Meconium - Stained Amniotic Fluid in Labour – its Significance and Correlation to Early Maternal and Neonatal Outcome – A Prospective Case Control Study in A Tertiary Care Center

Samarawickrama NGCL[1*], Pathiraja R[2], Gunasekara D[3], Withanathantrige MR[4]

[1] *Consultant Obstetrician & Gynaecologist, Colombo South Teaching Hospital, Colombo, Sri Lanka*

[2]*Professor, Department of Obstetrics & Gynaecology, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka.*

[3] *Professor, Department of Paediatric, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka*

[4] *Consultant Obstetrician & Gynaecologist, Teaching Hospital Mahamodara, Sri Lanka*

**Correspondence*

Abstract:

Background: **Meconium-stained amniotic fluid (MSAF) is a well-known factor which associated with significant adverse pregnancy outcomes. Meconium Aspiration Syndrome (MAS) occurs in about 5% of deliveries with MSAF and death occurs in about 12% of infants with MAS. The significance of meconium claimed to be varied from being entirely physiological, which exhibits sign of fetal maturity, to a sign of fetal distress as a response to hypoxic insult to the foetus. This study was carried out in a tertiary care centre; with the aim of detecting the significance of MSAF. Additionally, this study compares the fetal and maternal outcome in deliveries complicated by meconium-stained amniotic fluid and critically evaluates the associated predisposing maternal and fetal factors for MSAF.**

Method: **This prospective case-control study was carried out in Colombo South Teaching Hospital (University Professorial Obstetrics Unit), Sri Lanka. Women who presented to the unit with pre-defined selection protocol were recruited to the study until the sample size (n = 216 in each arm) is achieved. The Sample was categorized in to two groups depend on the presence or absence of Meconium-stained amniotic fluid. Mean, standard deviation, median and 95% confidence interval are computed for quantitative variables. Chi-square test is applied for calculating the statistical significance of variables such as grades of meconium and Apgar score at 95% confidence interval. The p-value <0.05 and 95% confident interval was utilised to assess the statistical significance.**

Results: **Presence of diabetes in current pregnancy was a significant risk factor for meconium-stained amniotic fluid at delivery with odd ratio of 2.397 (95% Confident Interval 1.203 - 3.568) and p value of <0.00.1.**

There is a statistically significant association between the mode of delivery and the nature of meconium with odd ratio of 3.029 (95% Confident Interval 1.887 – 3.136) and p value < 0.001, when its moderate to thick meconium staining. Presence of moderate to thick meconium increase the risk of neonatal respiratory morbidity with increased NICU admissions, which is both statistically and clinically significant with odd ratio of 2.412 (95% Confident Interval 1.674 - 3.199) and p value 0.005 when compared with thin meconium staining.

Overall, there is a 2-fold rise in operative vaginal deliveries and EM-LSCS (Emergency Lower Segment Caesarean Section) in the presence of MSAF which accountable for 67.3% of the deliveries compared to 37.2% in the clear liquor group.

The follow up of neonates at one month and three months of life, revealed no statistically significant concerns on the development of these babies in either arm of the study population.

Conclusion: **Presence of meconium-stained amniotic fluid is one of the common indications for caesarean delivery. Therefore, the results of this study may help to reduce the number caesarean sections carried out when the meconium is detected during labour. Presence of thin MSAF can be physiological following gut maturation of term foetuses, thus utilization of continuous electronic fetal monitoring can reliably cut down the caesarean section rates without adding numbers to the adverse perinatal outcomes. On the other hand, timely interventions upon detection of abnormal Cardiotocography (CTG), such as operative vaginal delivery or EM-LSCS, can significantly minimise these adverse neonatal outcomes. Abnormal CTG in a clinical background of moderate to thick meconium is more alarming, which warrant urgent interventions compared to the presence of thin / lightly stained meconium.**

Key Words: **Meconium stained amniotic fluid, Meconium Aspiration Syndrome, APGAR, Cardiotocography, EM-LSCS**

I. INTRODUCTION

Meconium is a thick black material that collects in the distal portion of the small intestine and colon of the foetus and constitute of intestinal secretions, bile, desquamated cellular debris and amniotic fluid. Although 69% of the new-borns pass meconium by 12 hours of birth, many infants may pass meconium prior to birth (1). Various studies have reported an incidence of meconium-stained

amniotic fluid ranging between 1.5% and 18% (2). The significance of meconium claimed to be vary from being entirely physiological, which exhibits sign of fetal maturity, to a sign of fetal distress as a response to hypoxic insult to the foetus (3). In the process of maturational event, meconium staining of amniotic fluid (MSAF) may occur in 35% or more of infants born at 42 weeks' gestation (4) and is seldom noted in infants born before 37 weeks. Closer to term, the gastrointestinal tract of the foetus matures, and head or cord compression causes commencement of bowel peristalsis with the relaxation of the rectal sphincter, leading to meconium passage. Recent data also support the role of motilin, a peptide produced mainly in the jejunum, which stimulates peristalsis. Motilin is low in preterm infants and non-asphyxiated infants but raised in infants who are term or asphyxiated (5).

Among pre-term infants, the evidence suggests that MSAF may be more prevalent than previously understood, and appears to be independently associated with higher levels of neonatal morbidity and mortality. It is unclear if the associated morbidity and mortality is a consequence of MSAF or if MSAF is correlated to other causative factors such as chorioamnionitis (6).

Meconium-stained amniotic fluid, which associated with significant adverse pregnancy outcomes, is a clinical diagnosis at the time of rupture of membranes with no practical antenatal confirmatory tests (7). However, various methods have been tried to detect the presence of meconium in the amniotic fluid and to prevent MAS. These methods include amnioinfusion, oropharyngeal suction, endotracheal intubation, amnioscopy and early induction of labour. The common maternal risk factors for meconium-stained amniotic fluid are maternal hypertension, gestational diabetes mellitus, maternal chronic respiratory or cardiovascular diseases, post term pregnancy, pre-eclampsia, Eclampsia, oligohydramnios, intrauterine infections and intrauterine growth restriction (8).

Meconium directly alters the amniotic fluid, reducing its antibacterial activity thus predisposed to increased risk of perinatal bacterial infections. The most significant complication of meconium passage in utero is aspiration of meconium-stained amniotic fluid before, during or after the birth (9). MAS occur in 2-22% of babies who born with meconium-stained amniotic fluid and carries significantly higher morbidity and mortality rates (10).

Presence of meconium below the vocal cords is known as meconium aspiration and it is seen in around 20-30 % of all infants with meconium-stained amniotic fluid (11). Aspiration can occur in utero with foetal gasping, or after birth, with the first breaths of life. Meconium Aspiration Syndrome (MAS), which explained by using radiographic evidence of pneumonia in the clinical presence of respiratory distress, occurs in about 5% of deliveries with MSAF (11). It's estimated that death can occurs in about 12% of infants with MAS (12).

The positive predictive value for meconium-stained amniotic fluid and its complications is higher when it occurs in high-risk patients and when it is thick, dark and tenacious. On the other hand, lightly stained meconium had a poor correlation with fetal hypoxia (13) as it can be a sign of gut maturity of the term foetuses. The moderate and thick meconium groups have significantly greater risk of abnormal fetal heart rate tracings, low Apgar scores, low cord blood pH, sepsis, need for O2 support and level III neonatal intensive care (14).

In recent years, there is a significant fall in rates of stillbirths and neonatal deaths due to improvement in antenatal, intra partum and neonatal care (15). Appropriate intrapartum care with early detection and management of fetal hypoxia is paramount in minimizing the risk of meconium staining of amniotic fluid (16).

The morbidity and mortality associated with MAS can be brought down by early identification of high-risk patients during the antenatal period in addition to careful and timely decision making on the mode of delivery along with comprehensive intrapartum fetal monitoring.

This study was carried out in a tertiary care centre; with the aim of detecting the significance of MSAF. Additionally, this study compares the fetal and maternal outcome in deliveries complicated by meconium staining with clear liquor and critically evaluates the associated maternal and fetal factors.

Scientific scope, General objective:

To assess the significance of meconium-stained amniotic fluid (MSAF) at term on maternal and neonatal outcomes (a prospective case control study)

Specific objectives:

1. To predict the association between maternal and fetal risk factors for the presence of MSAF
2. To assess the relationship between the presence of MSAF and adverse perinatal outcomes (both maternal and neonatal)
3. To evaluate the relationship between types MSAF on maternal and neonatal outcomes

II. METHODOLOGY

This prospective case-control study was carried out in Colombo South Teaching Hospital (University Professorial Obstetrics Unit), Sri Lanka. Women who presented to the unit with pre-defined selection protocol were recruited to the study until the sample size (n = 216 in each arm) is achieved. The Sample was categorized in to two groups depend on the presence or absence of Meconium-stained amniotic fluid. The relevant descriptive statistics, frequencies and percentages are computed for categorical variables such as booking status, parity, Bishop's score at detection of MSAF, stage of labour, CTG classification, mode of delivery, Apgar score and fetal/neonatal outcome. Mean, standard deviation, median and 95% confidence interval are computed for quantitative variables. Chi-square test is applied for calculating the

statistical significance of variables such as grades of meconium and Apgar score at 95% confidence interval. The p-value <0.05 and 95% confident interval was utilised to assess the statistical significance.

Sample selection criteria

1. Inclusion criteria

Pregnant women between 37 weeks and 42 weeks of gestational age, Singleton pregnancy with Vertex presentation.

Cases are those with meconium-stained amniotic fluid detected at or after the rupture of membranes and controls being those with clear liquor

2. Exclusion criteria

Breech presentation at term

Major congenital anomalies

Intrauterine fetal death

Multifetal pregnancies

Preterm or post-term pregnancies (<37 weeks or >42 weeks of gestation)

Patients who fulfilled the inclusion criteria were evaluated and enrolled in the study after explaining the purpose and procedures of the study. Informed written consent was taken from all the participants. Patient's bio data, detailed history, relevant clinical examination including general physical examination, abdominal examination, vaginal examination, speculum examination, and investigations including intermittent CTG, were recorded on a pre-designed proforma. The live births were categorized into MSAF and non-MSAF groups and compared for variables like maternal age, parity, antenatal complications (antepartum hemorrhage, pregnancy induced hypertension, Eclampsia, etc.) and complications during labor (obstructed or prolonged labor, fetal distress). Status of amniotic fluid was noted at amniotomy, during spontaneous rupture of membrane (SROM), during any point of labour and intra operatively in patients taken up for LSCS. MSAF was further categorized based on meconium consistency as follows.

Thin: Amniotic fluid tinted green with meconium without particulate matter

Moderate: Amniotic fluid with meconium and particulate matter

Thick: When consistency is pasty, viscous (pea–soup) and plugs present

Following above categorization of amniotic fluid, perinatal outcomes were compared for maternal outcomes such as OVD or EM/LSCS and neonatal outcomes such as APGAR score at birth, NICU admissions, incidence of birth asphyxia, MAS and perinatal mortality. To minimize the observer mediated bias in obtaining the data, assessment of the meconium was performed by two different observers who are postgraduate trainees in obstetrics. The observers were trained by the principal investigator in view of assessing the meconium-stained amniotic fluid by using specially prepared visual charts to differentiate the types of meconium.

Exact time of MSAF was detected and dilatation of uterine cervix in centimeters at the time of detection of MSAF were recorded. The time interval between detection of meconium-stained amniotic fluid and delivery of the baby was recorded respective to the mode of delivery. A Paediatric medical officer was present for all deliveries to facilitate to the neonatal care. Those neonates, who needed observation were transferred to the neonatal intensive care unit as per the neonatology team guidance. Perinatal outcomes including low Apgar score, low birth weight and birth asphyxia were documented.

Participants were given an idea about the study and requested to sign a consent form as an agreement for the participation. All the women were informed that, they have the right to refuse to participate form beginning or at any point of the data collection period. The identities of participants were kept confidential in online data base with password protection. No identifying information shared during data analysis and processing; thus, the anonymity of participants was ensured.

Data analysis

The Statistical Package for Social Science (SPSS-10) was used to analyse the data. The relevant descriptive statistics, frequency and percentage, were computed for categorical variables like booking status, mode of delivery, stage of labour, parity, gravida, Apgar score, CTG and fetal outcome. Mean, Standard deviation, Median and 95% confidence interval were computed for quantitative variables.

The chi square test was applied between grades of meconium and Apgar score at 95% confidence interval and the p-value < 0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was obtained from the Ethical Review Committee, Faculty of Medical Sciences, University of Sri Jayewardenepura. Approval to conduct the study was also obtained from the Director of the Colombo South Teaching Hospital, Kalubowila. Informed written consent was obtained from all participants. Those who did not consent for the study were given due medical care without any discrimination. All participants had the right to withdraw from the study after enrolment, without any prejudice to their further management.

Strict confidentiality was maintained regarding individual patient’s data which were stored in an on-going workplace data sheet and only grouped data will be presented. Each patient was given a reference number and their anonymity will be maintained throughout the study. There are no major ethical issues that could be identified in this study.

III. RESULTS

According to the demographic data analysis, majority of the women recruited in to the study were between 26 and 30 years of age (n = 186, 43%) and Sinhalese in ethnicity (93.8%).

Among the study sample, 98.6% were married and 47.9% educated up to G.C.E. Ordinary Level. Majority of the study population, monthly income range between LKR 10000 and 50000. (**Table 1 & Figure 1**)

Overall, there is no statistically significant demographic variation between MSAF group and clear liquor group.

Table 1. Demographic characteristics of the study population

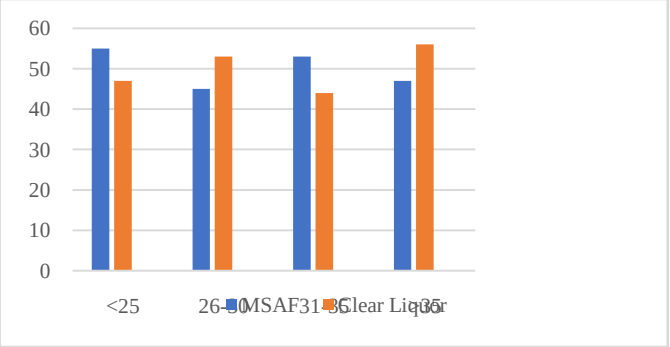
	N = 432	%
Age		
< 25	88	20.4
26 - 30	186	43.0
31 - 35	113	26.2
> 35	45	10.4
Ethnicity		
Sinhalese	405	93.8
Tamil	20	4.6
Muslim (Moor)	7	1.6
Education level		
No school education	2	0.5
Up to Grade 5	10	2.3
Up to GCE O/L	207	47.9
Up to GCE A/L	171	39.6
Other	42	9.7
Monthly income (LKR)		
< 10,000	9	2.1
10,000 – 50,000	260	60.2
50,000 – 100,000	156	36.1
> 100,000	7	1.6

*(G.C.E - O/L – General Certificate of Education Ordinary Level, G.C.E - A/L – General Certificate of Education Advanced Level, LKR – Sri Lankan Rupee)

There is a statistically significant association between the mode of delivery and the nature of meconium with odd ratio of 3.029 (95% Confident Interval 1.887 – 3.136) and p value < 0.001 when its moderate to thick meconium staining. Therefore, the presence of moderate to thick meconium increase the operative delivery rates (OVD and EM-LSCS) when compared to the presence of thin meconium-stained amniotic fluid. (**Table 2**)

Presence of moderate to thick meconium increase the risk of neonatal respiratory morbidity with increased NICU admissions. This finding is both statistically and clinically significant with odd ratio of 2.412 (95% Confident Interval 1.674 - 3.199) and p value 0.005 when compared to thin meconium staining. (**Table 2 & Table 5**)

Figure 1. Age distribution of participants among each arm of the study (%)



* All the values in the chart are representation of the respective percentages

There is no statistically significant relationship between the type of meconium-stained amniotic fluid on neonatal jaundice or neonatal intravenous antibiotic requirement. (**Table 2**)

Table 2. The effect of grade of meconium - stained amniotic fluid on obstetric and neonatal outcomes

Maternal & Neonatal outcomes	Nature of meconium		OR (95% CI)	p value
	Thin	Moderate to Thick		
Mode of delivery				
EM/LSCS or OVD	16	129	3.029	<0.001
VD	43	28	(1.887 – 3.136)	
Respiratory morbidity				
Yes	12	63	2.412	0.005
No	56	85	(1.674 - 3.199)	
Neonatal jaundice				
Yes	2	11	2.527	0.197
No	66	137	(0.081 - 2.952)	
IV antibiotic requirement				
Yes	5	22	2.021	0.121
No	63	126	(0.164 - 2.455)	

* OR – Odd ration, CI – Confident Interval, EM/LSCS – Emergency Lower Segment Caesarean Section, OVD – Operative vaginal delivery, VD – Vaginal Delivery, IV – Intra-venous, NICU – Neonatal Intensive Care Unit

Presence of diabetes in current pregnancy is a significant risk

factor for meconium-stained amniotic fluid at delivery with odd ratio of 2.397 (95% Confident Interval 1.203 - 3.568) and p value of <0.001. There is no statistically significant relationship between the presence of hypertensive disorders in current pregnancy and MSAF. (**Table 3**)

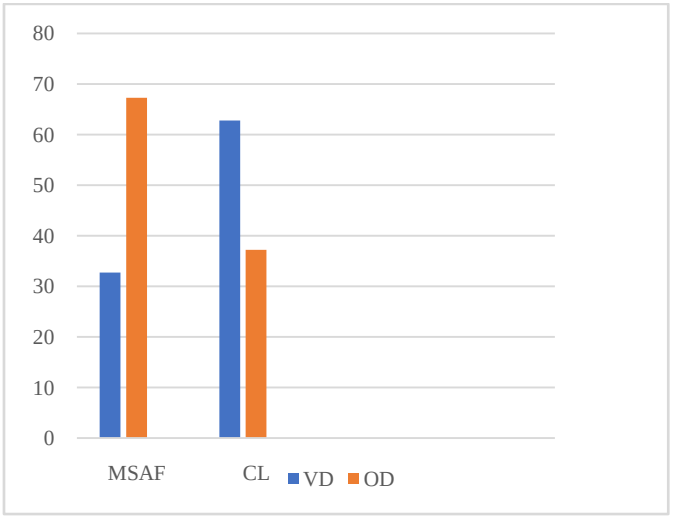
Table 3. The association between maternal and fetal factors on the presence of MSAF

Maternal and fetal factor			OR (95% CI)	p - Value
	Case	Control		
Diabetes in current pregnancy			2.397	<0.001
Yes	43	18	(1.203 – 3.568)	
No	173	198		
PIH/PE/Chronic HT in current pregnancy			3.762	0.052
Yes	23	12	(0.981-4.184)	
No	193	204		

*OR – Odd ration, CI – Confident Interval, DIP – Diabetes in pregnancy, PIH – Pregnancy Induced Hypertension, PE – Preeclampsia, Chronic HT – Chronic Hypertension

Overall, there is a 2-fold rise of operative vaginal deliveries and EM-LSCS (Emergency Lower Segment Caesarean Section) in the presence of MSAF which accountable for 67.3% (n = 145) of the deliveries compared to 37.2% (n = 80) in the clear liquor group.(**Figure 2**)

Figure 2. Comparison of Mode of delivery rates between MSAF and clear liquor group (%)



*MSAF – Meconium-stained amniotic fluid, CL – Clear liquor, VD – Vaginal delivery, OD – Operative delivery

The caesarean section rate is nearly two-fold higher among the MSAF group when compared with clear liquor group. In MSAF group, total 59.8% (n = 129) of women underwent EM-LSCS. Among the clear liquor group, 30.1% (n = 65) of women underwent EM-LSCS. There is no significant difference in operative vaginal delivery rates between the two groups (**Table 4**).

Table 4. The comparison between meconium-stained amniotic fluid group and clear liquor group on mode of delivery

Type	OVD		EM - LSCS	
	n	%	n	%
MSAF	16	7.5	129	59.8
Clear Liquor	15	7.1	65	30.1

* EM-LSCS – Emergency Lower Segment Caesarean Section, OVD – Operative vaginal delivery, MSAF-meconium-stained amniotic fluid

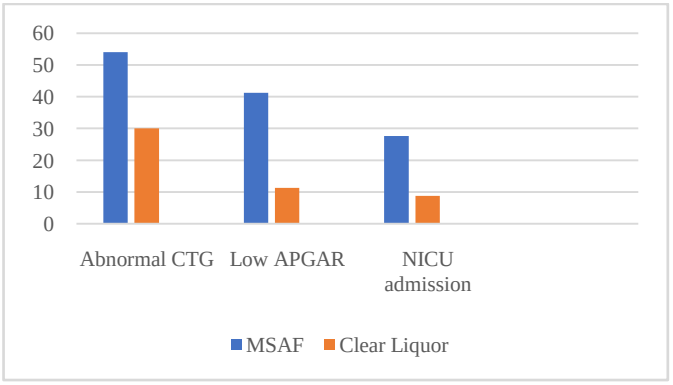
Continuous electronic fetal monitoring detect pathological Cardiotocography (CTG) traces [Classified according to the NICE (National Institute for health and Care Excellence) intrapartum guideline - CG 190] in 117 women in MSAF group. All these women underwent either OVD or EM-LSCS. Eighty-nine babies (41.2%) observed to have low APGAR score at 5 minutes of life where, 27.6% (60 babies) of MSAF group were admitted to NICU for further observations due to persistent low 5 min APGAR and/or presence of features of respiratory instability including transient tachypnoea of newborn. In comparison, the clear liquor group, there were 65 pathological CTGs, with 8.8% of babies (19 babies) admitted to the NICU. Among these, 24 babies (11.3%) found to have low 5 min APGAR score of <7. (**Table 5 & Figure 3**)

Table 5. The comparison of fetal and neonatal outcomes between MSAF and clear liquor group

N = 216	% from total	
MSAF		
Abnormal CTG	117	54.1
Low APGAR at 5 minutes	89	41.2
NICU Admission	60	27.6
Clear liquor		
Abnormal CTG	65	30.1
Low APGAR at 5 minutes	24	11.3
NICU Admission	19	8.8

*CTG – Cardiotocograph, NICU – Neonatal Intensive Care Unit

Figure 3. Comparison of fetal and neonatal outcomes between MSAF and clear liquor group (%)



*MSAF – Meconium-stained amniotic fluid, CL – Clear liquor, VD – Vaginal delivery, OD – Operative delivery

The follow up of neonates at one month and three months of life, revealed no statistically significant concerns on the development of these babies in either arm of the study population.

IV. DISCUSSION

Detection of meconium-stained amniotic fluid (MSAF) during labour is associated with significant anxiety among both health care providers and patients, as it is often considered as an indicator of fetal distress (17). It is a frequent causative factor for poor fetal outcome, which increases the number of neonatal intensive care unit admissions and interventions. However, the literature in obstetrics still has many unanswered questions regarding the significance of MSAF & seeks appropriate protocols and guidelines for the management of labors complicated by MSAF.

MSAF is a clinical diagnosis without any efficient practical confirmatory test. It is possible that in some cases in which MSAF was diagnosed, there may have been an alternative explanation for the discoloured liquor, such as congenital obstruction of gastro-intestinal tract or congenital infections other than the fetal distress. None of the neonates who diagnosed as having anatomical or functional intestinal obstruction after the birth were included in to the final data analysis in this study to eliminate such controversies.

Observers and the literature describe meconium as old Vs. new, thin Vs. moderate Vs. thick or particulate. All these categorizations have not been reliably defined, thus were not consistently recorded in this study. Therefore, all MSAF was considered equivalent except for thin versus moderate to thick MSAF.

Saunder's et al. reported that caesarean sections were performed twice as frequently as in subjects with MSAF when compared to women with clear liquor at labour (18). This is also compatible with our research findings, where we found Emergency Lower Segment Caesarean Sections (EM-LSCS) and operative vaginal deliveries (OVD) are more common among MSAF group. In addition to the presumed fetal distress diagnosed by using CTG criteria, presence of moderate to thick meconium at early stage of labour itself is an indication for these statistically and clinically significant increased operative delivery rates.

Becker S et al. identified that meconium consistency is directly correlated to the perinatal outcomes. The risk of perinatal morbidity and mortality increases when meconium is present at the onset of labour and is moderate to thick in consistency (19). Our study agreed with the fact that, moderate to thick meconium is associated with increased rate of caesarean sections and OVD in addition to increase perinatal morbidity such as low APGAR score at 5-minute, respiratory morbidity and admission to NICU when compared to thinly stained amniotic fluid.

This study also able to demonstrate the significance of respiratory morbidity associated with MSAF (20) and agrees with study carried out by Ratnam SS. et al. (1992) which identified a significantly increased risk between MSAF and respiratory morbidity requiring interventions (13).

Even though we found a statistically significant association between diabetes in pregnancy and MSAF, there were limited data and research available enquiring this topic. Given the nature of adverse pregnancy outcome associated with DIP, this is a good area of research with more defined criteria in order to predict and employ early interventions for such high-risk pregnancies to minimize such adverse pregnancy outcomes.

Tybulewicz AT et al. (2004) demonstrate that there is no statistically significant association between maternal hypertension and the MSAF, which is comparable with our study findings (7).

Our limited follow up revealed no statistically significant outcomes at intervals of one month and three months of life. This may be due to prompt interventions upon identifying alarming features of the CTG. Our aim is to follow up these babies up to the age of 10 years as a follow up study to detect any emergence of statistically significant outcome among these babies.

V. CONCLUSIONS AND RECOMMENDATIONS

Presence of meconium-stained amniotic fluid remains a management dilemma to the obstetricians and equally worries the paediatricians. This study helped to determine the significance of meconium staining of amniotic fluid and the association of its nature to the maternal and fetal outcome. Additionally, this study asses the associated risk factors as predictors to the MSAF.

Presence of meconium-stained amniotic fluid is one of the common indications for caesarean delivery. Therefore, the results of this study may help to reduce the number of caesarean sections carried out when the meconium is detected during labour. Presence of thin MSAF can be physiological following gut maturation of term foetuses, thus utilization of continuous electronic fetal monitoring can reliably cut down the caesarean section rates without adding numbers to the adverse perinatal outcomes. Thus, we recommend continuing electronic fetal monitoring for such complicated labors with comprehensively defined Cardiotocography (CTG) criteria. According to the available data, the NICE categorization of CTG gives comprehensive guidance to clinicians on managing these MSAF complicated labors, while significantly minimizing adverse pregnancy outcomes.

On the other hand, timely interventions upon detection of abnormal CTG, such as operative vaginal delivery or EM-LSCS, can significantly reduce these adverse neonatal outcomes. Abnormal CTG on a clinical background of moderate to thick meconium is more alarming, which warrant urgent interventions compared to the presence of thin / lightly stained meconium.

We believe the long-term effect of MSAF and its sequalae is a good research topic to be carried out. Our limited follow up revealed no statistically significant outcomes at intervals of one month and three months of life. This may be due to prompt interventions upon identifying alarming features of the CTG. Our aim is to follow up these babies up to the age of 10 years as a follow up study to detect any emergence of statistically significant outcome among these babies.

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