

Investigation of Meconium Aspiration Syndrome in Newborns, after NRP Protocol Changing

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ABSTRACT

Meconium is a thick green-black odorant substance, which is produced in the embryo's gut at the 12th week of gestation, and then stored in the colon throughout the pregnancy. Meconium can lead to pulmonary injury by various mechanisms, which in the presence of respiratory distress and other radiological findings in neonates born with meconium-stained amniotic fluid (MSAF), are defined as meconium aspiration syndrome (MAS). Given the frequent need for newborns to be resuscitated at birth, educated people are needed to resuscitate them. In the United States, the Neonatal Resuscitation Program (NRP) is a training guideline for newborns. The purpose of the NRP is to provide the cognitive, technical, and behavioral skills needed to resuscitate neonates after delivery. Due to the changes of NRP 6 and 7 guidelines in using PPV, Tracheal intubation and suctioning and using both guidelines in Shahid Mostafa Khomeini and Taleghani hospitals of Ilam, during 2015-2019, we decided to compare these two methods in terms of infant mortality and morbidity over the mentioned years. In this study, we aimed to determine the Meconium Aspiration Syndrome in neonates, born between the years 2015 and 2019, in Shahid Mostafa Khomeini and Taleghani Hospitals of Ilam, before and after the NRP protocol change.

Keywords: Meconium aspiration, meconium aspiration syndrome, infancy

INTRODUCTION

Meconium is a thick green-black odorant substance, which is produced in the embryo's gut at the 12th week of gestation, and then stored in the colon throughout the pregnancy¹⁻³. Meconium excretion occurs naturally within the first 24 to 48 hours after the birth, although the fetus may excrete meconium into the amniotic fluid for various reasons during pregnancy. Amniotic fluid impregnated with meconium before week 37 of gestation is uncommon, but its occurrence increases with gestational age⁴⁻⁶. For this reason, MSAF is found in 9 to 20% of term and post-term pregnancies, but its onset is only 5% in pre-term pregnancies^{7,8}. The exact cause of meconium excretion in amniotic fluid remains unclear. However, previous studies have suggested the role of labor factors (such as prolonged labor, post-term pregnancy, low birth weight neonates, oligohydramnios, intrauterine growth retardation, pregnancy hypertension), medical factors (anemia and cholestasis), ethical and social factors, and demographic factors (such as high maternal age, maternal drug abuse, especially tobacco and cocaine) are the major contributing factors to the excretion of meconium into the amniotic fluid⁸⁻¹⁰. Meconium can lead to pulmonary injury by various mechanisms, which in the presence of respiratory distress and other radiological findings in neonates born with meconium-stained amniotic fluid (MSAF), are defined as meconium aspiration syndrome (MAS)¹¹⁻¹³. Clinical manifestations vary from mild respiratory distress to severe respiratory failure. Hypoxic encephalopathy, air leakage, persistent pulmonary hypertension may be added to these manifestations^{14,15}. Meconium-impregnated amniotic fluid has long-term and short-term adverse effects in neonates,

especially increasing neonatal resuscitation, respiratory distress, low Apgar score, MAS, neonatal sepsis, and pulmonary diseases¹⁵⁻¹⁸. MAS worldwide has a 5 to 10 percent incidence in infants born from MSAF, accounting for 12 percent of all neonatal deaths. Besides, the severity of mental retardation and cerebral palsy in these newborns is significantly higher than that of MSAF-born neonates^{17,19-21}. MSAF increases the rate of congenital complications such as: amniotic fluid embolism, chorioamnionitis, wound infection, endometritis, and delivery complications^{17,22}. Approximately 4 million live births occur in the United States annually, of which approximately 400,000 infants require adjuvant breathing and/or positive pressure ventilation (PPV) to continue their lives outside the uterus, and about 12,000 infants need ion with chest compressions and cardiac medications²³⁻²⁶. Given the frequent need for newborns to be resuscitated at birth, educated people are needed to resuscitate them. In the United States, the Neonatal Resuscitation Program (NRP) is a training guideline for newborns. The purpose of the NRP is to provide the cognitive, technical, and behavioral skills needed to resuscitate neonates after delivery²³ successfully. The NRP curriculum is reviewed and investigated at five-year intervals in coordination with the International Liaison Committee on Resuscitation (ILCOR)^{18,27}. According to the ILCOR, the American Heart Association has developed newborn resuscitation guidelines²⁸. Due to the changes of NRP 6 and 7 guidelines in using PPV, Tracheal intubation and suctioning and using both guidelines in Shahid Mostafa Khomeini and Taleghani hospitals of Ilam, during 2015-2019, we decided to compare these two methods in terms of infant mortality and morbidity over the mentioned years. In this study, we

aimed to determine the Meconium Aspiration Syndrome in neonates, born between the years 2015 and 2019, in Shahid Mostafa Khomeini and Taleghani Hospitals of Ilam, before and after the NRP protocol change.

MATERIALS AND METHODS

Type of Study and Statistical sample: This cross-sectional study was performed on live neonates born with meconium aspiration syndrome in Mostafa Khomeini and Taleghani hospitals of Ilam during 2015-2019.

Sample Size and Method of Calculation: All neonates born with meconium aspiration syndrome in Mostafa Khomeini and Taleghani hospitals of Ilam during 2015-2019.

Type and Specifications of Data Collection Tool: Sample collection is done through a census of all live births in the years 2015 to 2019.

Data analysis method: Relevant information is extracted from patient records and included in pre-prepared forms—the data extracted after the analysis was processed by SPSS software version 19.

Method: This cross-sectional, retrospective study is a census sampling of all live births between 2015 and 1977. The inclusion criteria were all neonates born with meconium aspiration syndrome during the years 2014 to 2017 at Shahid Mostafa Khomeini (RAH) and Taleghanillam hospitals. Exclusion criteria included those with insufficient information in patient records, intrauterine death, neonatal congenital heart disease, out-of-hospital birth, neonatal congenital anomaly, systemic diseases during pregnancy, and before maternal and neonatal births.

Among the cases the information on maternal age, the number of pregnancies, type of delivery (cesarean section, normal, assisted delivery), duration of delivery, PROM, induction of delivery, preeclampsia, placental ductal, fetal distress, meconium class, gestational age, Apgar score at birth and 5 minutes later, neonatal weight and sex, symptoms of asphyxia, admission to NICU and cause and duration of hospitalization, need or not for the ventilator, symptoms of meconium aspiration syndrome, neonatal resuscitation process, and neonatal mortality and morbidity were examined.

RESULTS AND DISCUSSION

The results of the study showed that the mean age of mothers was 27.5 ± 15.7 NRP years before the change of protocol and after the change was 28.4 ± 29.48 NRP years, which was not statistically significant.

Gestational age in this study was reported 55.6% NRP in the pre-change group, and the post-change group WAS 44.4% NRP, and the post-term and pre-term gestational age was lower in the post-change NRP group.

The results of the amniotic fluid status of meconium before and after NRP changes were 9.1% thin and 12.1% thick and in the group after NRP changes (thin and thick) were 4.4%. Still, there was no statistically significant relationship between meconium amniotic status and NRP changes.

Table 1. Determining the relationship between maternal age and gestational age and neonatal morbidity and mortality

| Age | P | Mean±STD | |
|-----------|-----|-------------|------------|
| | | After NRP | Before NRP |
| Mother | .42 | 4.48 ±28/29 | 5/7±27/15 |
| Pregnancy | .93 | 2/23±38/82 | 1/67±38/86 |

Maternal age and gestational age were somewhat homogeneous before and after NRP protocol change, and there was no statistically significant relationship between maternal age and gestational age with NRP protocol change.

Table 2. Determination of the relationship between the type of delivery (cesarean section, normal, with device) and neonates with meconium sphincter syndrome

| Type of delivery | Frequency% | |
|-------------------|------------|------------|
| | After NRP | Before NRP |
| Caesarean section | 18(42.9%) | 24(57.1%) |
| Normal | 6(40%) | 9(60%) |

P value 0.54

Table 3. Determination of relationship between weight and sex of infant and meconium spirosis syndrome.

| Variable | Frequency% | |
|-----------------------------------|------------|------------|
| | After NRP | Before NRP |
| Baby gender (P value 0.56) | | |
| Girl | 12(42.9%) | 16(57.1%) |
| Boy | 12(41.4%) | 17(58.6%) |
| Baby weight (P value ./4) | | |
| <3500 | 19(44.2) | 24(55.8%) |
| >3500 | 5(35.7%) | 9(64.3%) |

There was no significant relationship between gender and infant weight before and after NRP changes.

Table 4. Determination of the relationship between meconium aspiration syndrome and length of stay in NICU before and after NRP protocol modification

| Duration of hospitalization | Mean±STD | |
|-----------------------------|-----------|------------|
| | After NRP | Before NRP |
| NICU | 3.99±6.29 | 9.02±6.09 |

P value 0.91

The length of stay in the ICU increased after the NHRP protocol change, but no significant relationship was observed.

Table 5. Determination of the association between meconium aspiration syndrome and the need for resuscitation before and after NRP modification.

| Variable/ Need to be revived | Frequency% | |
|------------------------------|------------|------------|
| | After NRP | Before NRP |
| Yes | 7(53.8%) | 6(46.2%) |
| No | 17(38.6%) | 27(61.4%) |

P value 0.25

Table 6. Determination of the relationship between ventilation requirement and meconium aspiration syndrome before and after NRP protocol modification

| Need ventilation | Frequency% | |
|----------------------|------------|------------|
| | After NRP | Before NRP |
| No need | 15(62.5%) | 25(75.8%) |
| Intube | 5(20.8%) | 7(21.2%) |
| Laryngoscope suction | 1(4.2%) | 1(3%) |
| PPV | 1(4.2%) | 0 |
| Intube+PPV | 2(4.2%) | 0 |

P value 0.34

Table 7. Determination of the relationship between neonatal mortality and meconium aspiration syndrome before and after NRP protocol modification

| Variable/ Infant mortality | Frequency% | |
|-------------------------------|------------|------------|
| | After NRP | Before NRP |
| - | 20(39.2%) | 31(60.8%) |
| + | 4(66.7%) | 2(33.3%) |

P value: 0.19

Table 8. Determination of the relationship between neonatal morbidity of meconium aspiration syndrome before and after NRP protocol modification.

| Morbidity | Frequency% | |
|--------------|------------|------------|
| | After NRP | Before NRP |
| Hypotonia | 1(4.2%) | 4(12.1%) |
| Pneumothorax | 1(4.2%) | 2(6.1%) |
| Sepsis | 0 | 1(3%) |

P value 0.45

DISCUSSION AND CONCLUSION

The results of the study showed that the mean age of mothers was 27.5 ± 15.7 NRP years before the change of protocol and after the change was 28.4 ± 29.48 NRP years, which was not statistically significant. Gestational age in this study was reported 55.6% NRP in the pre-change group and the post-change group WAS 44.4 % NRP, and the post-term and pre-term gestational age was lower in the post-change NRP group. In the study of Ziadeh et al. In Amman and Jazayeri et al. In America, the mean age of mothers and gestational age was higher in the case group. But they also failed to show a significant difference between the mean age of mothers and gestational age between case and control groups^{12,29}.

The results of the amniotic fluid status of meconium before and after NRP changes were 9.1% thin and 12.1% thick and in the group after NRP changes (thin and thick) were 4.4%. Still, there was no statistically significant relationship between meconium amniotic status and NRP changes. In the group before the change, NRP 57.1% and the group after change NRP 42.9% cesarean section was reported, and there was no statistically significant relationship. Cesarean delivery in the pre-change group was more than the post-change group, and other studies in this field, both in Iran and in other countries (American-Israel, Oman, etc.) had similar results^{1,5,12,29}.

In our study, 73.7% of cases had a cesarean section, in Israel study 33.7%¹⁶, Spain 52.5%²³ and in Oman study, the rate of cesarean section increased by 14% -7% compared to normal⁷. In Zimbabwe, cesarean delivery rates are twice as high³⁰. This reference figure is 60% in the reference book¹. The results showed that 42.6% of neonates before and 53.8% after the changes of NRP needed to be resuscitated, but this relationship was not statistically significant. There was no significant relationship between gender and infant weight before and after NRP changes. The length of stay in the NICU increased after the NRP protocol change, but no significant relationship was observed.

Intubation was used in 21.2% of the the group before the changes of NRP preterm infants and 20.8 % of the group after the changes of NRP. But there was no significant relationship between the need for ventilation before and after NRP changes. Aspiration meconium

syndrome that needed ventilator estimated 21% in our study and 0.6% (15%) in the US, Singapore 1.4%³, Syria 5.5%¹⁹, Italy 28%²⁰. That our study is in line with the study of Italy.

The results of this study showed that in the group before NRP changes in mothers with cesarean section out of 6 patients with amniotic membrane dilated 8.3% thin and 16.7% thick and in the group of after NRP changes only one patient with the cesarean section with amniotic membrane thickness was reported.

Birth weight was reported 72.7% in the pre-changes group and 72.9% NRP in the post changes groups of less than 3500g. But t-test showed that there was no significant difference between the two groups in terms of mean neonatal weight. Mean weight was reported $3094/54 \pm 624/1$ in pre-group changes and $3002/08 \pm 590$ in the post changes group. Jazayeri et al., Maymon et al. Achieved similar results in their studies^{1,14}. But Ziadeh and colleagues observed a significant $P < 0.05$ difference in mean neonatal weight between the two groups²⁹.

In this study, the mean score of the first minute Apgar score in both homogeneous groups and the 5th minute was higher in the pre-change group than in the post-NRP group. This difference was not statistically significant. Whereas in Jazayeri et al.'s study, only the first minute Apgar score was significantly different between the two groups¹⁴.

First-minute Apgar was less than 7% in our study, while in another study, it was 1.9%¹⁹. It seems in our study that high meconium excretion, which is indicative of severe fetal distress, is higher than the above study, with a lower Apgar score in the study. In our study, as in other studies, fortunately, most of the studied units were discharged in two groups with improved outcomes. (Respectively 72.7% and 83/3%)^{1,29,31}. In the group before the changes, one death due to pneumothorax and the next group, four deaths due to no morbidity, pneumothorax, and one case occurred due to hypothermia and hyperkalemia.

REFERENCES

- Jain PG, Sharma R, Bhargava M. Perinatal outcome of meconium stained liquor in pre-term, term and post-term pregnancy. Indian J Obstet Gynecol Res. 2017;4(2):146-50.
- Addisu D, Asres A, Gedefaw G, Asmer S. Prevalence of meconium stained amniotic fluid and its associated factors among women who gave birth at term in Felege Hiwot comprehensive specialized referral hospital, North West Ethiopia: a facility based cross-sectional study. BMC pregnancy and childbirth. 2018;18(1):429.
- Alimohammadi E, Maleki R, Akbarialiabad H, Dahri M. Atomistic insight into novel co-delivery of doxorubicin and paclitaxel using fullerene modified by dimethyl acrylamide trimethyl chitosan: A computational study. 2020.
- Khatun MHA, Arzu J, Haque E, Kamal M, Al Mamun MA, Khan MFH, et al. Fetal outcome in deliveries with meconium stained liquor. Bangladesh Journal of Child Health. 2009;33(2):41-5.
- Suthee Panichkul M, Boonprasert K, Komolpis S, Panichkul P. The association between meconium stained amniotic fluid and chorioamnionitis or endometritis. J Med Assoc Thai. 2007;90(3):442-7.
- Taghrir MH, Akbarialiabad H, Marzaleh MA. Efficacy of mass quarantine as leverage of health system governance during COVID-19 outbreak: a mini policy review. Archives of Iranian medicine. 2020;23(4):265-7.

7. Gomella T. Neonatal sepsis. Dalam: Gomella TL, Cunningham MD, Eyal FG, Zenk KE penyunting. *Neonatology Management Procedures on Call Problem Diseases Drugs*. Edisi ke-4. New York: Lange Medical Books/McGraw Hill; 1999.
8. Kumari R, Srichand P, Devrajani BR, Shah SZA, Devrajani T, Bibi I, et al. Foetal outcome in patients with meconium stained liquor. *JPMA*. 2012;62(474):474-6.
9. Mahapatro A, Ghose S. Obstetrics outcome at term in meconium stained amniotic fluid-retrospective study. *Int J pharm Bio Sci*. 2014:866-71.
10. Paydar S, Akbarialiabad H. Utilizing Novel Assessment and Instructional Methodologies of Trauma for Residents; A Case of Blended Learning in Shiraz Medical School. *Bulletin of Emergency & Trauma*. 2020;8(1):1.
11. Akbarialiabad H, Dahroud MD, Khazaei MM, Razmeh S, Zarshenas MM. Green Tea, A medicinal food with promising neurological benefits. *Current Neuropharmacology*. 2020.
12. Wiswell TE, Bent R. Meconium staining and the meconium aspiration syndrome. *Pediatr Clin North Am*. 1993;40(5):955.
13. Akbarialiabad H, Dalfardi B, Bastani B. The Double-Edged Sword of the Dark Web: Its Implications for Medicine and Society. 2020.
14. Yuksel B, Greenough A, Gamsu H. Neonatal meconium aspiration syndrome and respiratory morbidity during infancy. *Pediatric pulmonology*. 1993;16(6):358-61.
15. Shaikh EM, Mehmood S, Shaikh MA. Neonatal outcome in meconium stained amniotic fluid-one year experience. *JPMA*. 2010;60(9):711-4.
16. Rajput U, Jain A. Impact of meconium stained amniotic fluid on early neonatal outcome. *Journal of Evolution of Medical and Dental Sciences*. 2013;2(45):8788-95.
17. Desai D, Maitra N, Patel P. Fetal heart rate patterns in patients with thick meconium staining of amniotic fluid and its association with perinatal outcome. *Int J Reprod Contracept Obstet Gynecol*. 2017;6(3):1030-5.
18. Mamizadeh N, Mohammadi J, hossein Hosseini S, Asadzadeh R. Investigating the prevalence of congenital renal anomalies and urinary tract infections in infants, using ultrasound (sonography).
19. Sharma U, Garg S, Tiwari K, Hans PS, Kumar B. Perinatal outcome in meconium stained amniotic fluid. *Journal of Evolution of Medical and Dental Sciences*. 2015;4(48):8319-28.
20. Akbarialiabad H, Hesami S, Zahrayi SA, Vafabin M, Gheisari F. Study of Common Artifacts of Myocardial Perfusion Scan in Patients with Chronic Renal Failure and Liver Cirrhosis in Nuclear Medicine Ward of Namazi Hospital in 2019.
21. Eskandari E, Aliyazdi H, Farahani RH, Nezami-Asl A, Laripour R, Roudgari H, et al. Sniffer Dogs as a Screening/Diagnostic Tool for COVID-19: A Proof of Concept Study. 2020.
22. Hamilton BE, Martin JA, Osterman MJ. Births: preliminary data for 2015. 2016.
23. Halamek LP. Educational perspectives: the genesis, adaptation, and evolution of the Neonatal Resuscitation Program. *NeoReviews*. 2008;9(4):e142-e9.
24. Barber CA, Wyckoff MH. Use and efficacy of endotracheal versus intravenous epinephrine during neonatal cardiopulmonary resuscitation in the delivery room. *Pediatrics*. 2006;118(3):1028-34.
25. Perlman JM, Risser R. Cardiopulmonary resuscitation in the delivery room: associated clinical events. *Archives of pediatrics & adolescent medicine*. 1995;149(1):20-5.
26. Akbarialiabad H, Fard HA, Abbasi HR, Bolandparvaz S, Mohseni S, Mehrnous V, et al. Our Experience of Trauma Management During Novel Coronavirus 2019 (COVID-19) Pandemic in a Busy Trauma Center in Southern Iran. 2020;8(3):199.
27. Wyckoff MH, Aziz K, Escobedo MB, Kapadia VS, Kattwinkel J, Perlman JM, et al. Part 13: neonatal resuscitation: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation*. 2015;132 (18_suppl_2): S543-S60.
28. Singh B, Clark R, Powers R, Spitzer A. Meconium aspiration syndrome remains a significant problem in the NICU: outcomes and treatment patterns in term neonates admitted for intensive care during a ten-year period. *Journal of perinatology*. 2009;29(7):497-503.
29. Fedakar A. The incidence and clinical features of meconium aspiration syndrome: a two-year neonatal intensive care experience. *The European Research Journal*. 2019;5(5): 776-80.
30. Wyllie J, Perlman JM, Kattwinkel J, Wyckoff MH, Aziz K, Guinsburg R, et al. Part 7: neonatal resuscitation: 2015 international consensus on cardiopulmonary resuscitation and emergency cardiovascular care science with treatment recommendations. *Resuscitation*. 2015;95:e169-e201.
31. Sori D, Belete A, Wolde M. Meconium stained amniotic fluid: factors affecting maternal and perinatal outcomes at Jimma University specialized teaching hospital, south West Ethiopia. *Gynecol Obstet (Sunnyvale)*. 2016;6(394):2161-0932.1000394