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Factors associated with mortality in newborn infants with meconium aspiration syndrome

Asril Aminullah, Jonardi Sarmili, Sudigdo Sastroasmoro

Department of Child Health, Medical School, University of Indonesia, Cipto Mangunkusumo Hospital, Jakarta

ABSTRACT Meconium aspiration syndrome (MAS) is still one of the common causes of morbidity and mortality in neonatal period. A retrospective study was conducted from January 1993 to December 1999 to identify factors associated with mortality in MAS. Univariate analysis disclosed that preeclampsia/eclampsia, sex, Apgar scores, consistency of meconium, and use of mechanical ventilation were significantly associated with mortality in MAS, while gestational age, mode of delivery, hypertension, birth weight, tracheal suctioning, blood cultures, and complications were not. Logistic regression analysis showed that mode of delivery, preeclampsia/eclampsia, Apgar scores, consistency of meconium, and use of mechanical ventilation were associated with mortality in MAS, while other variables were not. **[Paediatr Indones 2001;41:6-10]**

Keywords: *meconium aspiration syndrome, risk factors, infants morbidity and mortality*

MECONIUM ASPIRATION SYNDROME (MAS) IS STILL ONE of the major causes of morbidity and mortality in neonatal period. This syndrome is found in 0.2-6 per 1000 live born neonates and it is mostly occurred in babies with meconium-stained amniotic fluid. It is reported that meconium-stained liquor occurs in 10 to 20% of all deliveries and increases to over 30% after 42 weeks gestation. From those cases about 2 to 5% suffered from MAS and with high incidence of morbidity and mortality. About a quarter of those patients were admitted to intensive care units and the mortality rate ranged from 36 to 46%.[1,2]

The aspiration of meconium to the respiratory tract can cause physical obstruction of the airways, chemical pneumonitis and surfactant inactivation; all of these can lead to hypoxemia, hypercapnia, inflammatory changes and dysfunction of alveoli. This conditions sometimes required mechanical ventilation, and mortality is usually associated with complications such as pneumothorax, respiratory failure or persistent hypertension.[1-4] All kinds of effort have been done to decrease the mortality of patients with this syndrome; however it seems that the mortality rate is still significant. In an attempt to decrease the mortality of MAS, some investigators have tried to find out factors that are associated with the prognosis of infants with the syndrome. Many perinatal factors are proved to be associated with the mortality of the disease. Thick meconium and low Apgar scores are among those are reported to have influence on the mortality of newborn infants with MAS.[5] This study was initiated in our clinic as an effort to identify the perinatal factors that might play a role in the mortality of newborn babies with MAS.

Correspondence: Asril Aminullah, MD, Department of Child Health, Medical School, University of Indonesia, Jakarta, Jl. Salemba 6, Jakarta 10430, Indonesia. Tel. 62-21-3907742, Fax. 3907743.

Methods

This was a retrospective review of medical records of infants diagnosed to have MAS admitted to Department of Child Health, Medical School, University of Indonesia, Cipto Mangunkusumo Hospital, Jakarta between January 1993 and December 1999. They represented babies who were born in Cipto Mangunkusumo Hospital and patients referred by other clinics in Jakarta. Identification was done to all factors (independent variables) i.e., gestational age, mode of delivery, birth weight, sex, Apgar scores, consistency of meconium, history of tracheal suction-ing, use of mechanical ventilation, blood cultures, and complications that might associate with mortality of MAS (dependent variable).

The significance of each factor associated with mortality of infants with MAS was first analyzed using univariate analysis. Thereafter a multivariate analysis (logistic regression model) was applied to find out the contribution of each risk factor after ruling out confounding factors. The level of significance was $p<0.05$.

TABLE 1. DISTRIBUTION OF FACTORS ASSOCIATED WITH MORTALITY IN MAS

Characteristics		n	%
Gestationat age	• Preterm	0	0.0
	• Term	78	72.2
	• Postterm	30	27.8
Mode of delivery	• Spontaneous	47	43.5
	• Forcipal/Vacuum extraction	21	19.5
	• Cesarean section	40	37.0
Risk factors	• No	34	31.5
	• Yes :	74	68.5
	Post term	30	27.8
	Hypertension	13	12.0
	Pulmonary/cardiac disease	1	0.9
	Smoking	3	2.8
	Preeclampsia/eclampsia	37	34.3
	Diabetus mellitus	2	1.9
Sex	• Male	83	76.9
	• Female	25	23.1
Birth weight	• Low	13	12.0
	• Normal	89	82.4
	• High	6	5.6
Apgar scores	• Severe asphyxia	10	9.3
	• Mild-moderate asphy ia	30	27.8
	• No as hyxia	68	62.9
Consistency of meconium	• Mild	20	18.5
	• Moderate	57	52.8
	• Thick	31	28.7
Tracheal suctioning	• No	102	94.4
	• Yes	6	5.6
Use of ventilation	• No	90	83.3
	• Yes	18	16.7
Blood culture	• No	93	86.1
	• Yes;	15	13.9
	Negative	13	12.0
	Positive	2	1.9
Complication	• No	105	37.2
	• Yes:	3	2.8
	Pneumothorax	3	2.8
Mortality	• Survived	71	65.7
	• Expired	37	34.3

TABLE 2. ASSOCIATION OF INDEPENDENT VARIABLES AND MORTALITY (UNIVARIATE ANALYSIS)

Characteristics	Survived (n=71)	Expired (n=37)	Hypotesis testing
Gestational age			
Preterm	0	0	p=0.149
Term	47	31	
Postterm	24	6	
Mode of delivery			
Spontaneous	29	18	p=0.505
FE - VE	16	5	
Cesarean section	26	14	
Risk factors			
No	27	7	OR = 2.63 (0.93:7.71) p=0.042
Yes	44	30	
Post-term	24	6	OR = 0.37 (0.11:3.21) p=0.064
Hypertension	10	3	OR = 0.54 (0.11:2.36) p=0.365
Preeclampsia/e clampsia	15	22	OR = 5.48 (2.10:14.55) p=0.000
Sex			
Male	59	24	OR = 2.66 (0.96:7.43) p=0.033
Female	12	13	
Birth weight			
Low	7	6	p=0.438
Normal	59	30	
High	5	1	
Apgar scores			
Severe asphyxia	1	9	p<0.0001
Mild-moderate asphyxia	17	13	
No asphyxia	53	15	
Consistency of meconium			
Mild	18	2	p<0.0001
Moderate	42	15	
Thick	11	20	
Tracheal suctioning			
No	67	35	OR = 0.96 (0.11:6.62) p=0.961
Yes	4	2	
Use of ventilation			
No	67	23	OR = 10.20 (2.71:41.77) p=0.000
Yes	4	14	
Blood cultures			
No	59	34	p=0.2873
Yes	12	3	
Complication			
No	70	35	OR = 4 (0.27:117,70) p=0.230
Yes	1	2	

Results

There were 108 cases of MAS identified from January 1993 to December 1999. Most of them were term neonates (72.2%), who were delivered spontaneously (43.5%), had risk factors (68.5%) i.e., preeclampsia/ eclampsia (34.3%). Three-quarter of the patients were male (76.9%). Most of the patients had a normal birth weight (82.4%), no asphyxia (62.9%), and had a moderate consistency of meconium (52.8%). Only few cases received tracheal suctioning (5.6%) or use of mechanical ventilation (16.7%). Blood cultures were positive for *E. coli* in 2 patients (1.9%), and complication such as pneumothorax was found in only 3 patients (2.8%) (Table 1).

Univariate analysis disclosed that preeclampsia or eclampsia, sex, Apgar scores, consistency of meconium, and use of mechanical ventilation were signifi-

TABLE 3. RESULTS OF BIVARIATE ANALYSIS AND LOGISTIC REGRESSION AMONG FACTORS ASSO

VARIABLE	BIVARIATE ANALYSIS		LOGISTIC REGRESSION	
	Odds ratio	p	Odds ratio	p
Gestational age		0,149	0,38	0,284
Mode of delivery (spontaneous)		0,505		0,044
Risk factors	2,63	0,042	1,47	0,543
Hypertension	0,54	0,365	3,89	0,094
Preeclampsia/eclampsia	5,48	0,000	0,22	0,010
Sex (male)	2,66	0,033	0,72	0,386
Birth weight		0,438	1,51	0,710
Apgar scores		0,000	0,161	0,008
Consistency of meconium		0,000		0.002
Tracheal suctioning	0,96	0,961	1,646	0,476
Use of ventilation	10,20	0,000	0,294	0,005
Blood cultures		0,287		0,142
Complication	4,00	0,230	1,745	0,571

cantly associated with mortality in MAS, while gestational age, mode of delivery, hypertension, birth weight, tracheal suctioning, blood culture, and complication were not (Table 2).

Logistic regression analysis with mortality of MAS as dependent variable showed that mode of delivery, preeclampsia/eclampsia, Apgar scores, consistency of meconium, and use of mechanical ventilation were associated with mortality in MAS, while other variables were not (Table 3).

Discussion

It is reported in many studies that MAS is a disease seen primarily in full-term or post-term infants, and also usually occurs in babies who have experienced some degree of chronic asphyxia which lead to dysmaturity.[1,2] This condition was also seen in our series of 102 cases of MAS in which there was no single preterm baby was found. On the other hand almost 12% of the patients were low birth weight babies with some degree of intrauterine growth retardation. It is also seen in our studies, as well as in others;[1,2] male neonates were more prone to this disorder than female neonates (76.9% vs. 23.1%). Whether this is related to the difference of chromosome of male and female infants still needs further investigation.

The syndrome of meconium aspiration usually occurs in babies delivered with meconium stained amniotic fluid. In utero passage of meconium occurs following stimulation of the gut and relaxation of the anal sphincter. It is usually a sign of fetal distress due to intrauterine hypoxia. Therefore all pregnancies associated with fetal distress should be terminated as soon as possible.[1,5] Several investigators reported that almost all patients with MAS were delivered through cesarean section.[6,7] In this study, mode of delivery (spontaneous) is related significantly with mortality of MAS. The negative result of mode of delivery in univariate analysis is most probably due to the role of confounding factor.

In preeclampsia/eclampsia there are incomplete invasion of trophoblast into spiral arteries and incomplete denervation of adrenergic nerves in uteroplacental bed. Both resulting in vasoconstriction of the spiral arteries and cause minimal interchange of nutrient-gases and finally affect the fetus condition.[8] Mothers with complicated pregnancy such as preeclampsia/eclampsia often come or are referred late to hospital, therefore no optimal labor monitoring could be done. As noted by Adhikari et al,[2] labor monitoring is the most significant factor in reducing the occurence of MAS, leading to better survival and less prolonged resuscitation and mechanical ventilation required. In this study, both univariate and multivariate analysis showed strong correlation between preeclampsia/eclampsia and mortality of MAS.

Apgar scores were included among factors that associated with MAS mortality because review of literature showed that severe asphyxia combined with

MAS had the gravest prognosis.[5] Asphyxia inhibits pulmonary capillary flow and reabsorption of fetal lung fluid, resulted to lung unresponsiveness to the insult produced by meconium.[9] According to literature the consistency of meconium play a great role in the prognosis of MAS. Thin meconium flow easily to terminal bronchioles from which it can be absorbed without causing any problem; complication is therefore not produced and absorption of meconium is complete.[5] Our study showed that both Apgar scores and consistency of meconium were significantly associated with mortality of MAS.

Mechanical ventilation is used for MAS infants who have respiratory acidosis or severe respiratory distress. Vidyasagar[5] reported that mortality among infants who required mechanical ventilation was around 30%. This is the reason for authors to include the use of mechanical ventilation as a factor associated with mortality. Statistical analysis significantly confirmed the relation of mechanical ventilation and mortality. However, tracheal suctioning and complication, which reported to be associated with mortality, were not proved in this study, most probably because of limited patients who received tracheal suctioning or those who developed complications.

To sum up, we have proven that mortality of newborn babies with MAS is associated with several perinatal factors, i.e. mode of delivery, preeclampsia/eclampsia, Apgar scores, consistency of meconium, and use of mechanical ventilation. This result should be considered in preventing the development of MAS.

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