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Research

Meta-Analysis: Amniotic Meconium and Low Birth Weight as Predictors of Asphyxia in Newborns

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ABSTRACT

Background: Preterm birth, intrapartum-related complications (birth asphyxia or difficulty breathing at birth), infections and birth defects accounted for the majority of neonatal deaths in 2017. Low birth weight and amniotic fluid with meconium are factors associated with perinatal asphyxia. The aim of this study was to conduct a meta-analysis to estimate the influence of meconium in the amniotic fluid and low birth weight on the risk of asphyxia in newborns based on the results of previous similar studies.

Subjects and Method: This was a systematic review and meta-analysis following the PRISMA flow diagram. The formula for PICO is as follows: P= newborn, I= mixed amniotic fluid with low birth weight, C = clear amniotic fluid and normal birth weight (≥2,500 g). Database: PubMed, Google Scholar, Clinical Key, Springer Link and Science Direct with keywords ("asphyxia" OR "birth asphyxia") AND ("meconium stained amniotic" OR "meconium stained liquor" OR "meconium stained amniotic liquor") AND "Low birth weight" AND "newborns" AND "cross sectional". The research inclusion criteria were full text articles and in English. Articles published from 2010 to 2020. The study design was cross-sectional with multivariate analysis using Revman 5.3 and results reported in adjusted odds ratio (aOR).

Results: The results of the meta-analysis in 11 primary studies showed that the effect of meconium in the amniotic fluid was statistically significant in increasing the risk of asphyxia in newborns by 5.16 times compared to clear membranes (aOR 5.16; 95% CI = 3.73-7.13; p <0.001). The effect of low birth weight was statistically significant in increasing the risk of asphyxia in newborns by 2.94 times compared to normal birth weight (aOR 2.94; 95% CI = 1.84-4.70; p <0.001).

Conclusion: Amniotic meconium and low birth weight increase the incidence of newborn asphxia. Early detection in proper control and monitoring of labor, development of a comprehensive partograph and adequate prenatal care with the provision of social support reduces the frequency and negative effects of perinatal asphyxia.

Keywords: meconium in the amniotic fluid, low birth weight, asphyxia, newborns

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BACKGROUND

Globally, in 2018, 2.5 million children died in the first month of life. Sub-Saharan Africa had the highest neonatal mortality rate in 2018 with 28 deaths per 1,000 live births, followed by Central and South Asia with 25 deaths per 1,000 live births. South Asia has the highest proportion of neonatal deaths at 62%. The majority of all neonatal deaths (75%) occur during the first week of life, and approximately 1 million newborns die within the first 24 hours of birth.

Premature birth, intrapartum-related complications (birth asphyxia or difficulty breathing at birth), infections and birth defects accounted for the majority of neonatal deaths in 2017 (WHO, 2019).

Twenty-three percent of deaths annually worldwide and 31.6% in Ethiopia are due to birth asphyxia. Studies conducted in Osogbo, Southwest Nigeria, Southern Nepal, and Khulna Urban Slum, Bangladesh also show that birth asphyxia is responsible for approximately 23.9%, 30%, and 39% of deaths, respectively (Wosenu et al., 2018).

A study conducted in China reported 18.6% of deaths due to intrapartum asphyxia due to meconium aspiration syndrome (MAS) amniotic fluid aspiration, or 8 out of 43 births (Deng et al., 2019).

Low birth weight, amniotic fluid with meconium, prolonged labor are factors associated with perinatal asphyxia (Gebreheat et al., 2018) besides medical complications, absence of antenatal care (ANC) visits, incomplete antenatal visits, non-cephalic presentations, Caesarean section (SC) is also a risk factor for asphyxia (Wayessa et al., 2018).

Low birth weight has a 6.9 times greater risk of asphyxia than normal body weight (≥2,500 g). Amniotic fluid with meconium has a 7.9 times higher risk than those without meconium to give birth to asphyxia (Tasew et al., 2018)

Most of the factors associated with birth asphyxia can be managed by means of good pre-natal care and improving antenatal, intrapartum, and neonatal care with good care (Wayessa et al., 2018).

This study is done by collecting and aggregating all relevant and pre-existing research results on the magnitude of the influence of meconium in the amniotic fluid, and low birth weight, on the risk of asphyxia in the newborn.

SUBJECTS AND METHOD

1. Study Design

Systematic review and meta-analysis were carried out by following the PRISMA flow diagram. Its article search databases include: PubMed, Google Scholar, Clinical Key, Springer Link and Science Direct. Keywords ("asphyxia" OR "birth asphyxia") AND ("meconium stained amniotic" OR "meconium stained liquor" OR "meconium stained amniotic liquor") AND "low birth weight" AND "newborns" AND "cross sectional". The formula for PICO is as follows: P= newborn, I= mixed amniotic fluid with low birth weight, C= clear amniotic fluid and normal birth weight (≥2,500 g).

2. Inclusion Criteria

The inclusion criteria in this study were full text articles and in English. The articles were published from 2010 to 2020. The research design was an observational, cross sectional study. Selected articles discussed predictors for asphyxia in newborns (meconium and low birth weight). The sample in the study was newborns. The study articles were processed by multivariate analysis and reported results in adjusted odds ratio (aOR).

3. Exclusion Criteria

The study was conducted with RCT, case control, quasi experiment, protocol study and pilot study. Articles are those published in a language other than English. His research articles are those with reported results not adjusted odds ratio (aOR).

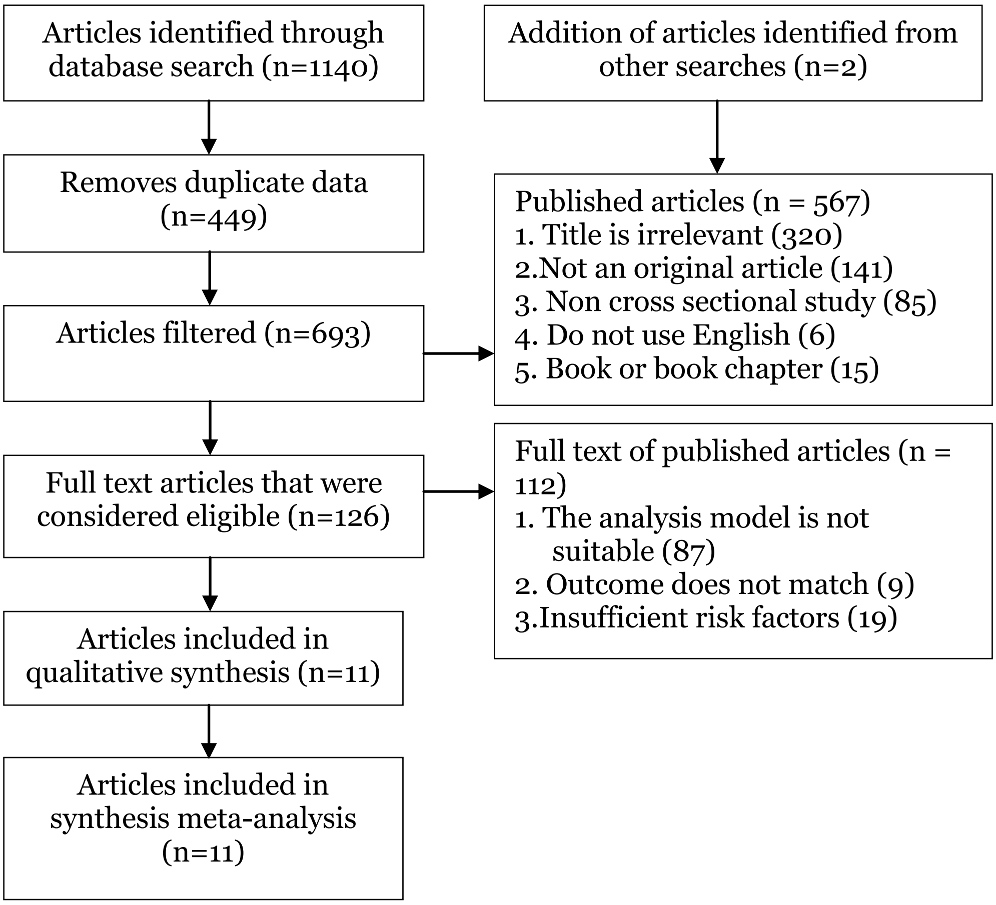

Figure 1. PRISMA flow diagram

4. Operational Definition of Variables

Asphyxia: a condition in newborns that fails to breathe spontaneously and regularly immediately after birth

Meconium mixed amniotic fluid: the condition of the amniotic fluid is not clear, tends to be greenish or cloudy

Low birth weight: low birth weight of the newborn or <2500 grams

5. Study Instrument

The research stages followed the PRISMA flow diagram and the assessment of the quality of research articles, using the Critical Appraisal Checklist for Cross-Sectional Study from the Center for Evidence Based Management.

6. Data Analysis

The data analysis process in this study was to use the Review Manager application (RevMen 5.3), to determine the effect size and heterogeneity of the study. The results of the meta-analysis data are presented in the form of a forest plot and a funnel plot.

RESULTS

The process of searching for articles on the electronic data base according to PRISMA flow diagrams can be seen in Figure 1. Eleven articles out of 1142 were reviewed in this study, 11 from Ethiopia, Nepal and Pakistan. Furthermore, the researchers conducted an assessment of the quality of the articles (Table 1).

1. The effect of meconium in the amniotic fluid on the risk of asphyxia

Table 2 provides information on 8 articles with a cross-sectional study design of the effect of meconium in the amniotic fluid on the risk of asphyxia in newborns.

a. Forest plot

Figure 2.forest plot shows that meconium-mingled amniotic fluid increases the risk of asphyxia in newborns by 5.16 times greater than clear membranes, which is statistically significant (aOR 5.16; 95% CI= 3.73 to 7.13; p<0.001). There is heterogeneity between experiments (I^2= 22%) Fixed Effect Model is used.

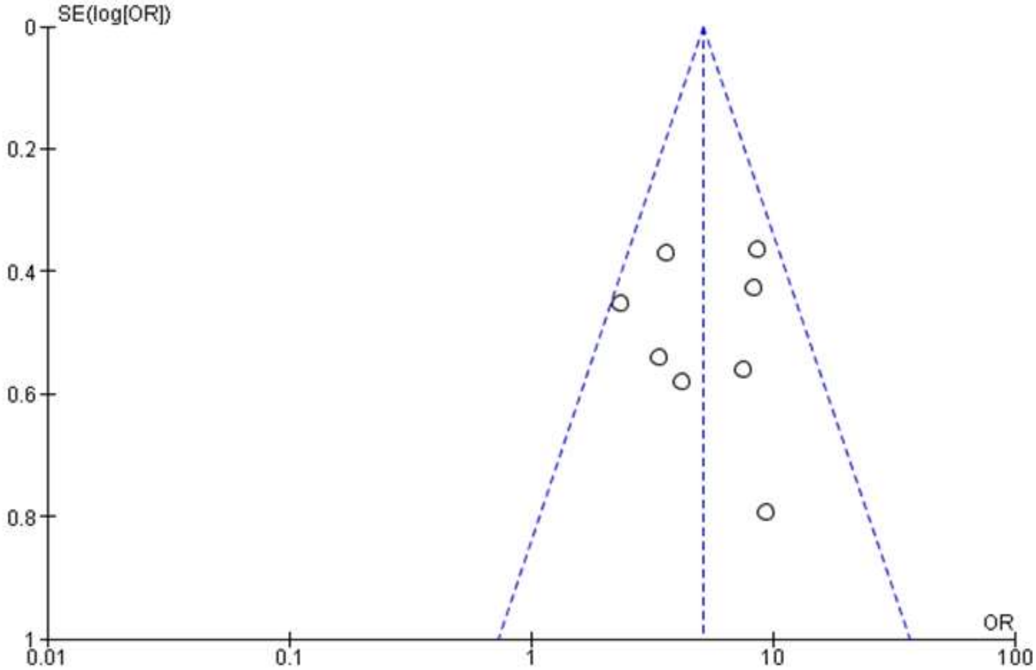

Figure 3. Funnel Plot of the Effect of Amniotic Meconium on the Risk of Asphyxia

b. Funnel Plot

Figure 3. Funnel plot Effect of meconium in amniotic fluid on the risk of plots on the right and left sides not symmetrical with each other and forming an inverted funnel. The left plot has a standard error of 0.6, while the plot on the right has a standard error of> 0.6. There is 1 plot on the right side away from the vertical center line. This indicates that there is a publication bias in the study;

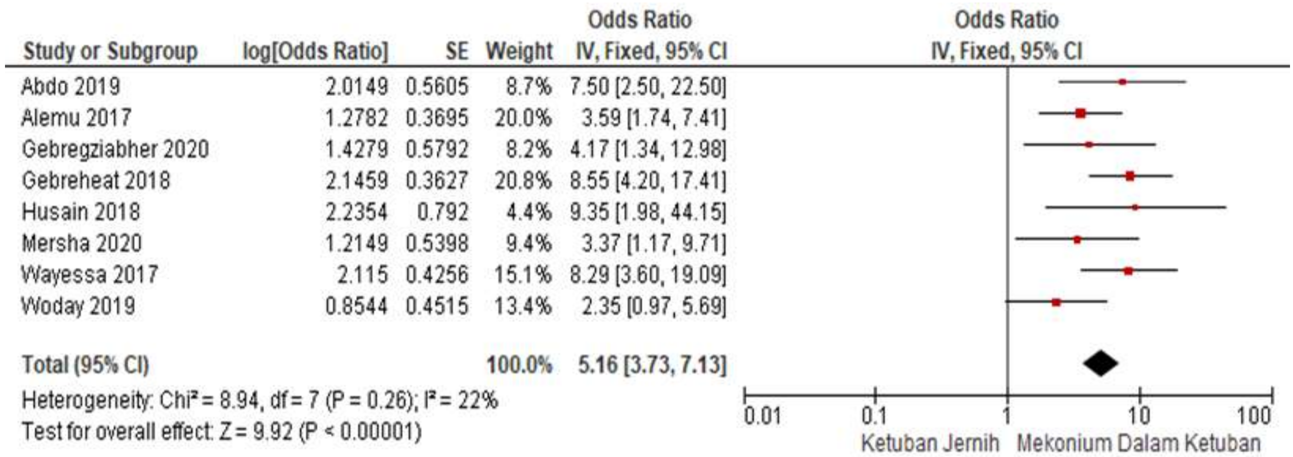

Figure 2. Forest Plot of the Effect of Amniotic Meconium on the Risk of Asphyxia

Table 2. Summary Source of Effect of Meconium in Amniotic Risk of Asphyxia

Author (Year)	Country	Study design and number of subjects	Inclusion Criteria	Effect	
				AOR	95% CI
(Mersha et al., 2020)	Ethiopia	Study design: cross-sectional study. Subjects: 286 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	3.37	1.17-9.74
(Gebreheat et al., 2018)	Ethiopia	Study design: cross-sectional study. Subjects: 421 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	8.55	4.20-17.39
(Woday et al., 2019)	Ethiopia	Study design: cross-sectional study. Subjects: 357 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	2.35	0.97-5.68
(Abdo et al., 2019)	Ethiopia	Study design: cross-sectional study. Subjects: 279 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	7.5	2.5-21.4
(Alemu et al., 2019)	Ethiopia	Study design: cross-sectional study. Subjects: 262 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	3.59	1.74-7.42
(Gebregziabher et al., 2020)	Ethiopia	Study design: cross-sectional study. Subjects: 267 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	4.17	11.34-12.98
Husain et al. (2018)	Pakistan	Study design: cross-sectional study. Subjects: 200 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome is low APGAR value and asphyxia	9.35	1.98-44.21
Wayessa, et al. (2018)	Ethiopia	Study design: cross-sectional study. Subjects: 368 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	8.29	3.6-18.9

Table 1. Research Quality Assessment

Publication	Clear purpose/ research focus	Cross sectio-nal	Me-thod	Selecti on Bias	Sam-ple	Size of sample	Reached response	Instru ment	Stastistic Signifi-cance	Confi-dence interval	Con-found-ing	Results can be applied	Total
(Mersha et al., 2020)	2	2	2	1	2	2	1	2	2	2	1	2	21
(Gebreheat et al., 2018)	2	2	2	1	2	2	2	2	2	2	1	2	22
(Woday et al., 2019)	2	2	2	1	2	2	1	2	2	2	1	2	21
[illegible]	2	2	[illegible]	[illegible]	[illegible]	[illegible]	2	1	2	2	1	2	21
[illegible]	2	2	[illegible]	[illegible]	[illegible]	[illegible]	2	2	2	2	1	1	21
(Gebregziabher et al., 2020)	2	2	2	1	2	2	2	2	2	2	1	2	22
(Husain et al., 2018)	2	2	2	1	2	2	1	2	2	2	1	2	22
(Wayessa, et al., 2018)	2	2	2	1	2	2	2	1	2	2	1	2	21
(Getachew et al., 2020)	2	2	2	1	2	2	1	2	2	2	1	2	21
(Lindbäck et al., 2014)	2	2	2	1	2	2	2	2	2	2	1	2	22
(Jamie dan Abdosh, 2019)	2	2	2	1	2	2	2	2	2	2	1	2	22

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Note:
Yes = 2
Unexplained = 1
No= 0

Table 3. Summary Source of the Effects of Low Birth Weight against the Risk of Asphyxia

Author (Year)	Country	Study Design and the number of subjects	Inclusion Criteria	Effect	
				AOR	95% CI
Mersha et al., (2020)	Ethiopia	Study design: cross-sectional study. Subjects: 286 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	3.37	1.17- 9.74
Gebreheat et al., (2018)	Ethiopia	Study design: cross-sectional study. Subjects: 421 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	8.55	4.20-17.39
Woday et al., (2019)	Ethiopia	Study design: cross-sectional study. Subjects: 357 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	2.35	0.97-5.68
Abdo et al., (2019)	Ethiopia	Study design: cross-sectional study. Subjects: 279 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	7.5	2.5-21.4
Alemu et al., (2019)	Ethiopia	Study design: cross-sectional study. Subjects: 262 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	3.59	1.74-7.42
Gebregziabher et al., (2020)	Ethiopia	Study design: cross-sectional study. Subjects: 267 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	4.17	11.34-12.98
Husain et al., (2018)	Pakistan	Study design: cross-sectional study. Subjects: 200 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome is low APGAR value and asphyxia	9.35	1.98-44.21
Wayessa, et al., (2018)	Ethiopia	Study design: cross-sectional study. Subjects: 368 newborn babies	Full paper article, observational study design, multivariate analysis (aOR), outcome was asphyxia	8.29	3.6-18.9

2. The Effect of low birth weight on the risk of asphyxia

Table 3. provides information on 7 articles with a cross-sectional study design of the effect of low birth weight on the risk of asphyxia in newborns.

a. Forest plot

Figure 4. Forest plot shows that low birth weight increases the risk of asphyxia in newborns by 2.94 times greater than normal birth weight, statistically significant (aOR= 2.94; 95% CI= 1.84-4.70; p<0.001). There is heterogeneity between experiments (I^2= 62%) and the Random Effect Model is used.

b. Funnel Plot

Figure 5. The funnel plot of the effect of low birth weight on the risk of asphyxia in newborns The plots on the right and left sides are not symmetrical with each other and do not form an inverted funnel. The left plot has a standard error of 0.2 while the plot on the right has a standard error of 0.6. There is 1 plot on the right side away from the vertical center line. This indicates that this study has a publication bias in the study.

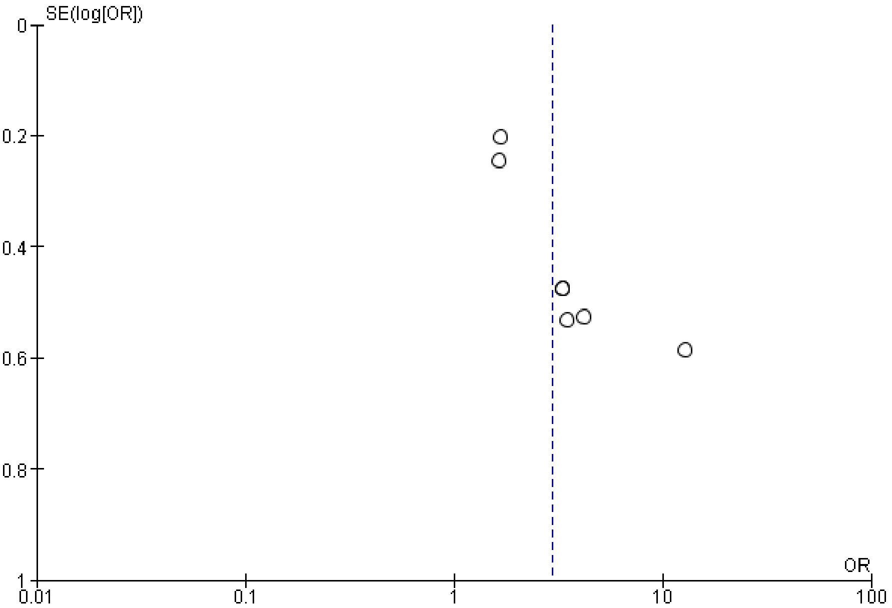

Figure 4. Forest Plot of the Effect of low birth weight on the risk of asphyxia

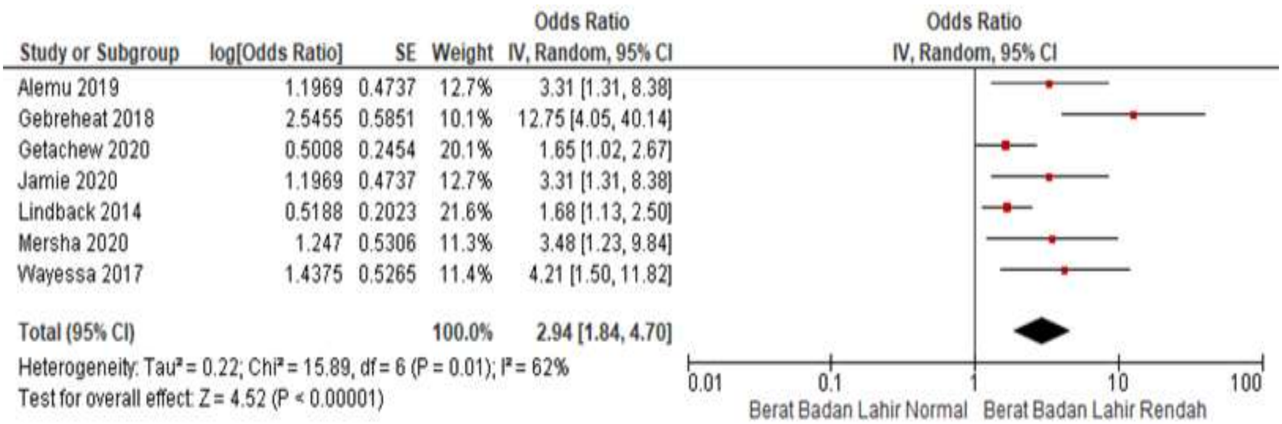

Figure 5. Funnel Plot of the Effect of Low Birth Weight against the Risk of Asphyxia

DISCUSSION

Perinatal asphyxia is one of the leading causes of perinatal mortality and morbidity worldwide (Torres-Muñoz et al., 2017) the effect of failure to initiate or maintain spontaneous breathing at birth (Moshiro et al., 2019). Other effects of asphyxia vary, from no adverse effects to multi-organ complications and death. This diversity varies according to the severity and duration of asphyxia (Aslam et al., 2014).

Some of the organs that will experience dysfunction due to perinatal asphyxia are the brain, lungs, liver, kidneys, gastrointestinal tract and blood system. Long-term effects of infants with severe asphyxia include hypoxic-ischemic encephalopathy, transient myocardial ischemia, tricuspid insufficiency, myocardial necrosis, acute renal failure, acute tubular necrosis, enterocolitis, SIADH (inappropriate antidiuretic hormone syndrome), liver damage, intra-vascular coagulation dissemination (KID), bleeding and pulmonary edema, secondary HMD hyaline membrane disease and meconium aspiration (Manoe and Amir, 2016).

Amniotic fluid mixed with meconium has a major impact on the mode of delivery and neonatal outcome. GDM (gestational diabetes mellitus) and PIH (pregnancy induced hypertension) are risk factors associated with meconium aspiration syndrome. Therefore, the presence of thick meconium requires close monitoring, early and timely obstetric intervention and appropriate postpartum care to minimize meconium-related complications and improve fetal outcome (Mohammad et al., 2018).

Complications that often occur in LBW include hypothermia, respiratory disorders, gastrointestinal disorders, immunological disorders, liver disorders, renal immunity and bleeding. In LBW, there can be a lack of surfactant and immature growth and development of the lungs so that it is difficult to start breathing which results from neonatal asphyxia (Wiadnyana et al., 2018).

1. The effect of Meconium in the amniotic fluid on the risk of asphyxia

The results of a meta-analysis of 8 articles on the effect of meconium in the amniotic fluid on the risk of asphyxia in newborns were summarized in a forest plot. Based on the results of the forest plot in Figure 4.2, it can be seen that meconium in the amniotic fluid is one of the causes of asphyxia in newborns. Meanwhile, there was heterogeneity between experiments (I^2= 22%; p <0.001). Thus, the Fixed Effect Model is used. Meconium mixed amniotic fluid increases the risk of asphyxia in newborns by 5.16 times greater than clear amniotic fluid. These results were statistically significant (aOR 5.16; 95% CI = 3.73-7.13; p <0.001).

This is in line with the research of Tasew et al., (2018) which states that mothers with meconium mixed membranes have a significant relationship with asphyxia at birth. They had a 7.9 times higher risk than those without meconium stain at birth with asphyxia. In a healthy, well-oxygenated fetus, this dilute meconium is readily cleared from the lungs by normal physiological mechanisms, but in some cases meconium aspiration syndrome occurs.

The incidence of MSAF (meconium-stained amniotic fluid) was associated with a low Apgar score due to the presence of meconium aspiration syndrome (Yang et al., 2019). Meconium-mixed amniotic fluid is a commonly observed phenomenon. The viscous consistency of meconium is associated with an increased incidence of perinatal morbidity and mortality. Based on the study, it was concluded that meconium-meconium-mixed amniotic fluid was associated with an increased incidence of caesarean section, low APGAR scores, special newborn care and meconium aspiration syndrome (Shaikh et al., 2010).

However, not all neonates with MSAF develop respiratory distress at birth, some develop problems after a few hours of birth. Close monitoring of all neonates born with MSAF is necessary and infants with this condition should be monitored to reduce morbidity and mortality. MSAF complications include MAS (Meconium Aspiration Syndrome), HIE (Hypoxic Ischemic Encelopathy), NEC (Necrotizing Enterocolitis), ARF (Acute Renal Failure) and severe thrombocytopenia (S. B., Devaraj and E., 2019).

Meconium aspiration syndrome (MAS) can be avoided with timely antenatal care. Babies born with meconium-mixed membranes should be treated aggressively to prevent complications such as perinatal asphyxia and respiratory failure that can lead to death. Neonates at risk of poor outcome should be managed with a particular focus on respiratory care with the use of assisted ventilation and nitric oxide inhalation and extracorporeal membrane oxygenation where available (S. B., Devaraj and E., 2019).

2. The Effect of Low Birth Weight on the Risk of Asphyxia

The results of a meta-analysis of 7 articles on the effect of low birth weight on the risk of asphyxia in newborns were summarized in a forest plot. Based on the results of the forest plot in Figure 4.4., It can be seen that low birth weight is one of the causes of asphyxia in newborns. Meanwhile, there was heterogeneity between experiments (I^2= 62%; p <0.001). Thus the Random Effect Model is used. Low birth weight increases the risk of asphyxia in newborns by 2.94 times greater than normal birth weight. These results were statistically significant (aOR= 2.94; 95% CI= 1.84-4.70; p <0.001).

This is in line with the research of Tasew et al., (2018). Birth weight was significantly associated with birth asphyxia. Low birth weight was 6.9 times more likely to experience shortness of breath than normal body weight (≥ 2500 g). This finding is similar to studies conducted in Pakistan and Thailand which stated that low birth weight is a risk factor for the birth of asphyxia. This may be due to the fact that low birth weight occurs as a result of maternal complications such as hypertension, diabetes mellitus that occurs before conception or antepartum.

According to Utomo (2011), prematurity and low birth weight increase the risk of asphyxia 4 and 5.8 times, respectively. Preterm and low births usually have pulmonary immaturity and limited respiratory muscle strength. Ventilatory or resuscitation support is required during labor of preterm infants.

Complications such as maternal hypertension and diabetes that are present before conception or antepartum are risk factors that are often associated with low birth weight infants (Aslam et al., 2014). Most cases of early neonatal mortality are associated with asphyxia, and prematurity and LBW are things that need attention. Reducing perinatal mortality requires a multifaceted approach by taking into account the problems associated with newborn asphyxia, potential complications of prematurity and low birth weight (Ersdal et al., 2012).

AUTHOR CONTRIBUTION

Alfiati Nanda Widiyaningrum is the main researcher who chooses topics, collects research data, formulates articles, and processes data. Bhisma Murti formulated background, research data analysis. Eti Poncorini Pamungkasari helped formulate the framework and document review.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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