Commentary

The Significance of 'Non-Significant' Meconium Stained Amniotic Fluid (MSAF): Colour versus Contents

Running Head: The Significance of Non-Significant Meconium

Abstract

The presence of 'thin' or 'non-significant' meconium stained amniotic fluid (MSAF) is currently being considered by some intrapartum guidelines as 'low risk', requiring only an intermittent auscultation and not continuous electronic fetal heart rate monitoring using the cardiotocograph (CTG). Clinicians not only must exclude 'non-physiological' causes of MSAF but consider the potential effect of MSAF on fetal wellbeing, irrespective of whether the passage was secondary to a normal physiological process or due to an underlying pathology. Management decisions should be made based on the parity, rate of progress of labour, cervical dilatation at diagnosis, and observed CTG changes and the risk factors such as multiple pregnancy and intra-uterine growth restriction. Presence of any meconium within the amniotic fluid should be considered as an important intrapartum risk factor. The thin meconium may be 'non-significant' on visual inspection, but it is very significant from the point of view of a fetus, who is covered with toxic materials within the surrounding amniotic fluid.

Keywords: Meconium, Stained Amniotic Fluid, fetal wellbeing, cardiotocograph

UNDER PEER REVIEW

Introduction

The presence of 'thin' or 'non-significant' meconium stained amniotic fluid (MSAF) is currently being considered by some intrapartum guidelines as 'low risk', requiring only an intermittent auscultation and not continuous electronic fetal heart rate monitoring (CEFM) using the cardiotocograph (CTG). It is true that the majority of fetuses pass meconium at term due to the physiological maturation of fetal gut. Accumulation of digested lanugo hair, vernix, cellular matter from the swallowed amniotic fluid as well as the regular shedding of epithelial cells from the gastrointestinal tract and intestinal secretions cause progressive distension of the bowel as the gestation advances. As the gut is mature at term, initiation of peristalsis and dilatation of the anal sphincter due to the 'loading' of faecal matter results in normal defaecation in-utero. If there is a copious amount of amniotic fluid to dilute the meconium, this would result in a 'thin' or 'non-significant' meconium. Conversely, if the amount

of amniotic fluid is reduced (e.g. oligohydramnios secondary to ongoing chronic utero-placental insufficiency), a 'thick' or 'significant' meconium would be noted. However, clinicians not only must exclude 'non-physiological' causes of MSAF (e.g. ongoing hypoxia or chorioamnionitis), but consider the potential effect of MSAF on fetal wellbeing, irrespective of whether the passage was secondary to a normal physiological process or due to an underlying pathology.

Why is the mere presence of meconium within the amniotic fluid harmful?

Meconium refers to the first stool passed by the fetus, usually within the first 48 hours of birth and consists of gastrointestinal contents of the fetus [1]. It is detectable at 11 to 14 weeks gestation [2] The greenish colour is due to bile pigments [3[. Although, 80% of meconium consists of water, in addition to bile salts, bile acids and bile pigments, it contains gastro-intestinal digestive enzymes (amylases, lipases and proteases), intestinal epithelial cells as well as materials which are constantly swallowed from the amniotic fluid (e.g. fetal lanugo hair, vernix caseosa, inflammatory mediators and desquamated epithelial cells). Therefore, if a fetus is surrounded by amniotic fluid contaminated by meconium with all its toxic contents, several local effects may occur. In autopsy examinations, meconium exposure was associated with damage to the umbilical cord such as severe ulceration [4]. The effects of bile salts and bile acids on the blood vessels in the umbilical cord may lead to the spasm of the blood vessels, resulting in an acute reduction in fetal oxygenation. Prolonged contact of the potentially toxic contents of meconium with the fetal skin may cause skin damage, such as physiological desquamation of the skin or even erythema toxicum neonatorum [4]. Scientific evidence suggests a stronger association between the passage of meconium and a higher incidence of chorioamnionitis and endometritis [1]. The presence of the meconium within the amniotic cavity has been shown in experimental studies to promote bacterial growth as a result of the inactivation of neutrophil phagocytosis [5]. Therefore, even a 'thin' or 'non-significant' meconium may be associated with significant fetal harm secondary to the presence of digestive, toxic and inflammatory contents.

Systemic effects include meconium aspiration syndrome (MAS), which occurs in approximately 11% of all cases of MSAF and is associated with a neonatal mortality rate of 20% [6]. Whilst MAS does occur more commonly with thick meconium, one should not dismiss the 'thin' meconium staining of amniotic fluid as 'non-significant'. This is because the concentration of toxic mediators may be lower compared to 'thick' or 'significant' meconium, however, the thin meconium may also exert biochemical and inflammatory effects on the alveoli. It has been shown that MSAF induces the activation of alveolar macrophages and neutrophils, leading to the release of cytokines including tumour necrosis factor α and interleukins [6]. In addition, displacement of the surfactant may lead to respiratory distress syndrome even in a term fetus [6]. Moreover, the MSAF-induced release of inflammatory mediators can directly damage pulmonary parenchymal tissue or damage the pulmonary vasculature resulting in vascular leakage and damage to the type 2 pneumocytes and decrease surfactant production [6]. MSAF-induced release of the surfactant may lead to a decreased lung compliance, hypoxia and acidosis [2]. Compared to thin meconium, if there is 'thick' meconium or a 'meconium plug', this can cause obstruction of the airways [6]. The obstruction of relatively larger airways may result in an airway obstruction, resulting in ventilation/perfusion mismatch [2]. In

UNDER PEER REVIEW

severe cases of ventilation-perfusion mismatch, or if there is damage to the pulmonary vasculature secondary to inflammatory damage to the alveolar epithelium and the underlying endothelium, then, a persistent pulmonary hypertension (PPH) may occur in up to 40% of cases of severe MAS [7]. PPH can worsen fetal condition and result in poor neonatal adaptation resulting in hypoxia and severe metabolic acidosis, which cause further pulmonary vasoconstriction [7.8]. Hence, a vicious cycle may be established leading to a very poor perinatal outcome.

Time to question the significance of 'non-significant' meconium

Some have considered that 'non-significant' meconium has a lower risk of fetal complications, and therefore, they have recommended intermittent auscultation [10]. Those who advocate this management consider that reduced concentration of meconium within the amniotic fluid may not be sufficient to cause poor perinatal outcomes. However, it has been shown that, irrespective of whether it is 'thin' or 'thick', the mere presence of meconium within the amniotic fluid is associated with increased risk of neonatal sepsis and admission to neonatal intensive care units [7-9]. Therefore, it is illogical and possibly dangerous to suggest that in the presence of 'thin' or 'non-significant' meconium, it is appropriate to recommend intermittent auscultation [10]. This is because doing so, would lead to underestimation the local and systemic effects of the potentially toxic contents of the meconium on the fetus. Whilst the presence of thick meconium is known to be significantly associated with severe fetal complications [11.12], one should not forget that even thin or 'non-significant` meconium in the amniotic fluid containing bile salts and bile acids, pancreatic enzymes and inflammatory mediators reduces the phagocytotic activity of the amniotic fluid and should be seen as a strong risk factor towards the development of chorioamnionitis. Therefore, the presence of *any* meconium, irrespective of whether it is significant or 'non-significant' as deemed by clinicians which has a considerable inter- and intra-observer variability, warrants continuous intrapartum fetal heart rate monitoring to timely recognize the onset of chorioamnionitis and evolving hypoxic stress.

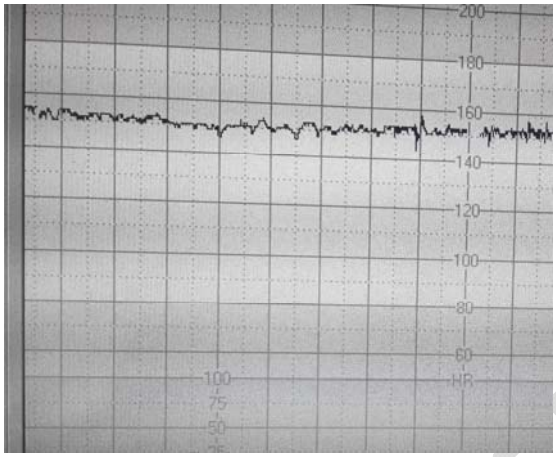
Role of CTG Guidelines in managing fetuses with MSAF

The guidelines produced by national [10] and international [13] bodies on CTG interpretation are specifically designed to timely detect intrapartum hypoxia and not infection. It is important to appreciate that MSAF may result in chorioamnionitis, which does not operate through the hypoxic pathway of fetal injury, but through the inflammatory pathway. It has been shown that in the presence of fetal tachycardia associated with MSAF, the risk of fetal infection is increased by 51 fold [14]. It is important to appreciate that a fetus beyond 40 weeks of gestational may have a lower baseline FHR due to the vagal dominance. Therefore, when there is an intrauterine fetal infection, a rise of fetal temperature by 1°C secondary to the fetal inflammatory response may only increase the baseline FHR by approximately 10%. Therefore, a fetus with a baseline FHR of 130 bpm may not increase the FHR beyond 150 bpm to demonstrate tachycardia (i.e. > 160 bpm). Hence, it should be noted that a rise in the fetal heart rate, even within the normal range may be abnormal for a fetus who has developed chorioamnionitis. Arbitrary cut offs (i.e. baseline of 110-160 bpm) which have been developed for a population of human feuses cannot be blindly applied to individual fetuses with MSAF. Moreover, contrary to the earlier belief, it is now accepted that fetuses do not always pass meconium when they are subjected to intrapartum hypoxia [15]. Therefore, the absence of

UNDER PEER REVIEW

ongoing decelerations should not provide a false sense of security in fetuses with MSAF. CTG features suggestive of non-hypoxic pathways fetal neurological injuries such as higher than expected baseline, absence of cycling and accelerations (Figure 1) and loss of baseline variability should be considered [16]. Recently, it has been reported that absence of cycling, a rise in the baseline FHR and saltatory patterns are associated with chorioamnionitis [17].

Figure 1. Note higher than expected baseline FHR for 41 weeks of gestation with absence of cycling and accelerations indicative of ongoing chorioamnionitis in a fetus with MSAF



Moreover, a rise in the baseline and repetitive atypical variable decelerations which have been associated with in-utero gasping and meconium aspiration syndrome should be avoided. The use of oxytocin should be critically reviewed because the onset of additional hypoxic stress in a fetus with MSAF during labour may increase the risk of meconium aspiration syndrome by hypoxia-acidosis mediated damage to the alveolar macrophages and alveolar membrane. Moreover, co-existing chorioamnionitis can also independently damage alveolar membrane predisposing to meconium aspiration syndrome. Scientific evidence suggests that the synergistic effect of intrapartum hypoxia (e.g. due to the injudicious use of oxytocin) and fetal infection increases the risk of cerebral palsy by up to 78 fold [18]. Management decisions should be made based on the parity, rate of progress of labour, cervical dilatation at diagnosis, and observed CTG changes and the risk factors such as multiple pregnancy and intra-uterine growth restriction.

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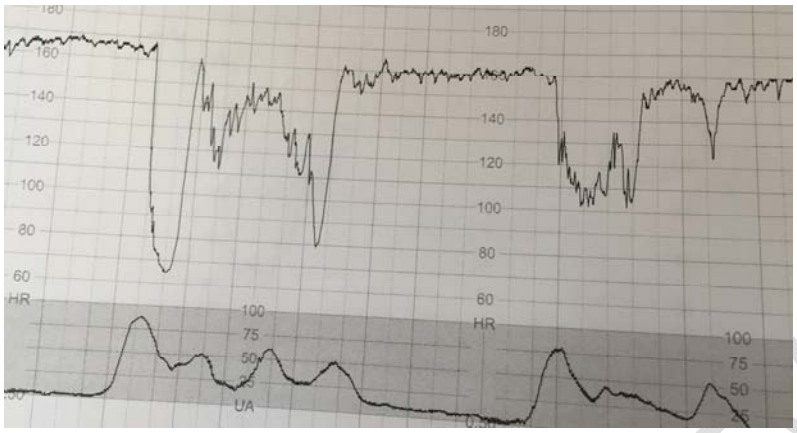
Figure 2. Note ongoing Atypical variable decelerations after the commencement of oxytocin in a fetus with MSAF, which increases the risk of meconium aspiration syndrome by inducing fetal gasping.



How to avoid poor perinatal outcomes in fetuses with MSAF?

Clinicians should consider the presence of any meconium (thick, thin, significant or non-significant) as an important risk factor for poor perinatal outcomes due to its detrimental local and systemic effects. The use of intermittent auscultation for 'non-significant' meconium should be strongly discouraged as this technique is not sensitive to detect features of non-hypoxic causes of fetal neurological injury secondary to the harmful effects of meconium. Auscultation once in every 15 minutes would delay the detection of a prolonged deceleration which may occur as a result of umbilical cord spasm during the interval between auscultations. Moreover, intermittent auscultation cannot detect a subtle rise in the baseline fetal heart rate, loss of cycling, sinusoidal or saltatory patterns which are seen in chorioamnionitis secondary to MSAF. Considering the 'non-significant' meconium as 'low risk' reflects the lack of understanding by some clinicians of the biochemical, inflammatory, digestive and toxic contents which constitute the meconium. Presence of any meconium, irrespective of how thick it appears to a clinician's eyes, should be viewed with caution, due to the local and systemic side effects (Table 1).

Management decisions should be made based on the parity, rate of progress of labour, cervical dilatation at diagnosis, and observed CTG changes and the risk factors such as multiple pregnancy and intra-uterine growth restriction. In the presence of MSAF, caution should be exercised whilst commencing oxytocin infusion, especially in early labour, because a super-imposed hypoxic stress (Figure 3), especially if there was a meconium-induced chorioamnionitis, may worsen perinatal outcomes and increase the likelihood of meconium aspiration syndrome.

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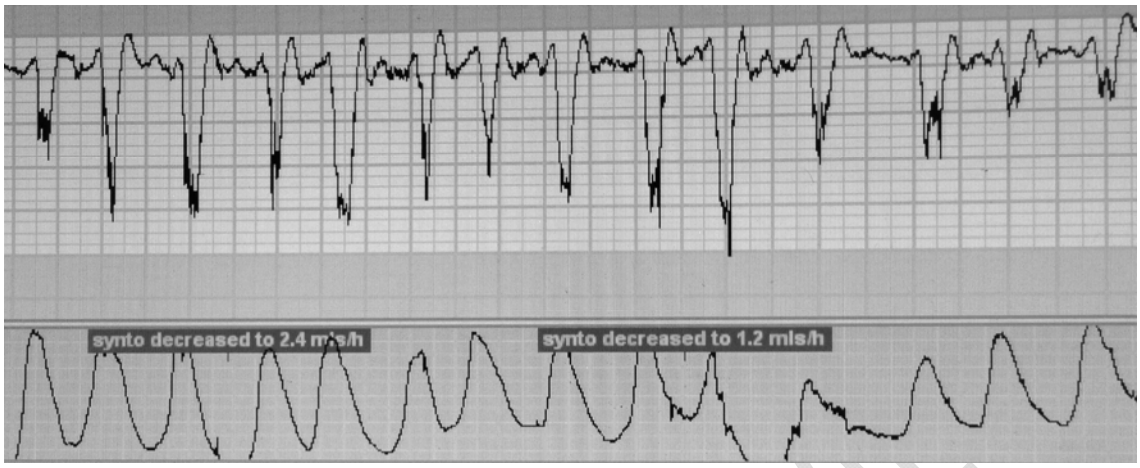
Figure 3. Note the onset of repetitive deceleration in a fetus already experiencing chorioamnionitis (raised baseline FHR for 40 weeks + 6 days), which resulted in meconium aspiration syndrome.



Conclusion

The presence of meconium within the amniotic fluid should be considered as a significant risk factor for poor perinatal outcomes. The terminologies 'light', 'thin' or 'non-significant' should be used with caution and should not lead to a false reassurance because the presence of meconium within the amniotic cavity increases the risk of local and systemic adverse effects to a fetus regardless of the concentration. Recently it has been reported that there was an 8-fold increase in the incidence of MSAF in fetuses with chorioamnionitis [19].Therefore, one should not recommend intermittent auscultation for 'non-significant meconium' because this technique would not be able to reliably detect features of non-hypoxic injury such as absence of cycling, loss of baseline FHR variability and a rise in the baseline by 10-15 bpm in a term fetus. In addition, if there is umbilical cord spasm secondary to meconium within the amniotic fluid, awaiting the next auscultation after 15 minutes may miss a prolonged deceleration secondary to vasospasm of the umbilical arteries. Meconium, regardless of how it looks to the human eye, contains the same digestive and toxic agents, and should be treated with caution and should be considered as an important intrapartum risk factor. Presence of any meconium within the amniotic fluid should alert the clinician to the increased risks of fetal hypoxia and infection and their association with MSAF. The thin meconium may be 'non-significant' on visual inspection, but it is very significant from a from a point of view of a fetus covered with toxic materials within the surrounding amniotic fluid. Scientific evidence suggests that even thin meconium may accelerate the growth of GBS and E.Coli within 6 hours, indicating that neutrophil phagocytosis may be inactivated within a few hours of contamination of the amniotic fluid [20].

Conflict of Interest

None

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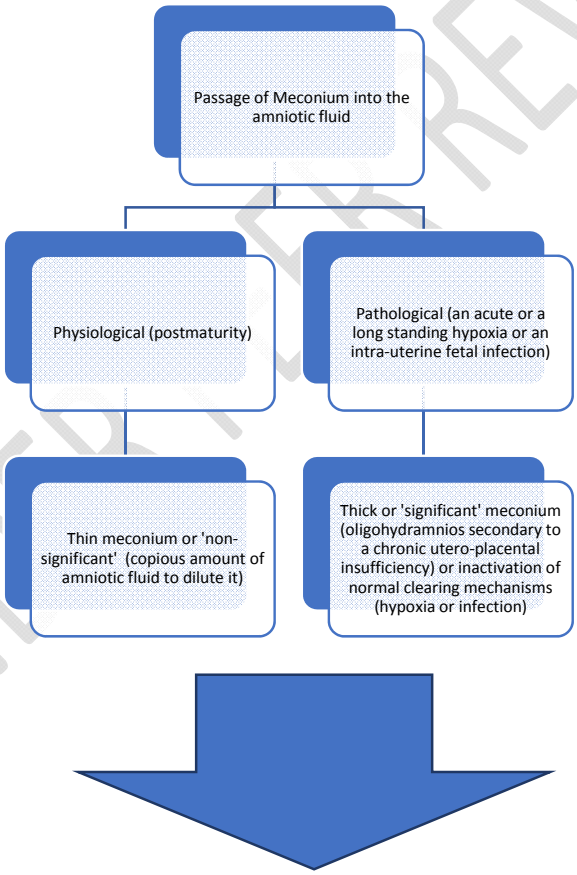
Table 1. Impact of ‘Significant’ and ‘Non-Significant’ Meconium



Local effects: Spasm of umbilical cord vessels leading to an acute hypoxic insult, inactivation of neutrophil phagocytosis leading to chorioamnionitis, ulceration of the fetal skin or the umbilical cord due to a prolonged contact with bile salts and digestive enzymes

UNDER PEER REVIEW

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