; until the desired number of patients was completed.

Respiratory distress was defined as respiratory rate more than 60 breaths per minute, with intercostal or subcostal in drawing, sternal retraction and a predominantly diaphragmatic breathing pattern.<sup>13</sup>

Pulmonary hypertension (PHN) was defined on the basis of pre- and post-ductal oxygen saturation difference of >10% with or without the presence of chocardiographic evidence of PHN, i.e., peak velocity of a tricuspid regurgitate jet with a peak pulmonary pressure gradient of >20 mmHg.<sup>11</sup>

Air leak was defined as an accumulation of extra-pulmonary air within the chest and chemical pneumonitis was defined as signs of respiratory distress with reduced air entry or crepitation with radiological evidence of diffuse patchy infiltrates, atelectasis mixed with areas of hyperinflation throughout the lung fields.<sup>14,15</sup>

Babies with congenital lung anomalies, congenital heart diseases or respiratory distress due to any other disease that could not be explained on meconium aspiration syndrome were excluded from the study.

Data include, history, examination and outcome was collected on specially designed pro forma. Investigations included CBC, CRP and chest X-Ray was done. Echocardiography of all patients was done by a consultant Paediatric Cardiologist at the Department of Paediatric Cardiology, The Children's Hospital & The Institute of Child Health, Lahore. All patients were managed in with minimal handling; haemoglobin was maintained above 12 g/dl, oxygen inhalation to maintain oxygen saturation above 95%. Patients not maintaining blood pressure were given inotropic support in the form of dopamine and dobutamine and blood glucose was maintained above 45 mg/dl. Arterial blood gases were done 12 hourly. Patients were intubated and started on mechanical ventilation if PO2<50mmHg, PCO2>60mmHg, PH<7.2 and FIO2 >0.6.

Patients not maintaining oxygen saturation on conventional ventilation were shifted on high frequency oscillatory ventilation. PPH was managed by vasodilator (sildenafil 0.25–0.5 mg/kg/dose 6 hourly per orally; increasing to 2mg/kg/dose 6 hourly; total 8 doses). Repeat echocardiography was done after 48 hours in all patients with PPH.

All patients were monitored for development of complications including chemical pneumonitis, air leak and pulmonary hypertension. Short-term outcomes of the neonate that were measured in terms of discharge and death and duration of hospital stay. Results were analysed using SPSS-20. Qualitative variable were presented as mean and standard deviation, while quantitative variables presented in frequency and percentages. Chi-square test was used to compare the variables. *p*-value  $\leq 0.05$  was considered statistically significant.

## RESULTS

A total of 96 cases of MAS were initially included in the study. Out of those 4 cases were found to have congenital lung anomalies, 12 had congenital heart diseases and 8 had respiratory distress due to other causes which could not be explained on meconium aspiration syndrome. Therefore, total of those 24 babies were excluded from the study and the remaining 72 patients were finally included in the study and their data was subjected to further analysis. Out of 72 babies 44 were males (61.11%) and 28 were females (38.9%) resulting in male: female ratio of 1.57:1. Mean age at admission was  $9.59\pm5.27$ hours (Figure-1), mean birth weight was  $2.87\pm0.49$ kg (Figure-2) and mean gestational was  $37\pm0.56$ weeks.

The deliveries through caesarean section were carried out in 33 (45.8%) cases while 39 (54.2%) babies were born through spontaneous vaginal delivery. Mean age at the onset of respiratory distress was  $3.02\pm2.20$  hours.

Out of 72 babies with MAS, 21 babies (29.2%) did not develop any studied complication while 51 (70.8%) were found to have one or more complications. Chemical pneumonitis was found in 17 (23.6%), PHN in 15 (20.8%) and chemical pneumonitis with PHN was observed in 19 (26.4%) neonates. None of the patients had air leak.

The mean duration of the hospital stay among those who survived was  $87.41\pm54.60$  hours while the mean duration of the hospital stay among those who expired was  $122.28\pm55.89$  hours. Hospital stay among patients with different complications is described in (Figure-3). Out of 72, 14 (19.44%) patients died while 58 (80.56%) were discharged. The mortality was highest in babies having chemical pneumonitis along with PHN (6/19, *p*-value=0.013) followed by chemical pneumonitis (3/17, *p*-value=0.02) and PHN alone (5/15, *p*-value=0.032).

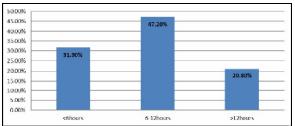
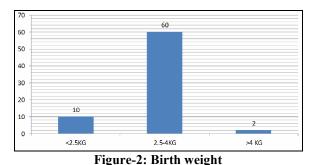


Figure-1: Age at the time of admission



160 148 3 134.4 140 120 109. NO COMPLICATION 100 94.8 01.2 84.6 CHEMICAL PNEUMONITIS 80 DUN 56.8 60 CHEMICAL VEUMONITIS PHN 40 20 n 0 DISCHARGE DEATH

Figure-3: Duration of hospital stay in hours associated with complication

### DISCUSSION

The mortality of MAS in children born with MSAF has decreased over the years particularly in the developed countries. Dargaville estimated the neonatal mortality in Australian population due to MAS to be 2.5%.<sup>16</sup> In a study conducted in a tertiary hospital in Lahore-Pakistan, Anwar found the mortality rate in MAS was 32%.<sup>9</sup>The mortality rate of 19.4% in our study is quite different from the studies done by Dargaville & Anwar.9,16 The difference in results can be explained on the basis of variation in study population. The Australian study by Dargaville is focused only on babies delivered in the institution while Anwar included both babies delivered in the institution and those delivered at home or other clinics. Current study was based only on out of institution born babies.

Bonde and Wilcox have highlighted the issue of gender discrimination in South Asia results in seeking less care for the girls as compared to boys.<sup>17</sup> A similar trend is also reflected in our study with1.5:1male to female ratio:

In a study conducted by Karabayir in Istanbul, Turkey, 43% of MAS new-borns were born through C-section.<sup>18</sup> Masood also presented the similar results in his study conducted in Lahore, Pakistan where 40% babies diagnosed as MAS were delivered through C-section.<sup>8</sup> The results are in conformity with our study where C-section was found to be the mode of delivery in 45.8% (n=33) of studied babies.

The mean duration of hospital stay in patients with MAS has been found to be variable in different studies.<sup>9,11</sup> In our study it was calculated to be 87.41±54.60 hours in those who were discharged and 122.28±55.89 hours in those who expired. This shows that the patients of MAS with severe complications had prolonged stay than the uncomplicated cases that recovered soon and were the discharged.

Zagariya demonstrated that meconium acts as a chemical irritant leading to pneumonitis and lung injury through cytokine mediated pathway.<sup>19</sup> In our study 23.6% cases were found to have features suggestive of chemical pneumonitis. Many studies have found MAS to be the commonest cause of PHN.<sup>12,20–23</sup> Pulmonary hypertension developed in 36 patients (50%) in our study which is consistent with a Korean study done by Lee.<sup>21</sup> Fischer has found a 17% incidence of pulmonary hypertension in French neonatal population having MAS.<sup>12</sup> This variation in results may be due to difference in guidelines for surfactant therapy whereby liberal use of surfactant in neonates with MAS was adopted in Fischer's study. which is known to reduce the development of pulmonary hypertension.<sup>12</sup> No baby in our study fulfilled the criteria of surfactant administration.

Air leak is another documented complication of MAS. Velaphi found its frequency to be 24% in neonates having MAS.<sup>24</sup> However, no patient developed air leaks in our study. Mechanical ventilation has been implicated as a risk factor for development of pneumothorax in MAS. The difference in our studies may be because 28.6% cases of MAS were ventilated in study by Velaphi as compared to only 8.3% cases in our study.

### CONCLUSION

About three fourth babies with MAS developed one or more complications. MAS complicated by PPHN and chemical pneumonitis has worst outcome in terms of both longer hospital stay and higher mortality, followed by PHN and Chemical pneumonitis alone. Patients without complications have excellent outcome with no mortality observed.

### **AUTHORS' CONTRIBUTION**

MS: Conceptualizing of study design, data collection, and literature search. KAIW, SJ and MAH: Help in write-up, data interpretation, proof reading. RG: Literature search, proof reading. STF: Data analysis.

### REFERENCES

1. Fanaroff AA. Meconium aspiration syndrome: historical aspects. J Perinatol 2008;28 (Suppl 3):S3-7.

- Satomi M, Hiraizumi Y, Suzuki S. Perinatal outcomes associated with meconium-stained amniotic fluid in Japanese singleton pregnancies. Open J Obstet Gynecol 2011;1(2):42–6.
- Yeh TF. Core Concepts: Meconium aspiration syndrome: pathogenesis and Current Management. NeoReviews 2010;11(9):e503–12.
- Swarnam K, Soraisham AS, Sivanandan S. Advances in the management of meconium aspiration syndrome. Int J Pediatr 2011;2012:359571.
- Zea-Vear A, Ochoa TJ. Challenges in the diagnosis and management of neonatal sepsis. J Trop Pediatr 2015;61(1):1–13.
- Nisar YB, Dibley MJ. Determinants of neonatal mortality in Pakistan: Secondary analysis of Pakistan demographic and health survey 2006-07. BMC Public Health 2014;14: 663.
- Khan A, Kinney MV, Hazir T, Hafeez A, Wall SN, Ali N, et al. Newborn survival in Pakistan: a decade of change and future implications. Health Policy Plan 2012;27(3):iii72–87.
- Masood MK, Sharif S, Butt NA. Meconium aspiration syndrome in meconium stained babies. Ann King Edw Med Univ 2011;17(4):429–32.
- Anwar Z, Butt TK, Kazi MY. Mortality in meconium aspiration syndrome in hospitalized babies. J Coll Physicians Surg Pak 2011;21(11):695–9.
- Emmerson AJ. Predictors of mortality in neonates with meconium aspiration syndrome. Indian Pediatr 2014;51(8):610–1.
- Louis D, Sundaram V, Mukhopadhyay K, Dutta S, Kumar P. Predictors of mortality in neonates with meconium aspiration syndrome. Indian Pediatr 2014;51(8):637–40.
- Fischer C, Rybakowski C, Ferdynus C, Sagot P, Gouyon JB. A population- Base study of meconium aspiration syndrome in neonates born between 37 and 43 weeks of gestation. Int J Pediatr 2012;2012:321545.
- 13. Kumar A, Bhatnagar V. Respiratory distress in neonates. Indian J Pediatr 2005;72(5):425–8.
- 14. Winnie GB, Lossef SV. Pneumothoax In: Kliegman R, Nelson WE, editors. Nelson textbook of pediatrics. 19th ed.

Philadelphia, PA: Elsevier/Saunders; 2011. p.1509-12.

- Goldsmith JP. Continuous positive airway pressure and conventional mechanical ventilation in the treatment of meconium aspiration syndrome. J Perinatol 2008;28(Suppl 3):S49–55.
- Dargaville PA, Copnell B. The epidemiology of meconium aspiration syndrome: incidence, risk factor, therapies, and outcome. Pediatrics 2006;117(5):1712–21.
- 17. Bonde JP, Wicox A. Ratio of boys to girls at Birth. BMJ 2007;334(7592):486-7.
- Karabayir N, Demirel A, Bayramoglu E. Blood lactate level and meconium aspiration syndrome. Arch Gynecol Obstet 2015;291(4):849–53.
- Zagariya A, Bhat R, Uhal B, Navale S, Freidine M, Vidyasagar D. Cell death and lung cell histology in meconium aspirated newborn rabbit lung. Eur J Pediatr 2000;159(11):819–26.
- Espinheira MC, Grilo M, Rocha G, Guedes B, Guimaraes H. Meconium aspiration syndrome-the experience of a tertiary center. Rev Port Pneumol 2011;17(2):71–6.
- Lee EC, Choi MG, Shim GH, Song YH, Chey MJ. Comorbid risk factors of persistent pulmonary hypertension of the newborn in infants with meconium aspiration syndrome. Neonatal Med 2014;21(3):166–71.
- 22. Choudhary M, Meena MK, Chhangani N, Sharm D, Choudhary JS, Choudhary SK. To study prevalence of persistent pulmonary hypertension in newborn with meconium aspiration syndrome in western Rajasthan, india: a prospective observational study. J Matern Fetal Neonatal Med 2016;29(2):324–7.
- Lin HC, Su BH, Lin TW, Peng CT, Tsai CH. Risk factors of mortality in meconium aspiration syndrome: review of 314 cases. Acta Paediatr Taiwan 2004;45(1):30–4.
- Velaphi S, Van Kwawegen A. Meconium aspiration syndrome requiring assisted ventilation:perspective in a setting with limited resources. J Perinatol 2008;28(Suppl 3):S36–42.

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