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REVIEW ARTICLE

Meconium aspiration syndrome, fetal heart rate, and stillbirth. Literature review

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Abstract

Meconium aspiration syndrome (MAS) is a medical condition that can affect newborn babies. It occurs when a newborn inhales meconium, which is the first stool (feces) that a baby passes in the womb. Normally, meconium is expelled after birth, but in some cases, it is released into the amniotic fluid and can be inhaled by the baby before or during delivery. This can lead to a range of respiratory problems and complications. The severity of MAS can vary, with some infants experiencing mild symptoms and others facing more severe respiratory distress. Babies with MAS may have symptoms such as rapid breathing, grunting, bluish or grayish skin color (cyanosis), and chest retractions (drawing in of the chest wall with each breath). Severe cases of MAS may require treatment in a neonatal intensive care unit. The prognosis for babies with MAS varies depending on the severity of the condition and the promptness of treatment. Most infants recover with appropriate medical care, but in severe cases, complications can occur. It is important for health-care providers to closely monitor and provide care to babies with MAS to ensure the best possible outcomes. We present a document that results from the consultation of an updated bibliography on MAS, including aspects related to its pathophysiology and complications and the considerations to be taken into account by the obstetric service.

Keywords: *Meconium aspiration syndrome. Perinatal asphyxia. Stillbirth.*

Methods

A literature review was carried out with the keywords meconium aspiration syndrome (MAS), perinatal asphyxia, and stillbirth. The search included literature from the most recent 10 years, using the PUBMED databases, 65 articles with the topic linked to the keywords were selected, and then 28 manuscripts from those that included the items to be treated in the review (fetal distress vs. non-reassuring fetal state (NFRS), heart rate and fetal hypomotility, decreased fetal movements (DFM) and its risks, labor and fetal distress, fetal death, and its etiology) were selected.

Introduction

Most obstetric damage and risks to the health of the mother and child can be successfully prevented, detected, and treated through the application of standardized procedures for care, including the use of the risk approach and the performance of eminently preventive activities and the elimination or rationalization of some practices that, if carried out routinely, increase the risks. The proposed actions tend to favor the normal development of each of the stages of the gestational process and prevent the appearance of complications, improve maternal and child survival, and quality of life,

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and additionally contribute to providing care with greater warmth[1-3].

MAS is one of the most common causes of respiratory distress in neonates. The incidence is still high in the developing world. MAS is one of the most common causes of respiratory distress in a neonate which is associated with common maternal risk factors, especially in primigravida, which includes urinary tract infection, hypertension, and oligohydramnios. A study was conducted in Nepal, and a cross-sectional descriptive study was done among neonates admitted to the neonatal intensive care unit (NICU) with a diagnosis of MAS. The early outcome of those neonates was studied. Out of 140 neonates with a mean birth weight of 2865 + 543 g, 73.6% were male, of which 76.4% were referred cases, whereas 23.6% were inborn. Of them, 69.3% had a history of the thin type of meconium, whereas 30.7% had the thick type of meconium during delivery. Of all mothers, 74.3% were primigravida, 4.3% had an intrapartum fever of unknown source, 11.4% suffered from urinary tract infection, and 2.8% had hypertension. Premature rupture of membrane had occurred among 7.9%, and oligohydramnios was found in 10%. Half of them (50.7%) had a spontaneous vaginal delivery, 44.3% had a cesarean section, whereas 4.8% had assisted delivery. Around one-third of the neonates (37.1%) were given supplemental oxygen through nasal prongs, 25.7% through head box, 27.1% through continuous positive airway pressure, and 10% intubated. Around half of the neonates (42.1%) had no complications. Complications noted were sepsis, birth asphyxia, seizures, and polycythemia in 35%, 14.3%, 5.7%, and 2.9%, respectively. Mortality occurred among 5.0% of them[4].

Some stillbirths caused by placental abruption are potentially preventable. To prevent stillbirths caused by placental abruption, improvements should be implemented in obstetric management and assessment of fetal well-being, as well as in establishing a regional perinatal emergency transport system[5].

In the search for factors and conditions associated with fetal death, several types of exposures have been investigated, the study conducted in the United Kingdom published in 2023 found the following: In a population of women who had a stillbirth ≥ 28 weeks' gestation (n = 238) and women with an ongoing pregnancy at the time of interview (n = 597), a secondary analysis of data from the Midlands and North of England Stillbirth case-control study only included participants domiciled within 20 km of fixed air pollution monitoring stations. Pollution exposure was calculated using pollution climate modeling data for NO_2, NOx, and $PM_{2.5}$. The association between air pollution exposure and stillbirth risk was assessed using multivariable logistic regression adjusting for household income, maternal body mass index (BMI), maternal smoking, index of multiple deprivation quintile, and household smoking and parity. There was no association with whole pregnancy ambient air pollution exposure and stillbirth risk, but there was an association with pre-conceptual NO_2 exposure (adjusted odds ratio [aOR] 1.06, 95% confidence interval [CI] 1.01-1.08/$\mu g/m^3$). Risk of stillbirth was associated with maternal smoking (aOR 2.54, 95% CI 1.38-4.71), nulliparity (aOR 2.16, 95% CI 1.55-3.00), maternal BMI (aOR 1.05, 95% CI 1.01-1.08) and placental abnormalities (aOR 4.07, 95% CI 2.57-6.43). In conclusion, levels of ambient air pollution exposure during pregnancy in the UK, all of which were beneath recommended thresholds, are not associated with an increased risk of stillbirth. Periconceptual exposure to NO_2 may be associated with increased risk, but further work is required to investigate this association[6].

Exposure to high levels of $PM_{2.5}$, PM_{10}, SO_2, NO_2, and CO increases the risk of stillbirth, and the most susceptible gestational period to ambient air pollution exposure was in the third trimester. Further toxicological and prospective cohort studies with improved exposure assessments are needed to confirm the causal link between air pollutants and stillbirth[7].

Fetal distress versus NFRS

NRFS is associated with significant maternal complications, in the form of increased need for blood transfusions, intensive care unit (ICU) admissions, and increased infection and readmission rates. Strategies for minimizing maternal complications need to be proactively considered in the management of NRFS[8].

One of the largest clinical trials on this topic was conducted using the following methodology: a large retrospective cohort study of 27,886 women who delivered between January 2013 and December 2016 in a single health system was studied. Inclusion criteria included (1) women over the age of 18 at the time of admission; (2) singleton pregnancy; (3) live birth; and (4) gestational age ≥ 37 weeks at the time of admission. NRFS was defined as umbilical cord pH ≤ 7.00, fetal bradycardia, late decelerations, and/or umbilical artery base excess ≤ –12. Univariate and multivariate logistic regression and propensity score analyses were performed, and propensity score aORs (AORPS) were derived. $p < 0.05$ were considered statistically significant. Primary outcomes

are maternal blood transfusion, maternal readmission, maternal ICU admission, and cesarean delivery in relation to umbilical artery pH, fetal bradycardia, and late decelerations. Results: umbilical artery pH ≤ 7 was associated with maternal blood transfusion (AORPS 6.83 [95% CI 2.22-21.0, p < 0.001]), maternal readmission (AORPS 12.6 [95% CI 2.26-69.8, p = 0.0039]), and cesarean delivery (AORPS 5.76 [95% CI 3.63-9.15, p < 0.0001]). Fetal bradycardia was associated with transfusion (AORPS 2.13 [95% CI 1.26-3.59, p < 0.005]) and maternal ICU admission (AORPS 3.22 [95% CI 1.23-8.46, p < 0.017]). Late decelerations were associated with cesarean delivery (AORPS 1.65 [95% CI 1.55-1.76, p < 0.0001]), clinical chorioamnionitis (AORPS 2.88 [95% CI 2.46-3.37, p < 0.0001]), and maternal need for antibiotics (AORPS 1.89 [95% CI 1.66-2.15, p < 0.0001]). Umbilical artery base excess ≤ –12 was associated with readmission (AORPS 6.71 [95% CI 2.22-20.3, p = 0.0007]), clinical chorioamnionitis (AORPS 1.89 [95% CI 1.24-2.89, p = 0.0031]), and maternal need for antibiotics (AORPS 1.53 [95% CI 1.03-2.26, p = 0.0344]). Conclusion of the study: NRFS is associated with significant maternal complications, in the form of increased need for blood transfusions, ICU admissions, and increased infection and readmission rates. Strategies for minimizing maternal complications need to be proactively considered in the management of NRFS[8].

Heart rate and fetal hypomotility

With the objective of assessing this condition, artificial intelligence, inspired by clinical decision-making procedures in delivery rooms, can correctly interpret cardiotocographic (CTG) tracings and distinguish between normal and pathological events. In a study, a method based on artificial intelligence was developed to determine whether a cardiotocogram shows a normal response of the fetal heart rate (FHR) to frequency of uterine contractions (UCF) predicts a FHR response, under the assumption that the fetus is still in good condition and based on how that specific fetus has responded so far. It hypothesizes that this method when having only learned from fetuses born in good condition, is incapable of predicting the response of a compromised fetus or an episode of transient fetal distress. The (in)capability of the method to predict the FHR response would then yield a method that can help assess fetal condition when the obstetrician is in doubt. CTG data of 678 deliveries during labor were selected based on a healthy outcome just after birth. The method was trained on the CTG data of 548 fetuses in this group to learn their heart rate response. Subsequently, it was evaluated on 87 fetuses, by assessing whether the method was able to predict their heart rate responses. The remaining 43 cardiotocographies were segment-by-segment annotated by three experienced gynecologists, indicating normal, suspicious, and pathological segments, while having access to the full recording and neonatal outcome. The comparison between abnormalities detected by the method (only using past and present input) and the annotated CTG segments by gynecologists (also looking at future input) yields an area under the curve of 0.96 for the distinction between normal and pathological events in majority-voted annotations. The developed method can distinguish between normal and pathological events in near real-time, with a performance close to the agreement between three gynecologists with access to the entire CTG tracing and fetal outcome[9].

DFM and its risks

The presence of DFM is a marker associated with increased risk for a fetus. However, DFM is associated with increased odds of an infant being born small for gestational age (SGA), obstetric intervention, early-term birth, and a composite of adverse perinatal outcomes. The biggest trial related to this topic was conducted as follows: among 101,597 women with pregnancies that met the inclusion criteria, 8821 (8.7%) presented at least once with DFM, and 92,776 women (91.3%) did not present with DFM (i.e., the control population). Women presenting with DFM, compared with those presenting without DFM, were younger (mean [SD] age, 30.4 [5.4] years vs. 31.5 [5.2] years; p < 0.001), more likely to be nulliparous (4845 women [54.9%] vs. 42 210 women [45.5%]; p < 0.001) and have a previous stillbirth (189 women [2.1%] vs. 1156 women [1.2%]; p < 0.001), and less likely to have a previous cesarean delivery (1199 women [13.6%] vs. 17 444 women [18.8%]; p < 0.001). During the study period, the stillbirth rate was 2.0 per 1000 births after 28 weeks' gestation. Presenting with DFM was not associated with higher odds of stillbirth (9 women [0.1%] vs. 185 women [0.2%]; aOR, 0.54; 95% CI, 0.23-1.26, p = 0.16). However, presenting with DFM was associated with higher odds of a fetus being born SGA (aOR, 1.14; 95% CI, 1.03-1.27; p = 0.01) and the composite adverse perinatal outcome (aOR, 1.14; 95% CI, 1.02-1.27; p = 0.02). Presenting with DFM was also associated with higher odds of planned early-term birth (aOR, 1.26; 95% CI, 1.15-1.38; p < 0.001), induction of labor (aOR, 1.63; 95% CI,

1.53-1.74; p < 0.001), and emergency cesarean delivery (aOR, 1.18; 95% CI, 1.09-1.28; p < 0.001)[10].

Labor and fetal distress

Keeping in mind the large number of inflammatory mediators that are potentially released during labor, several studies have been conducted, one of the most transcendental is the following: to investigate the correlation between the intrapartum CTG findings "suggestive of fetal inflammation" ("SOFI") and the interleukin (IL)-6 level in the umbilical arterial blood a prospective cohort study conducted at a tertiary maternity unit and including 447 neonates born at term. IL-6 levels were systematically measured at birth from a sample of blood taken from the umbilical artery. The intrapartum CTG traces were retrospectively reviewed by two experts who were blinded to the postnatal umbilical arterial IL-6 values as well as to the neonatal outcomes. The CTG traces were classified into "suggestive of fetal inflammation (SOFI)" and "no evidence of fetal inflammation (NEFI) according to the principles of physiologic interpretation of the CTG traces. The CTG was classified as "SOFI: if there was a persistent FHR increase > 10% compared with the observed baseline FHR observed at the admission or the onset of labor without any preceding repetitive decelerations. The occurrence of composite adverse outcome (CAO) was defined as NICU or special care baby unit admission due to one or more of the following: metabolic acidemia, Apgar score at 5 min ≤ 7, the need for neonatal resuscitation, respiratory distress, tachypnea/polypnea, jaundice requiring phototherapy, hypotension, body temperature instability, poor perinatal adaptation, suspected, or confirmed early neonatal sepsis. To compare the umbilical IL-6 values between the cases with intrapartum CTG traces classified as "SOFI" and those classified as "NEFI"; to assess the correlation of umbilical IL-6 values with the neonatal outcome. 43 (9.6%) CTG traces were categorized as "SOFI"; IL-6 levels were significantly higher in this group compared with the "NEFI" group (82.0 [43.4-325.0] pg/mL vs. 14.5 [6.8-32.6] pg/mL; p < 0.001). The mean FHR baseline assessed 1 h before delivery and the total labor length showed an independent and direct association with the IL-6 levels in the umbilical arterial blood (p < 0.001 and p = 0.005, respectively). CAO occurred in 33 (7.4%) cases; IL-6 yielded a good prediction of the occurrence of the CAO with an AUC of 0.72 (95% CI 0.61-0.81). Intrapartum CTG findings classified as "SOFI" are associated with higher levels of IL-6 in the umbilical arterial blood[11].

There are significant differences in perinatal outcomes when fetuses were exposed to evolving intrapartum hypoxic stress culminating in an abnormal baseline FHR variability, which was preceded by repetitive decelerations, followed by an increase in the baseline heart rate. Therefore, the knowledge of fetal physiological response to evolving hypoxic stress can be reliably used to determine fetal compensation[12].

The absence of cycling is associated with intrapartum maternal pyrexia, and fetuses with the absence of cycling are more likely to have poorer perinatal outcomes measured by Apgar ≤ 7 at 5 min, despite no association with fetal acidosis[13].

Contrary to continued use in some clinical areas, we found no evidence of benefit for the use of the admission CTG for low-risk women on admission in labor. Furthermore, the probability is that admission CTG increases the cesarean section rate by approximately 20%. The data lacked the power to detect possible important differences in perinatal mortality. However, it is unlikely that any trial, or meta-analysis, will be adequately powered to detect such differences. The findings of this review support the recommendation that the admission CTG not be used for women who are at low risk of admission in labor. Women should be informed that admission CTG is likely associated with an increase in the incidence of cesarean section without evidence of benefit[14].

Fetal death (stillbirth)

India contributes the highest absolute number of stillbirths in the world. This systematic review and meta-analysis were conducted to synthesize the burden, timing, and causes of stillbirths in India. Forty-nine reports from 46 studies conducted in 21 Indian states and union territories were included. It was found that there was no uniformity/standardization in the definition of stillbirths and in the classification system used to assign the cause. The share of antepartum stillbirths was estimated to be two-thirds whereas the remaining were intrapartum stillbirths. Maternal conditions and fetal causes were found to be the leading cause of stillbirth in India. The maternal condition was assigned as the most common cause (25%) followed by fetal (14%), placental cause (13%), congenital malformation (6%), and intrapartum complications (4%). Approximately 20% of the stillbirths were assigned as unknown or unexplained[15]. One of the biggest studies conducted with the aim of identifying stillbirth risk conditions was done. The study population of 131,514 pregnancies

included 131,037 live births and 477 (0.36%) stillbirths. There are four main findings of this study. First, 92.5% (441/477) of stillbirths were antepartum and 7.5% (36/477) were intrapartum, and 59.2% (261/441) of antepartum stillbirths were observed in association with placental dysfunction, and 40.8% (180/441) were unexplained or due to other causes. Second, placental dysfunction accounted for 80.1% (161/201) of antepartum stillbirths at < 32 weeks gestation, 54.2% (52/96) at 32 + 0 to 36 + 6 weeks, and 33.3% (48/144) at ≥ 37 weeks. Third, the risk of placental dysfunction-related antepartum stillbirth increased with increasing maternal weight and decreasing maternal height, was 3-fold higher in African-american than in Caucasian women, was 5.5-fold higher in parous women with previous stillbirth than in those with previous live birth, and was increased in smokers, in women with chronic hypertension and parous women with a previous pregnancy complicated by pre-eclampsia, and/or birth of a small-for-gestational-age baby. Fourth, in screening for placental dysfunction-related antepartum stillbirth by a combination of maternal risk factors, estimated fetal weight (EFW), and uterine artery (UtA)-pulsatility index (PI) in the validation dataset, the DR at a 10% FPR was 62.3% (95% CI, 57.2-67.4%) and the AUC was 0.838 (95% CI, 0.799-0.878); these results were consistent with those in the dataset used for developing the algorithm and demonstrate high discrimination between affected and unaffected pregnancies. Similarly, the calibration slope was 1.029 and the intercept was −0.009, demonstrating good agreement between the predicted risk and observed incidence of placental dysfunction-related antepartum stillbirth. The performance of screening was better for placental dysfunction-related antepartum stillbirth at < 37 weeks' gestation compared to at term (DR at a 10% FPR, 69.8% vs. 29.2%). Screening at mid-gestation by a combination of maternal risk factors, EFW and UtA-PI can predict a high proportion of placental dysfunction-related stillbirths and, in particular, those that occur preterm. Such screening provides poor prediction of unexplained stillbirth or stillbirth due to other causes[15,16].

EFW, UtA PI, umbilical artery (UA) PI, fetal middle cerebral artery PI, mean arterial pressure, serum placental growth factor, and soluble fms-like tyrosine kinase-1 for screening at 30-34 weeks gestation, biomarkers of impaired placentation and fetal hypoxemia provide a good prediction of PE, SGA, and fetal distress before labor, but poor or no prediction of stillbirth and adverse events in labor or after birth[17].

The survival of a fetus in utero is dependent on several factors. These factors can be broken down into the well-being of the host in its environment, the function of the uteroplacental unit, the condition of the environment in which the fetus lives, and the absence of lethal fetal factors. A single insult or a combination of factors may affect the function of these life-sustaining factors and lead to a stillbirth. The ability to maintain and support a pregnancy is dependent on multiple physiologic, hormonal, and anatomical adaptations[18].

The integrity of the uteroplacental unit may be compromised by structure, function, genetic anomalies, or insults such as hemorrhage or infection. Placental findings could include (1) single umbilical cord insertion, (2) velamentous umbilical cord insertion, (3) furcate umbilical cord insertion, (4) circummarginate insertion of the placental membranes, (5) circumvallate insertion of the placental membranes, (6) terminal villous immaturity, (7) terminal villous hypoplasia, (8) terminal villous hyperplasia, (9) acute chorioamnionitis of placental membranes, (10) acute chorioamnionitis of the chorionic plate, (11) acute funisitis, (12) acute umbilical cord arteritis, (13) acute umbilical cord phlebitis, (14) chorionic plate acute vasculitis of the fetal blood vessels, (15) chorionic plate vascular degenerative changes, (16) acute villitis, (17) chronic villitis, (18) avascular villi, (19) retroplacental hematoma, (20) parenchymal infarction, (21) intraparenchymal (intervillous) thrombosis, (22) perivillous fibrin deposition, (23) intervillous fibrin deposition, (24) placental weight, and (25) ratio placental weight/birth weight[18].

Etiology of fetal death

Placental abnormalities can also be found in stillbirths without evidence of impaired growth. Symphysis-fundal height, used to estimate serial fetal growth at prenatal visits, has a low sensitivity and specificity for detecting SGA infants. Placental factors such as a placental abruption are found in 6% of stillbirths[19].

Diabetes increases stillbirth risk up to 5 times. The highest rate for stillbirth is in the 38th week for type 1 diabetes and in the 39th week for type 2 diabetes, with type 2 diabetes, the risk for stillbirth was two-fold higher if the birth weight was over the 95th%[20].

Non-obese women have a stillbirth risk of 5.5/1000. The risk is 8/1000 for a BMI of 30-39.9 kg/m^2 and 11/1000 for a BMI > 40 kg/m^2. Overweight women with BMI 25-29.9 kg/m^2 have an OR 1.37 (95% CI: 1.02-1.85), and class IV obese women with BMI > 50 kg/m^2 have an OR 5.04 (95% CI: 1.79-14.07)[21].

The risk of stillbirth is augmented by advanced maternal age due to an increased risk for aneuploidy and medical complications of pregnancy. Even after controlling for these risk factors, maternal age over 35 has an increased risk for stillbirth, which is accentuated by nulliparity. At age 40, the risk is 1/116 for a nullipara and 1/304 for a multipara[22].

Smoking tobacco increases the risk of stillbirth, both antepartum and intrapartum (15/1000). The odds ratio for stillbirth associated with alcohol use is 1.36 (95% CI: 1.05-1.76). There is a 1.5 OR for stillbirth associated with opioid use in pregnancy (95% CI: 1.3-1.8) and a 5.1 OR for stillbirth associated with methamphetamine use in pregnancy (95% CI: 3.7-7.2)[23].

Chronic hypertension increases stillbirth risk 3-times. Hypertension is a common condition that complicates pregnancy; incidence is 9.6% (95% CI: 6.9-12.1)[19].

Congenital defects, defined as physical or biochemical abnormalities, occur in 1/33 of pregnancies and are associated with a higher risk of stillbirth. The detection of congenital defects prenatally may impact antenatal surveillance policy in hopes of reducing the risk of stillbirth. Stillbirth risk is 11/1000 for bladder exstrophy and 490/1000 for the limb-body-wall complex; even for isolated congenital defects not affecting major organs, the risk of stillbirth increases. The risk for stillbirth associated with cleft lip with cleft palate is 10/1000, transverse limb deficiencies are 26/1000, longitudinal limb deficiencies are 11/1000, and amniotic band-associated limb defects are 110/1000. The increased stillbirth risk for sacral agenesis is 13/1000, isolated spina bifida 24/1000, and holoprosencephaly 30/1000 may be underestimated due to failure to account for elective termination of pregnancy[24].

Infection as a cause of stillbirth may be underrepresented because signs and symptoms of infection are often undetected, and evaluation for infection is often not conducted. Stillbirth related to infection varies from 5% to 22%. In developed countries, infection accounts for 19% of stillbirths before 28 weeks, but only 2% of stillbirths at term. When an infection is the cause of stillbirth, spontaneous preterm delivery is common. A US cohort study demonstrated infection as the probable or possible cause of stillbirth in 12.9% of cases. Predominant bacteria cultured included *Escherichia coli* 29%, group B *Streptococcus* 12%, *Enterococcus* 12%, and rarely *Listeria monocytogenes*. The placental evaluation found evidence of infection in 99% of culture-positive cases. Non-bacterial organisms causing stillbirth included cytomegalovirus 8%, parvovirus 3%, syphilis 2%, and herpes simplex virus 2%. Infection is unlikely the cause of stillbirth unless it results in significant autopsy or placental findings. Serologic screening for toxoplasmosis, chlamydia, rubella, or herpes is usually not indicated when these infections are not detected on placental or autopsy examination. Malaria should be screened for in endemic areas. Human immunodeficiency virus increases the risk of stillbirth[25].

Antiphospholipid syndrome (APS), in addition to thrombotic events, has been linked to stillbirth since 1984. To diagnose APS, one clinical criterion plus one laboratory criterion must be met. The anticardiolipin antibodies, anti-β2 glycoprotein 1 antibody, or the lupus anticoagulant, have to be above the 99th% and present on two occasions at least 12 weeks apart. In some cases, these antibodies may not be detected due to the limitations of current assays. These antibodies may be found in 5% of people without clinical symptoms. Stillbirth risk is highest when all three laboratory criteria are positive and lowest when the lupus anticoagulant is negative. Recently, anti-β2 glycoprotein 1 domain-1 antibody has been linked to late pregnancy morbidity. Lupus anticoagulant positivity at baseline was associated with an odds ratio of 8.3 (95% CI: 3.6-19.3) for adverse pregnancy outcomes[26].

Intrahepatic cholestasis may affect 0.1%-2% of pregnant women. Cases of fetal arrhythmias have been documented in pregnancies complicated by cholestasis. Most of these stillborns have signs of acute anoxia but no signs of growth restriction or long-term uteroplacental compromise[27].

Conclusion

The prognosis for infants with MAS depends on the severity of the condition and the promptness of medical intervention. Most infants with mild-to-moderate MAS recover with appropriate care and do not experience long-term complications. However, severe cases can be life-threatening and may result in long-term respiratory issues or other health problems. Timely medical attention and support are crucial in managing MAS. The goal of antepartum surveillance is to identify any issues promptly so that appropriate medical interventions can be initiated to optimize the health of the fetus and the expectant mother. This close monitoring can help reduce the risk of complications, including stillbirth and perinatal asphyxia, and improve the chances of a healthy pregnancy and delivery.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript.

References

1. Official Mexican Guideline Nom-007-SSA2-2016, for the Care of Women During Pregnancy, Childbirth and Puerperium, and of the Newborn Person. Mexico: Ministry of Health; 2016. Available form: https://www.gob.mx.nom-007-ssa2-2016.pdf
2. Clinical Guidelines for Prenatal Control IMSS 028-08. Mexico: Ministry of Health; 2009. Available from: https://www.calameo.com/gpc-control/renatal/con/enfoque/de/riesgo
3. Clinical Practice Guideline Prenatal Control with Patient-Centered Care, Evidence, and Recommendations. Master Catalog of Clinical Practice Guidelines. Mexico: Mexican Institute of Social Security; 2017. Available from: https://imss.gob.mx/sites/all/statics/guiasclinicas/028ger.pdf
4. Bhandari I, Karmacharya-Malla K, Chaudhary BR, Ghimire P. Early outcome of neonates admitted with meconium aspiration syndrome. J Nepal Health Res Counc. 2023;21:165-9.
5. Kasahara M, Koshida S, Tokoro S, Katsura D, Tsuji S, Murakami T, et al. Potential prevention of stillbirth caused by placental abruption: a regional population-based study in Japan. J Matern Fetal Neonatal Med. 2024;37:2321485.
6. Hammer L, Heazell AE, Povey A, Myers JE, Thompson JM, Johnstone ED. Assessment of the association between ambient air pollution and stillbirth in the UK: results from a secondary analysis of the MiNESS case-control study. BJOG. 2024;131:598-609.
7. Yang S, Tan Y, Mei H, Wang F, Li N, Zhao J, et al. Ambient air pollution the risk of stillbirth: a prospective birth cohort study in Wuhan, China. Int J Hyg Environ Health. 2018;221:502-9.
8. Alhousseini A, Farr C, Ogunyemi D, Wharton K, Fawaz A, Bazzi N, et al. Delivery of a fetus with a non-reassuring status is associated with significant maternal morbidity. Gynecol Obstet Invest. 2023;88:359-65.
9. Melaet R, de Vries IR, Kok RD, Guid-Oei S, Huijben IA, van Sloun RJ, et al. Artificial intelligence based cardiotocogram assessment during labor. Eur J Obstet Gynecol Reprod Biol. 2024;295:75-85.
10. Turner JM, Flenady V, Ellwood D, Coory M, Kumar S. Evaluation of pregnancy outcomes among women with decreased fetal movements. JAMA Netw Open. 2021;4:e215071.
11. Di Pasquo E, Fieni S, Chandraharan E, Dall'Asta A, Morganelli G, Spinelli M, et al. Correlation between intrapartum CTG findings and interleukin-6 levels in the umbilical cord arterial blood: a prospective cohort study. Eur J Obstet Gynecol Reprod Biol. 2024;294:128-34.
12. Jia YJ, Chen X, Cui HY, Whelehan V, Archer A, Chandraharan E. Physiological CTG interpretation: the significance of baseline fetal heart rate changes after the onset of decelerations and associated perinatal outcomes. J Matern Fetal Neonatal Med. 2021;34:2349-54.
13. Pereira S, Lau K, Modestini C, Wertheim D, Chandraharan, E. Absence of fetal heart rate Cycling on the Intrapartum Cardiotocograph (CTG) is associated with intrapartum pyrexia and lower Apgar scores. J Matern Fetal Neonatal Med. 2022;35:7980-5.
14. Devane D, Lalor JG, Daly S, McGuire W, Cuthbert A, Smith V. Cardiotocography versus intermittent auscultation of fetal heart on admission to labour ward for assessment of fetal wellbeing. Cochrane Database Syst Rev. 2017;1:CD005122.
15. Sharma B, Aggarwal N, Suri V, Siwatch S, Kakkar N, Venkataseshan S. Facility-based stillbirth surveillance review and response: an initiative towards reducing stillbirths in a tertiary care hospital of India. J Perinat Med. 2022;50:722-8.
16. Sharma B, Lahariya C, Majella MG, Upadhyay A, Yadav S, Raina, A, et al. Burden, differentials and causes of stillbirths in India: a systematic review and meta-analysis. Indian J Pediatr. 2023;90:54-62.
17. Valiño N, Giunta G, Gallo DM, Akolekar R, Nicolaides KH. Biophysical and biochemical markers at 30-34 weeks' gestation in the prediction of adverse perinatal outcome. Ultrasound Obstet Gynecol. 2016;47:194-202.
18. Bukowski R, Hansen NI, Pinar H, Willinger M, Reddy UM, Parker CB, et al. Altered fetal growth, placental abnormalities, and stillbirth. PLoS One. 2017;12:e0182874.
19. Zile I, Ebela I, Rumba-Rozenfelde I. Maternal risk factors for stillbirth: a registry-based study. Medicina (Kaunas). 2019;55:326.
20. Mackin ST, Nelson SM, Wild SH, Colhoun HM, Wood R, Lindsay RS, et al. Factors associated with stillbirth in women with diabetes. Diabetologia. 2019;62:1938-47.
21. Jacob L, Kostev K, Kalder M. Risk of stillbirth in pregnant women with obesity in the United Kingdom. Obesity Res Clin Pract. 2016;10:574-9.
22. Urhoj SK, Andersen PK, Mortensen LH, Davey Smith G, Nybo Andersen AM. Advanced paternal age and stillbirth rate: a nationwide register-based cohort study of 944,031 pregnancies in Denmark. Eur J Epidemiol. 2017;32:227-34.
23. Miller CB, Wright T. Investigating mechanisms of stillbirth in the setting of prenatal substance use. Acad Forensic Pathol. 2018;8:865-73.
24. Heinke D, Nestoridi E, Hernandez-Diaz S, Williams PL, Rich-Edwards JW, Lin AE, et al. Risk of stillbirth for fetuses with specific birth defects. Obstet Gynecol. 2020;135:133-40.
25. Page JM, Bardsley T, Thorsten V, Allshouse AA, Varner MW, Debbink MP, et al. Stillbirth associated with infection in a diverse U.S. cohort. Obstet Gynecol. 2019;134:1187-96.
26. Chighizola CB, Pregnolato F, Andreoli L, Bodio C, Cesana L, Comerio C, et al. Beyond thrombosis: anti-β2GPI domain 1 antibodies identify late pregnancy morbidity in anti-phospholipid syndrome. J Autoimmun. 2018;90:76-83.
27. Geenes V, Chappell LC, Seed PT, Steer PJ, Knight M, Williamson C. Association of severe intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: a prospective population-based case-control study. Hepatology. 2014;59:1482-91.