"EFFECT OF DEXAMETHASONE IN THE OUTCOME OF MECONIUM ASPIRATION SYNDROME: A PROSPECTIVE STUDY"

By

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LIST OF ABBREVIATIONS

AMA	- Against Medical Advice
AGA	- Appropriate for Gestational Age
AP 1	- Protein Activator 1
B/N Ratio	- Band Neutrophil Ratio
COX- 2	- Cyclooxygenase- 2
CFT	- Capillary Filling Time
CRP	- C - Reactive Protein
DBF	- Direct Breast Feeding
ECMO	- Extracorporeal Membrane Oxygenation
ET-1	- Endothelin-1
GA	- Gestational Age
HC	- Head Circumference
HIE	- Hypoxic Ischemic Encephalopathy
HFV	- High Frequency Ventilation
ICAM-1	- Intercellular Adhesion Molecule 1
IL-1	- Interlukin- 1
IL-6	- Interlukin- 6
IL-8	- Interlukin- 8

iNO	- Inhaled Nitric Oxide
IPPV	- Intermittent Positive Pressure Ventilation
LSCS	- Lower Segment Caesarean Section
MAS	- Meconium Aspiration Syndrome
MSAF	- Meconium Stained Amniotic Fluid
NF-κB	- Nuclear Factor - κB
NICU	- Neonatal Intensive Care Unit
NVD	- Normal Vaginal Delivery
PAF	- Platelet Activating Factor
PEEP	- Positive End Expiratory Pressure
PLA2	- Phospholipase A2
PPHN	- Persistent Pulmonary Hypertension
RBS	- Random Blood Sugar
SD	- Standard Deviation
SGA	- Small for Gestational Age
TLC	- Total Leucocyte Count
TNFα	- Tumor Necrosis Factor α

ABSTRACT

BACKGROUND AND OBJECTIVE

Meconium aspiration syndrome (MAS) is an important cause of respiratory distress in term and post- term newborn babies.

The overall frequency of MAS varies between 5-25% (median 14%). It occurs in around 10% of babies born through meconium stained amniotic fluid (MSAF).

The pathophysiology of MAS is not completely understood. Meconium aspiration leads to activation of pulmonary macrophages producing an intense inflammatory response and infiltrations of polymorphonuclear lymphocytes diffusely through the lungs.

Since inflammation plays an important role in the pathophysiology of MAS, suppression of inflammation by corticosteroids appears to be of potential benefit.

Hence the present study is intended to assess the effect of Dexamethasone administration in the outcome of meconium aspiration syndrome.

METHODS

A late preterm (34 – 36 weeks), term and postterm babies born with meconium stained amniotic fluid with respiratory distress were included in the study.

The neonates were made into two groups, case group with steroid therapy along with routine treatment of MAS and control group only with routine treatment of MAS.

The severity of respiratory distress was assessed by Downe's scoring system. Recording of weight, vitals, RBS, $SPO_{2,}$ serum electrolytes (sodium, potassium,

calcium, chloride), sepsis screening including total leucocyte count, C-reactive protein, band neutrophil ratio and blood culture were recorded at the time of admission in both the groups. X – ray chest was done routinely on admission.

In case group intravenous dexamethasone was administered. The first dose was given starting from 2nd day of life (i.e 24hr to 36hrs) and given for another two days. In control group only routine treatment of MAS was given.

Period of oxygen dependency, duration of hospital stay, initiation of feeds, development of sepsis were assessed in both the groups.

RESULTS

70 neonates were included in the study, 34 neonates in case group and 36 neonates in control group. Clinical profile, period of oxygen dependency, hospital stay and initiation of feeds were similar in both the groups. No serious adverse effects were noted in steroid treated group (case group).

CONCLUSION

In our study we found that there was no significant difference in terms of oxygen dependency, duration of hospital stay and morbidity and mortality in between the steroid treated group and the control group. A further large randomised control trial is needed to study the effect of steroid in the outcome of meconium aspiration syndrome.

KEYWORDS

Meconium aspiration syndrome, Meconium stained amniotic fluid, Dexamethasone, Downe's score, Apgar score.

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INTRODUCTION

Meconium aspiration syndrome (MAS) is an important cause of respiratory distress in term newborn babies. The overall frequency of MAS varies between 5-25% (median 14%) MAS occurs in around 10% of babies born through meconium stained amniotic fluid (MSAF)[1].

The most important consequence of neonate born through meconium stained liquor is meconium aspiration syndrome (MAS). It is one of the major cause of severe respiratory distress in newborn[2].

The pathophysiology of MAS is not completely understood. Meconium aspiration leads to activation of pulmonary macrophages producing an intense inflammatory response and infiltrations of polymorphonuclear lymphocytes diffusely through the lungs[3].

There is associated increased pulmonary vascular permeability, leading to proteinaceous exudation into the alveolar spaces and thereby causing inactivation of pulmonary surfactant and decreased lung compliance.

Since inflammation plays an important role in the pathophysiology of MAS, suppression of inflammation by corticosteroids appears to be of potential benefit.

The synthetic glucocorticoid (dexamethasone) have metabolic and anti - inflammatory effects, their anti-inflammatory action results from inhibition of transcription factors including nuclear factor (NF)-κB and protein activator (AP)-1 inhibits the expression of pro-inflammatory cytokines (IL-1, IL-6, IL-8, TNF-α, etc.),

enzymes (PLA2,COX-2, iNOS, etc.) and other biologically active substances such as PAF, ET-1, ICAM-1, etc[4].

By stabilizing the cell membranes and decreasing the production of proinflammatory and vasoactive substances, glucocorticoid reduces microvascular permeability. In addition, by direct modulation of the pulmonary vasomotoric tone, glucocorticoid diminishes pulmonary vasoconstriction and inhibits fibrogenesis[5].

Hence the present study is intended to assess the effect of dexamethasone administration in the outcome of meconium aspiration syndrome.

AIMS AND OBJECTIVES

1) To evaluate the role of dexamethasone in meconium aspiration syndrome.
2) To compare the oxygen dependency, duration of hospital stay and any other morbidity and mortality in between the groups.

REVIEW OF LITERATURE

Definition:

Meconium aspiration syndrome (MAS) is defined as "respiratory distress in newborn infants born through meconium-stained amniotic fluid (MSAF) whose symptoms cannot otherwise be explained" [6].

Epidemiology:

In Europe the incidence is between 1:1000 and 1:5000, whereas in North America rates of 2-5: 1000 have been reported[7]. In Australia and New Zealand, the rate of MAS was 0.43:1000, with a decrease in incidence between 1995 and 2002 (Dargaville and Copnell 2006). However in developing countries, the incidence is considerably higher[8].

The overall frequency of MAS varies between 5-25% (median 14%). It occurs in around 10% of babies born through MSAF[1]. Most babies with MSAF are 37 weeks or older and many are postmature (>42 weeks).

Etiology:

Meconium aspiration was intially considered to be a postnatal event caused by aspiration of meconium at the first breath[9]. Suctioning of trachea and oropharynx at delivery decreased the incidence of mild and moderate MAS[10].

It is no longer considered to be a postnatal disorder caused by postnatal aspiration, but rather a disorder with antepartum, intrapartum and neonatal cause[11]. Meconium aspiration may occur in utero, during or after delivery. Chronic in utero insult may be responsible for severe MAS[12].

Vain et al showed that routine intrapartum oropharyngeal and nasopharyngeal suctioning of term gestation infants born through MSAF did not prevent MAS[13].

Ghidini et al reviewed the literature and concluded that severe MAS is caused by chronic asphyxia or intrauterine infection[14].

Meconium has been found in the lungs of stillborn infants and infants who died soon after birth without a history of aspiration at delivery[15].

Risk factors:

Signs of fetal compromise like abnormal fetal heart rate and/or low Apgar scores increase the risk of MASF leading to MAS[16].

There is an increased risk of MAS in Africans[17] and in Afro-Americans compared to other Americans. Advanced gestation is a risk factor of both MASF and MAS[18].

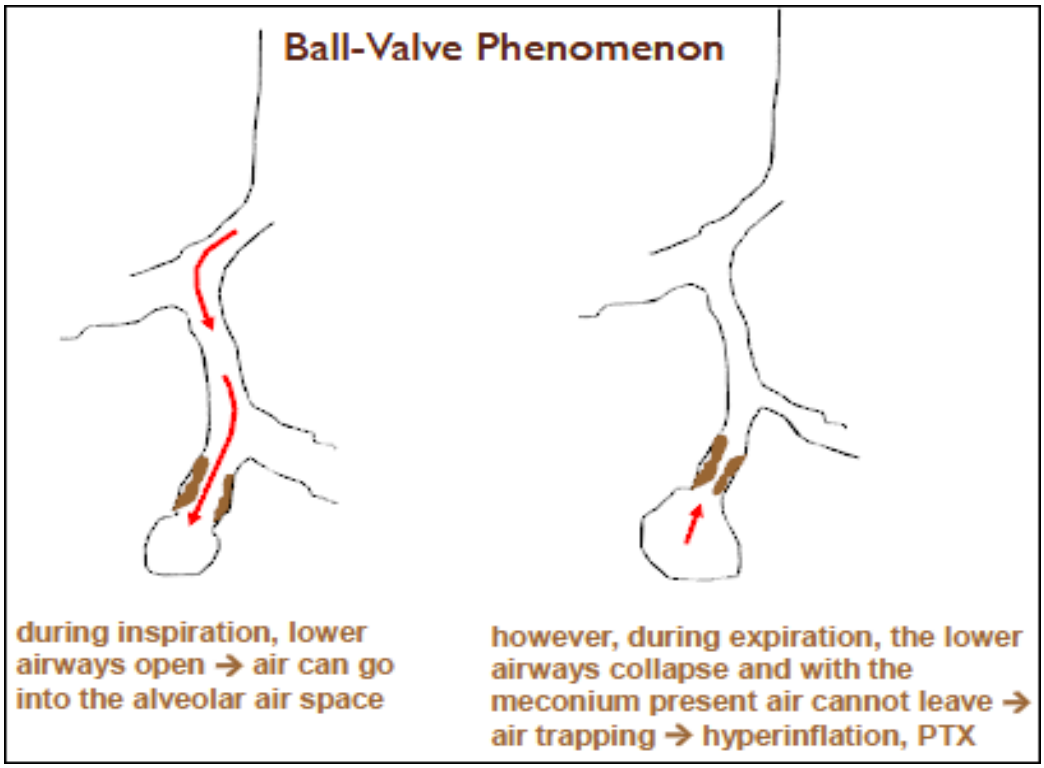
Risk factors for developing respiratory distress in infants born through meconium-stained amniotic fluid are male gender, abnormal biophysical profile, abnormal fetal heart rate, low Apgar score, oligohydramnios, caesarean section, preeclampsia or eclampsia and maternal diabetes mellitus[19].

Pathophysiology:

MAS has a complex not well defined pathophysiology[6]. Several factors are involved including -

1. Direct toxicity of meconium and its constituents resulting in alveolar and parenchymal inflammation with release of inflammatory mediators, edema and protein leakage into the alveoli, tissue necrosis and apoptosis in the lung and ulcerations of the umbilical cord.

2. Airway obstruction caused by meconium, edema fluid, protein exudates and blood cells.
3. Altered elastic forces in the lungs resulting in increased resistance and decreased compliance.
4. Inactivation and dysfunction of surfactant caused by meconium, protein and inflammatory cells leading to atelectases, air trapping, pneumothorax, right to left shunting,
5. In utero hypoxemia leading to pulmonary vascular remodelling and lung parenchymal changes, and vasoconstriction of placental and umbilical vessels.
6. Ventilation perfusion mismatch contribute further to acidosis, hypercapnia and hypoxemia.



Picture 1: Ball – valve phenomenon

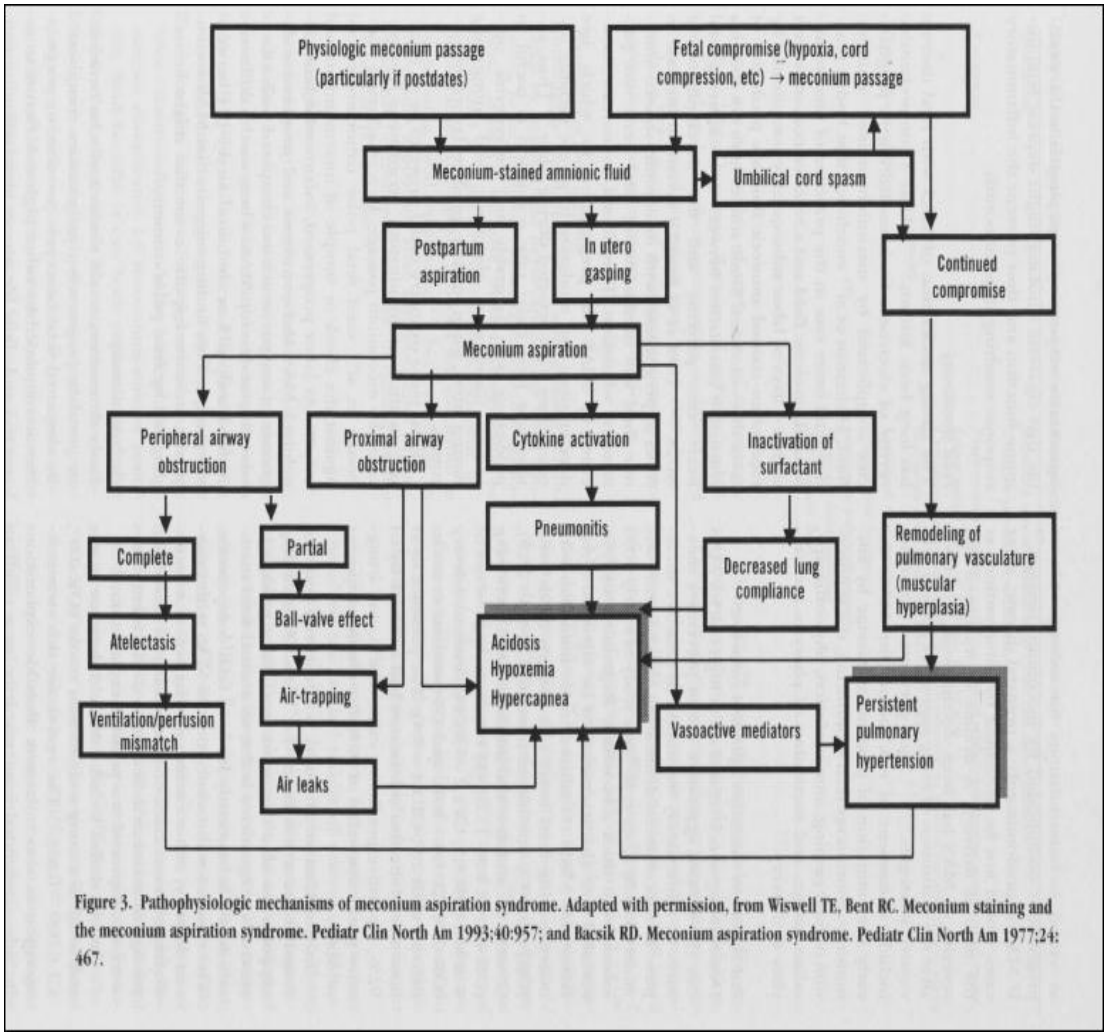


Figure 3. Pathophysiologic mechanisms of meconium aspiration syndrome. Adapted with permission, from Wiswell TE, Bent RC. Meconium staining and the meconium aspiration syndrome. Pediatr Clin North Am 1993;40:957; and Bacsik RD. Meconium aspiration syndrome. Pediatr Clin North Am 1977;24: 467.

Picture 2: Pathophysiologic mechanism of meconium aspiration syndrome

MSAF is rarely detected before 37 weeks of gestation[20], but occurs in more than one third of pregnancies lasting longer than 42 weeks[18]. Prenatal passage of meconium is normally prevented by lack of intestinal peristalsis caused by low motilin levels, tonic contraction of the anal sphincter[21].

The incidence of clinical chorioamnionitis is significantly higher in the presence of MAS[22]. Among women in preterm labor, the prevalence of positive amniotic fluid cultures after amniocentesis is significantly higher in those with MASF as compared to those with clear fluid[23].

Histological evidence of acute placental inflammation is present in majority of cases of severe MAS[24], supporting the fact that intrauterine infections may contribute to a proportion of cases of severe MAS. This is supported by the lack of studies that directly correlate the severity of MAS with the amount of meconium aspirated, the thickness of meconium and the duration of exposure to meconium[25].

Incidence of severe MAS is higher in post-term infants[26]. Placental ischemic changes suggesting long compromise of utero-placental bloodflow[27] leading to pulmonary vascular hypertrophy is found in almost all cases of severe MAS also may be found in the absence of meconium passage and chronic in utero hypoxia may lead to persistent pulmonary hypertension of the newborns (PPHN)[28].

Meconium:

Meconium is blackish-green, odourless and varies in amount from 60 to 200g[29]. Meconium consists of 72-80% water[15].

It is a sterile, thick, black-green, odourless and contains secretions from salivary and intestinal glands like mucus, bile and bile acids, fatty acids and steroids from the gut, cellular debris, lanugo hair, components of vernix caseosa, amniotic fluid and blood group specific glycoproteins, drug metabolites[30].

It may also contain various amounts of proinflammatory substances including TNF-α, IL-1, IL-6 and especially IL-8[31].

Description of meconium[15]:

1. Watery: Amniotic fluid that is thinly stained.
2. Moderately stained fluid: Opaque without particles.
3. Pea soup: Fluid with thick meconium with particles.

Effect of meconium on the lungs and vessels:

Respiratory symptoms may be secondary to meconium aspiration in utero or at birth, or to alterations in the pulmonary vasculature secondary to asphyxia or to meconium itself[32]. MAS is believed to be caused by a combination of mechanical blockage of the small airways and chemical pneumonitis induced by meconium particles aspirated[28].

Aspiration of meconium may cause partial obstruction of the airways with air trapping and atelectasis and development of air leaks or complete obstruction with alveolar collapse and ventilation-perfusion mismatch[33]. Estimated risk of pneumothorax is 15-33%[6].

Mechanical dysfunction of lungs is more severe during the early phase of MAS with lower dynamic and specific lung compliance and increased airway resistance[34]. Vasospasms, hypertrophy of the pulmonary musculature, and pulmonary hypertension lead to right to left shunting through the foramen ovale and ductus arteriosus. It is the most common cause of PPHN[35, 36], with abnormally constricted pulmonary vasculature.

Meconium injury triggers postnatal release of vasoactive mediators like endothelin-1, thromboxane-A2 and prostaglandin E2[37, 38]. Meconium induced a dose-dependent oxidative burst in neutrophils with increased levels of vasoactive peptides[39].

Surfactant displacement and inactivation:

Meconium, protein and inflammatory cells inactivate surfactant function and alter surfactant production[40]. Meconium displaces surfactant from the alveolar surface and inhibits surfactant function reducing its ability to reduce the surface tension.

In high enough concentrations, meconium has a direct cytotoxic effect on type II pneumocytes[41]. Bronchial lavage fluid from infants with MAS contained increased levels of albumin, total protein and membrane-derived phospholipids compared to controls. The inhibition of surfactant in the alveolar spaces may be mediated by meconium, plasma proteins, edema fluid and hemoglobin.

Meconium aspiration syndrome and inflammation:

Toxic effects of meconium trigger inflammation in the lungs[42]. Activated neutrophils and macrophages are detected in the lung parenchyma and alveoli only hours after meconium aspiration[43].

Meconium activates the complement system both in vitro[44] and in vivo in an experimental model of MAS in newborn pigs[45]which is associated with release of proinflammatory cytokines. The proinflammatory cytokines may directly injure the lung parenchyma resulting in vascular leakage causing pneumonitis and pulmonary edema[46]. Most proinflammatory cytokines and chemokines measured, as well as the anti-inflammatory cytokine IL-10, were significantly elevated in sera from neonates with MAS[47].

Meconium-induced inflammatory lung injury is associated with respiratory epithelial apoptosis in several animal models[48]. Meconium activates the pulmonary renin angiotensin system shown by an increase in angiotensinogen m-RNA associated

with apoptosis and cytokine release. Angiotensin-II receptor, which is expressed in several cell types in the newborn lung, including bronchial and alveolar epithelium and bronchial and vascular smooth muscles are up-regulated after meconium exposure[49].

Prenatal management:

Transcervical intrapartum infusion of saline into the amniotic cavity has been proposed to reduce the risk for MAS. An inverse relationship has been found between amniotic fluid volume and fetal heart rate decelerations. The proposed mechanism is mechanical cushioning of the umbilical cord to prevent recurrent umbilical compressions leading to fetal acidosis and dilution of meconium to reduce mechanical and inflammatory effects[50].

A systematic review of the literature by Xu concluded that only in settings with limited peripartum surveillance and where complications are common, amnioinfusion appeared to reduce the risk of MAS[50]. There are adverse outcomes of amnioinfusion, which include increased incidence of cord prolapse, infection and requirement of instrumental delivery.

Delivery room management:

Thorough oropharyngeal suctioning before delivery of the infants shoulders has long played an important role in preventing MAS. This approach has been recently challenged because despite effective suctioning at birth some babies develop MAS due to aspiration of meconium in- utero.

Carson et al demonstrated in 1976, a decreased incidence of MAS after intrapartum oropharyngeal suctioning[51].

Vain et al showed that routine intrapartum oropharyngeal and nasopharyngeal suctioning of term-gestation infants born through MSAF did not prevent MAS[52].

Rossi and colleagues recently reported oropharyngeal suctioning to result in higher 1 and 5 minute Apgar scores and less need for mechanical ventilation[53].

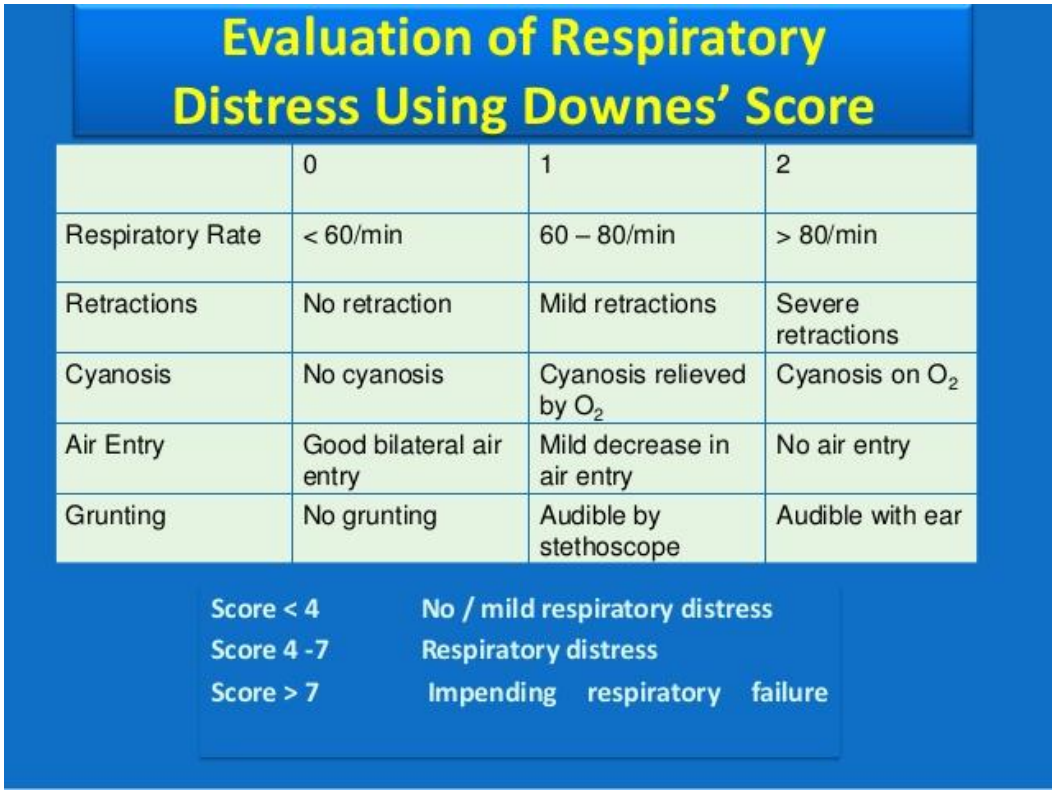
Still the American Academy of Pediatrics and American Heart Association recommends intubation of all infants born through moderately thick or thick consistency MSAF.

Clinical features:

Infants with meconium aspiration are often postmature and have visible meconium staining of the nails, skin and the umbilical cord. Thick pea soup consistency of MSAF is mostly associated with MAS compared to thin consistency[6].

Respiratory:

Infants with MAS typically have respiratory distress with marked tachypnoea, use of accessory muscles as evidence by intercostals and subcostal recession, flaring of nostrils and an expiratory grunt may be heard. It can cause air trapping and an overdistended chest with an increased anteroposterior diameter. Baby may remain symptomatic for only 24 hrs or may be dyspnoeic for 7 – 10 days before recovery[7].



Picture 3: Downe's score

Cardiovascular:

In the absence of asphyxia damage to the myocardium, there are no specific cardiovascular features of MAS. If PPHN develops, S_2 may remain single, and there may be murmur of tricuspid incompetence[7].

Gastrointestinal system:

Liver and spleen are palpable if there is downward displacement of the diaphragm caused by air trapping. In a severely affected infant, bowel sound may be absent, with delayed passage of meconium[7].

Central nervous system:

Depending on the severity of coexisting neurological insult, the baby can be neurologically normal or may show features of birth depression (HIE). Convulsion may occur[7].

Treatment:

Prevention of MAS:

The decrease in the incidence of MAS in the last decade is due to the reduction in postterm delivery, aggressive management of abnormal heart rate monitoring and decreased number of infants with low Apgar score.

It is important to observe and monitor all infants born through MSAF for hypoxia or respiratory distress for at least 6 hours. There is no specific treatment for MAS.

Management is primarily supportive. Maintenance of optimal thermal environment and minimal handling is essential because these infants are agitated easily, which causes right to left shunting leading to hypoxia and acidosis.

Maintenance of adequate oxygenation, correction of hypoglycaemia, acidosis and other metabolic disorders is the mainstay of treatment.

Role of Antibiotics:

The presence of meconium increases the chances of positive cultures from amniotic fluid in preterm and term infants. However, studies evaluating the development of sepsis in infants with MSAF failed to demonstrate that relationship[54].

Three randomized control studies reported that routine antibiotic prophylaxis is not recommended in the management of MAS for those without perinatal risk factors[55]. The role of antibiotics in the management of MAS may need to be re-evaluated in well designed trials. Unless there is definite risk for infection, prophylactic use of antibiotics in MAS did not reduce infection. If antibiotics are started for suspected infection due to perinatal risk factors, discontinuing antibiotics once the blood culture results are negative is being considered.

Ventilation:

Ventilator management of the neonate with MAS is challenging because of the complicated pulmonary pathophysiology resulting from areas of atelectasis and areas of hyperinflation, in association with ventilation perfusion mismatch and airway compromise[56].

Approximately 40% of babies with MAS require mechanical ventilation and additional 10% require continuous positive airway pressure[57].Ventilation should be aimed at increasing oxygenation while minimizing the barotrauma that lead to air leak syndromes.

The amount of ventilator support depends on severity of respiratory distress. Some infants only require oxygen by hood. In infants with MAS without PPHN, it is sufficient to maintain a pH of 7.3–7.4, with PaO_2 targeted between 60 and 80mmHg and $PaCO_2$ of 40–50mmHg. Infants may be started with a moderate peak inspiratory pressure (PIP) preferably not exceeding 25cm H_2O, a relatively rapid ventilator rate (40–60/min), a moderate positive end expiratory pressure (4–6 cm H_2O), and an adequate expiratory time (0.5–0.7 sec) to prevent gas trapping and air leaks.

If gas trapping is noticed, expiratory time may be increased and PEEP should be decreased (3-4 cm H_2O)[56,57]. In infants with MAS and concomitant PPHN, mild hyperventilation and higher FiO_2 can be considered. But the strategy of achieving hypocapnia and alkalosis by hyperventilation has adverse effects including cerebral vasoconstriction leading to long-term neurologic morbidity as well as air leaks[58]. In such situations other modalities like inhaled nitric oxide and high frequency ventilation should be considered early.

Theoretically High Frequency Ventilation (HFV) minimizes the barotrauma and reduce air leak syndrome in MAS. No prospective randomized trials have compared conventional ventilation versus HFV in MAS.

In pilot studies using inhaled nitric oxide (iNO), Kinsella and Abman found that the combination of HFV and iNO causes greatest improvement in oxygenation in some patients with severe PPHN[59].

Partial liquid ventilation was found to be a better method of delivering surfactant in an adult rat model of MAS when compared with conventional mechanical ventilation[60]. There is no randomized clinical trial about the use of partial liquid ventilation in neonates with MAS.

Surfactant Therapy:

In vitro studies have shown that meconium interferes with surfactant in several ways[6]:

1. Inactivation of its function depending on the concentration
2. Direct toxicity on type II pneumocytes
3. Displacement of surfactant from the alveolar surface
4. Decrease of surfactant protein A and B levels.

Canadian Pediatric Society position statement recommends that intubated infants with MAS requiring more than 50% oxygen should receive exogenous surfactant therapy[61].

Meta-analysis of 4 RCTs showed reduction in the severity of respiratory illness and decrease in the number of infants with progressive respiratory failure requiring ECMO. However, there was no significant difference in mortality, hospital stay, length of ventilation, duration of oxygen use, pneumothorax, pulmonary interstitial emphysema, or chronic lung disease. Dargaville and colleagues reported that lung lavage with dilute surfactant (Survanta) in ventilated infants with severe

MAS does not decrease the duration of respiratory support, but may produce a reduction in mortality[62].

Role of Steroids:

In 2003, Cochrane meta-analysis of two trials[63] including 85 infants with MAS showed that there was no difference in mortality but a small increase in the duration of oxygen treatment in steroid treated group[5].

Since then, two more trials reported that steroid therapy in MAS was associated with a decrease in the duration of oxygen therapy and hospital stay[2, 64]. The choice of steroid and duration of therapy was different between the studies.

Steroids may be beneficial in severe MAS with apparent lung edema, pulmonary vasoconstriction, and inflammation. At present, there is no conclusive evidence to propose routine steroid therapy in the management of MAS.

Further research is needed regarding the dosing, timing and ways of administration of steroids considering their individual properties and possible acute and long term side effects[4].

Nitric Oxide:

Severe MAS is often associated with PPHN, resulting in severe hypoxemia. Randomized clinical trials have demonstrated that iNO therapy decreases the need for ECMO in addition to mortality in full-term and near-term neonates with hypoxic respiratory failure and PPHN[65]. For hypoxic respiratory failure due to MAS, infants responded well to combined iNO and HFV as compared to either treatment alone[66].

Extracorporeal Membrane Oxygenation:

ECMO has been used as a final rescue therapy in infants with severe and refractory hypoxemia associated with MAS. Use of ECMO has been decreased significantly in developed countries with the availability of iNO and HFV. Infants with MAS make up approximately 35% of the infant population who require ECMO[67]. The survival rate has approached 95% of infants with MAS who underwent ECMO[68]. In the ECMO registry, the highest survival rates (>90%) were seen in the patients with MAS who qualified for ECMO[69].

Complications:

Despite advances in the understanding of pathophysiologic mechanisms of MAS and therapeutic advances in the management of respiratory failure and PPHN in newborn babies outcome of MAS is guarded[70].

The case fatality rate vary between 5 and 35 %[70]. The majority of deaths are from respiratory failure, PPHN and airleaks.

There is high risk of cerebral palsy, seizures and mental retardation depending on the severity and duration of perinatal hypoxia.

Pneumothorax, air leaks:

Pneumothorax, pneumomediastinum, pneumopericardium and pneumoperitoneum can all occur. Approximately 50% of ventilated MAS babies suffer some from air leak.[7]

Persistent pulmonary hypertension (PPHN):

It is a common complication of severe MAS and appears to be a frequent fatal case[7].

Bronchopulmonary dysplasia:

This is a rare complication of MAS, although it may occur in any baby who survives after long term high pressure IPPV.

Related studies:

In a study by Garg N et al, the role of early inhaled budesonide therapy in meconium aspiration syndrome, a randomized control study in 2016, a total of 78 neonates were included in the study. After randomization, intervention group received nebulization with budesonide (0.5 mg dissolved in 2.5ml sterile normal saline within 2 hours of birth and second dose was given at 12 hours of birth) whereas control group were nebulized with normal saline. All neonates were accessed for serial respiratory distress score (Downe's score), requirement of oxygen (in days), duration of neonatal intensive care unit stay. Budesonide nebulization in meconium aspiration results in significant early improvement in general condition (early improvement in respiratory distress and early normalization of Downe's score) of the newborn with lesser oxygen requirement, thus early discharge from NICU but has no impact on final outcome[7]

In a study by Suresh R et al, effect of nebulized budesonide in improving the clinical outcome of neonates with meconium aspiration syndrome done in Mysore Medical College and Research Institute, Department of Pediatrics, Mysore; involving a total of 60 patients with diagnosis of MAS were admitted to the NICU from August to October 2013. They found that the baseline clinical profile of both the groups were similar. Duration of respiratory distress in days (2.63 vs 5.24 p=0.0493), duration of oxygen dependency (2.37 vs 4.94 p=0.0406), duration of hospital stay (7.58 vs 10.47 p=0.0430), time taken for achievement of full feeds (3.79 vs 8.76 p-0.0002) and the need for mechanical ventilation (0 vs 0.2 p=0.0356) were statistically less in

budesonide treated group as compared to the controls. Incidence of sepsis is similar in both the groups. Complications were similar in both the groups and no specific adverse effects were noted in the steroid treated group[71].

In a study by Daniela Mokra et al in the year 2011 in a review article concluded that glucocorticoid may be beneficial particularly in severe form of MAS with apparent lung edema, pulmonary vasoconstriction and inflammation[4].

Ward MC et al in the year 2009 in a review article in the Cochrane collaboration concluded that the small number and sample sizes of randomized control trials undertaken to date, and the mortality and morbidity associated with MAS itself, the limited information available to date suggest early parenteral dexamethasone would be an appropriate intervention for further study[5].

In a study by Sriparna Basu et al, role of steroids on the clinical course and outcome of meconium aspiration syndrome a randomized controlled trial conducted in three groups over a period of 1 year i.e., 2007, at department of Pediatrics at Banaras Hindu University, Varanasi. Group A (control, n =33), group B (n = 34) received i.v methylprednisolone of 0.5mg/kg/day in two divided doses and group C (n =32) received nebulized budesonide in a dose of 50µg in 2.5 ml of normal saline. This was given for a period of 7 days starting after 24hrs and found that period of oxygen dependency and duration of hospital stay was significantly less in the steroid treated groups. Also enteral feeding and radiological clearance of chest was achieved earlier in steroid treated groups[2].

In a study by Tripathi S et al, effect of steroids on the clinical course and outcome of neonates with meconium aspiration syndrome, a double blinded randomized controlled trial conducted over a period of one year in 2007, in the neonatal unit of the Lady Hardinge Medical College and associated Kalawati Saran Children's hospital. 51 babies of MAS which were randomly distributed into three groups; control, systemic and nebulized steroids. Methyl prednisolone was given i.v. in dose of 0.5 mg/kg/day in two divided doses. Budecort was given by nebulization in dose of 50 microgram 12 hourly. Infants were assessed in terms of duration of stay, oxygen dependence, X-ray clearances and also assessed for short term adverse effects. There was statistically significant difference in the duration of stay, duration of oxygen dependence and radiological clearance. The use of steroids was not associated with an increased incidence of sepsis[64].

In a study by Yeh TF et al, hydrocortisone therapy in meconium aspiration syndrome: a double blinded controlled study, to evaluate the efficacy of glucocorticoids in the treatment of infants with meconium aspiration syndrome in 1977. Thirty-five infants were included in the study. No significant difference in requirement for assisted ventilation or in survival were domonstrated between the groups. In control group, a significant decrease (p less than 0.01) in respiratory distress score was found at 48 to 72 hours of age; in hydrocortisone group, it was seen only after 72 hours. The infants in the hydrocortisone group took a significantly longer (p less than 0.01) period of time to wean to room air than those in the control group (68.9 ± 9.6 hours vs 36.6 ± 6.9 hours). On the basis of these observations, hydrocortisone is not recommended for treatment of MAS[63].

MATERIALS AND METHODS

SOURCE OF STUDY

The study was conducted in the neonatal intensive care unit at Shri B.M Patil Medical College, Hospital and Research Centre, Vijayapur.

STUDY DESIGN

This was a hospital based prospective study. All neonates with meconium aspiration syndrome fulfilling the inclusion criteria were included in the study.

STUDY DURATION

This study was conducted over a period of one and half years beginning from October 2014 to April 2016 were included in the study.

METHODS OF COLLECTION OF DATA

A late preterm (34 – 36 weeks), term and post- term babies born with meconium stained amniotic fluid with respiratory distress with inspiratory costal retractions or expiratory grunt were included in the study and were made into two groups, case group with steroid therapy along with routine treatment of MAS and control group only with routine treatment of MAS.

The severity of respiratory distress was assessed by Downe's scoring system. Recording of weight, vitals, RBS, $SPO_{2,}$ serum electrolytes (sodium , potassium, calcium, chloride), sepsis screening including complete hemogram, C-reactive protein, band neutrophil ratio and blood culture were recorded at the time of admission in both the groups. Chest X -ray was done routinely on admission.

In case group, intravenous dexamethasone was administered in the dose of 0.5mg/kg/day given 12hrly for 3days. The first dose was given starting from 2nd day of life (i.e 24hr to 36hrs) and given for another two days.

Period of oxygen dependency, duration of hospital stay, initiation of feeds, development of sepsis were assessed in both the groups.

The following parameters were asked in all the neonates included in the study:

1. Detailed maternal history like age, parity, gestational age.
2. Details of labour, mode of delivery were recorded.
3. Details of baby like: sex, date of birth, time of birth.
4. Thorough clinical examination of the neonates were done.

SAMPLE SIZE

With the average value of SD duration of oxygen therapy in steroid treated group and control group 34(68.9±38.6 and 36.6±29.3)[3] at 99% level of confidence and at 80% power of the study , the sample size is calculated using

Statistical formula $n = \frac{(Z\alpha + Z\beta)^2 \times 2\times\sigma^2}{d^2}$

$Z\alpha$ = Z value at α level = 99%

$Z\beta$ = Z value at β level = 80%

σ^2 = Average SD of two groups

d = Difference between two groups

Hence a total of 70 neonates were included in the study of effect of corticosteroid (dexamethasone) in the outcome of meconium aspiration syndrome.

STATISTICAL ANALYSIS

All characteristics were summarized descriptively. For continuous variables, the summary statistics of n, mean, standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries. Chi-square (χ^2)/Freeman-Halton Fisher exact test was employed to determine the significance of differences between the groups for categorical data. The difference of the means of analysis variables was tested by unpaired t test. If the p-value was < 0.05, then the results will be considered to be significant.

Software used in analysis:

SPSS 23.0 version

INCLUSION CRITERIA:

Late preterm (34- 36weeks), term (≥37 weeks), post – term new born infants with meconium stained amniotic fluid with respiratory distress.

EXCLUSION CRITERIA:

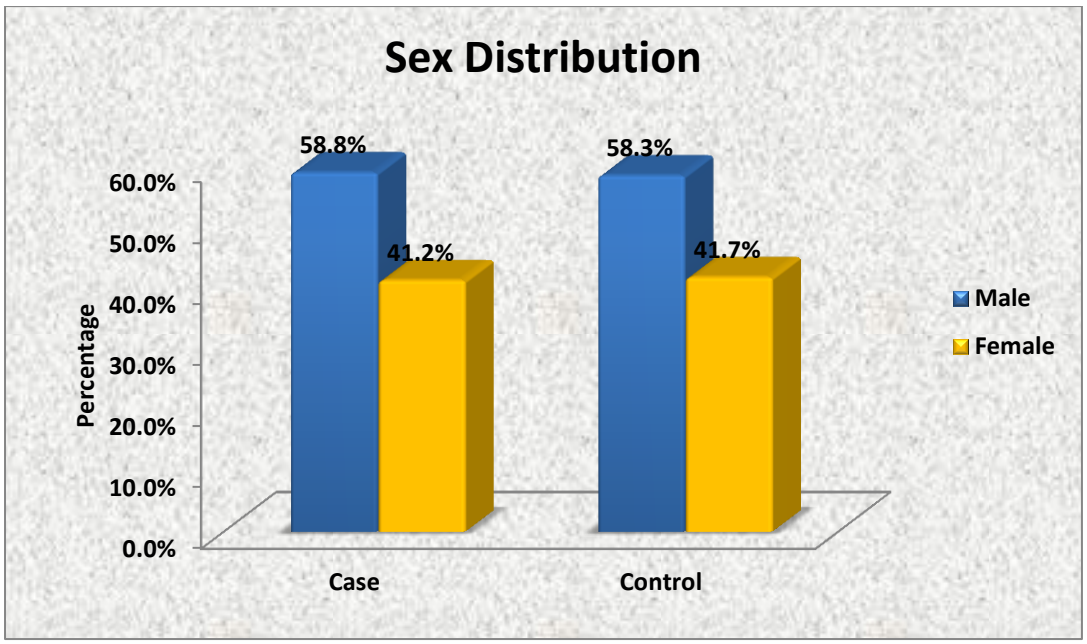
- Meconium aspiration with significant congenital malformations.
- Denial of consent.
- Sepsis at time of admission – presence of clinical signs e.g. poor feeding, lethargy, sclerema, delayed capillary filling time>3sec, with a positive blood culture.

RESULTS

Table 1: Distribution of neonates according to sex

SEX	Case		Control		p value
	n	%	n	%	
Male	20	58.8%	21	58.3%	0.967
Female	14	41.2%	15	41.7%	
Total	34	100.0%	36	100.0%	

Figure 1: Distribution of neonates according to sex

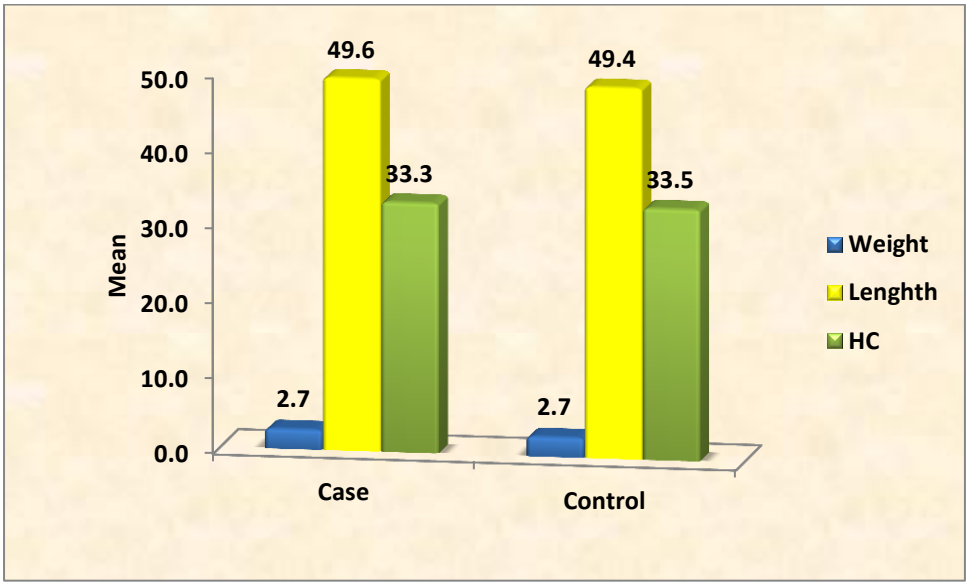


A total of 70 neonates were included in the study. 58.8%, 58.3% of neonates were males and 41.2% , 41.7% of neonates were females in the case and control group respectively. This shows that in both the groups male and female proportion were similar.

Table 2: Mean and SD of anthropometric parameters

Parameters (Mean ± SD)	Case	Control	p value
Weight (kg)	2.7±0.3	2.7±0.4	0.715
Length (cm)	49.6±1.1	49.4±1.4	0.64
Head circumference [HC] (cm)	33.3±1	33.5±1	0.543

Figure 2: Mean and SD of anthropometric parameters



Mean birth weight of neonates was 2.7 ± 0.3 kg in case group and 2.7 ± 0.4 kg in control group. Mean length was 49.6 ± 1.1cm in case group and 49.4 ± 1.4 cm in control group. Mean head circumference was 33.3 ± 1cm in case group and 33.5 ± 1cm in control group.

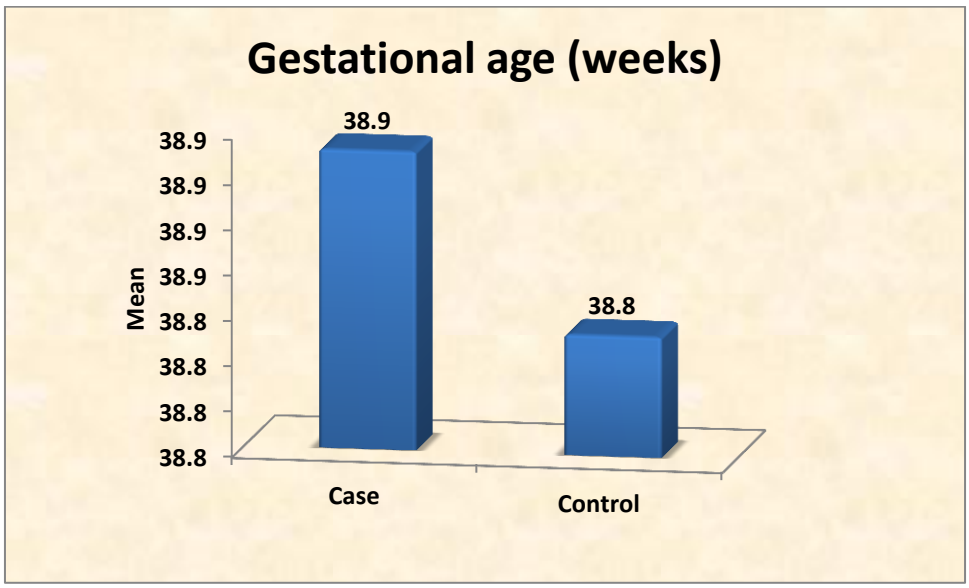
Table 3: Vital parameters

Parameters (Mean ± SD)	Case	Control	p value
Heart rate (/min)	139.5 ± 5.3	140.3 ± 4.8	>0.05
Respiratory rate(/min)	57.6 ± 6.8	57.5 ± 5.6	>0.05

Mean heart rate of newborn was 139.5 ± 5.3 beats per minute in case group and 140.3 ± 4.8 beats per minute in control group. Mean respiratory rate of newborn was 57.6 ± 6.8 per minute in case group and 57.5 ± 5.6 per minute in control group.

There was no significant difference in the vitals (heart rate and respiratory rate) in both the case and control group.

Figure 3: Mean gestational age group (weeks)

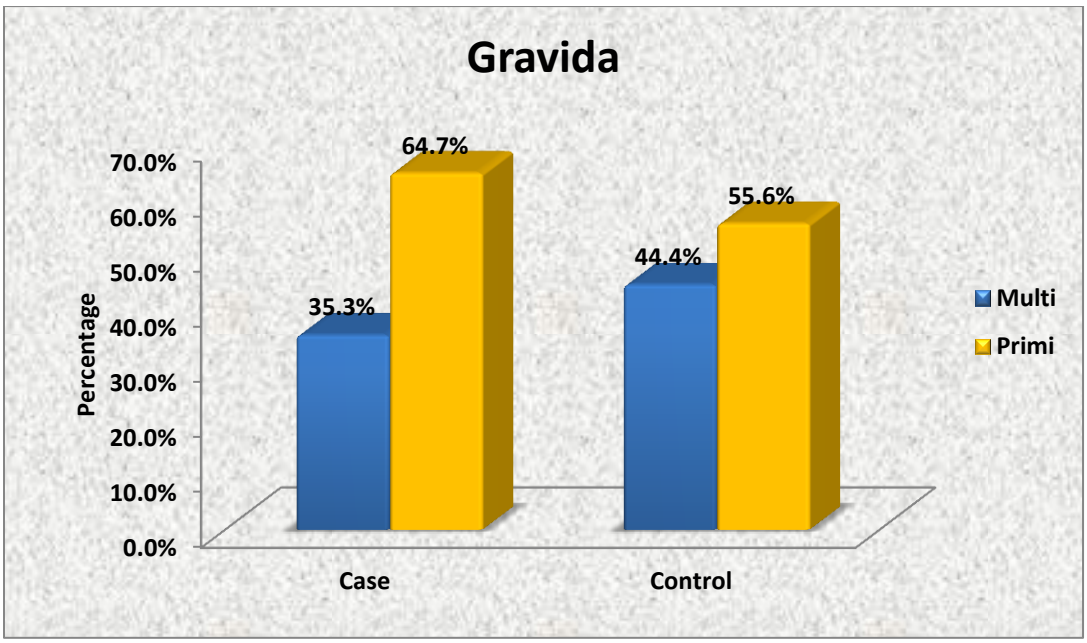


There was no significant difference in the gestational age in between the two groups. Mean gestational age group were 38.9± 1.2 weeks in case group and 38.8 ± 1.1 weeks in control group.

Table 4: Gravida of the mother

Gravida	Case		Control		p value
	n	%	n	%	
Multi	12	35.3%	16	44.4%	0.435
Primi	22	64.7%	20	55.6%	
Total	34	100.0%	36	100.0%	

Figure 4: Gravida of the mother

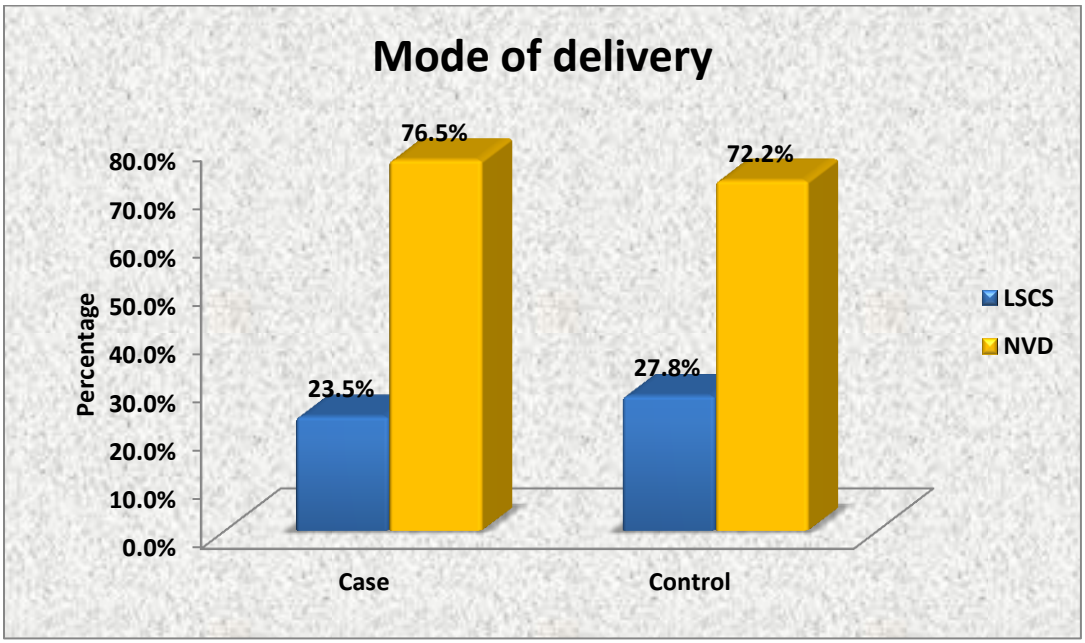


In our study we found that primigravida mothers (64.7%, 55.6%) was more as compared to multigravida (35.3%, 44.4%).

Table 5: Mode of delivery

Type of Delivery	Case		Control		p value
	n	%	n	%	
NVD	26	76.5 %	26	72.2%	0.684
LSCS	8	23.5%	10	27.8%	
Total	34	100.0%	36	100.0%	

Figure 5: Mode of delivery

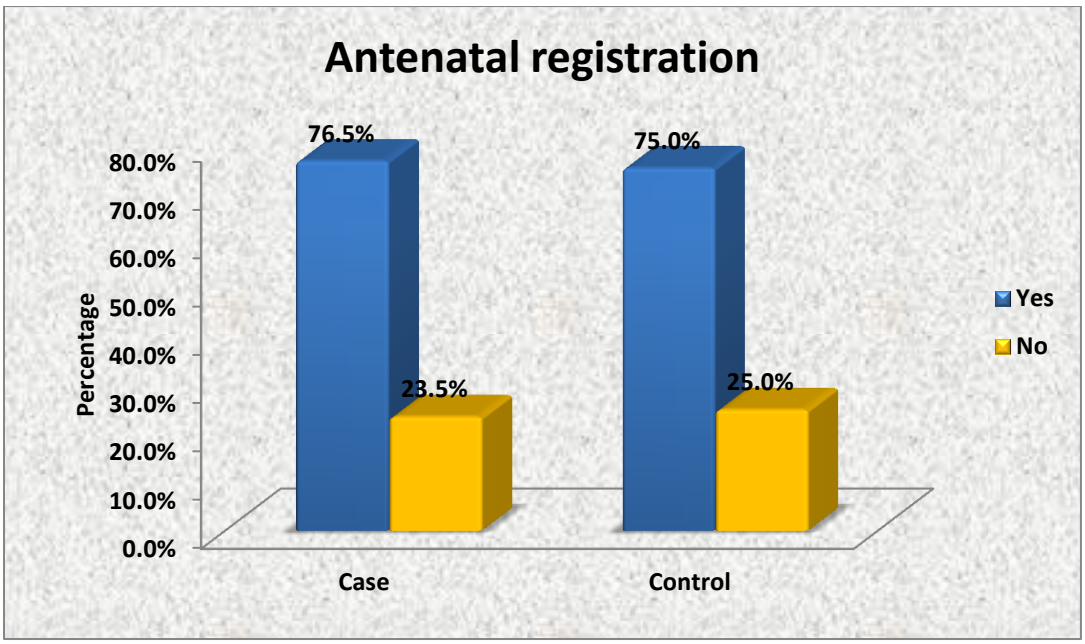


In our study we found that normal delivery was more i.e., 76.5% in the case group and 72.2% in the control group as compared to LSCS.

Table 6: Antenatal registration

Antenatal registration	Case		Control		p value
	n	%	n	%	
Yes	26	76.5%	27	75.0%	0.886
No	8	23.5%	9	25.0%	
Total	34	100.0%	36	100.0%	

Figure 6: Antenatal registration

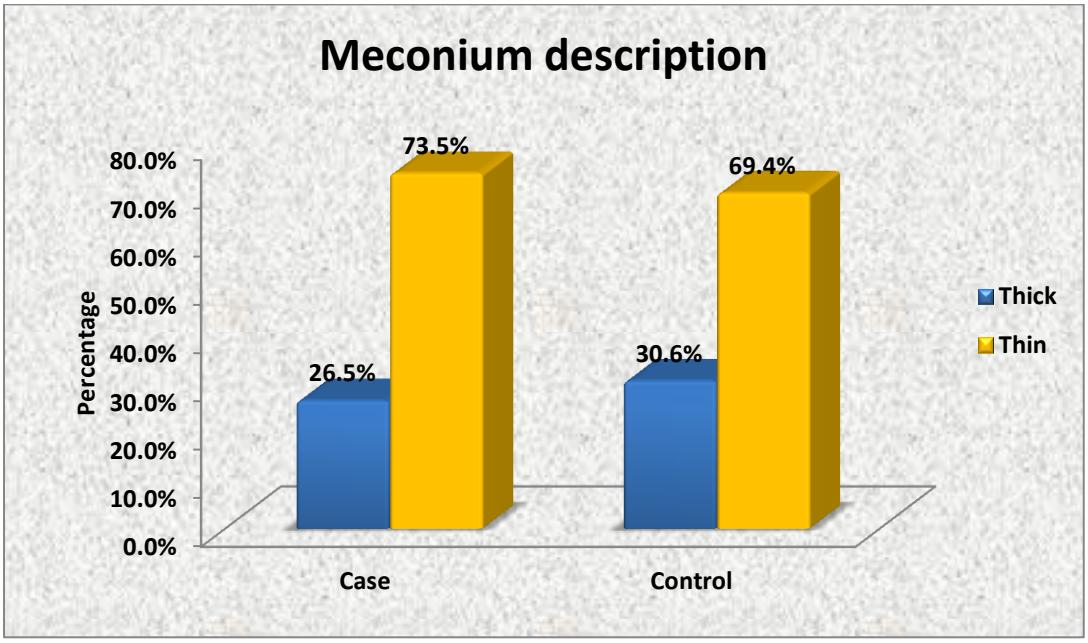


Antenatal registration was done in 77% in cases group and 75% in control group showing that MAS can occur even after regular antenatal check up.

Table 7: Description of meconium

Meconium	Case		Control		p value
	n	%	n	%	
Thick	9	26.5%	11	30.6%	0.705
Thin	25	73.5%	25	69.4%	
Total	34	100.0%	36	100.0%	

Figure 7: Description of meconium

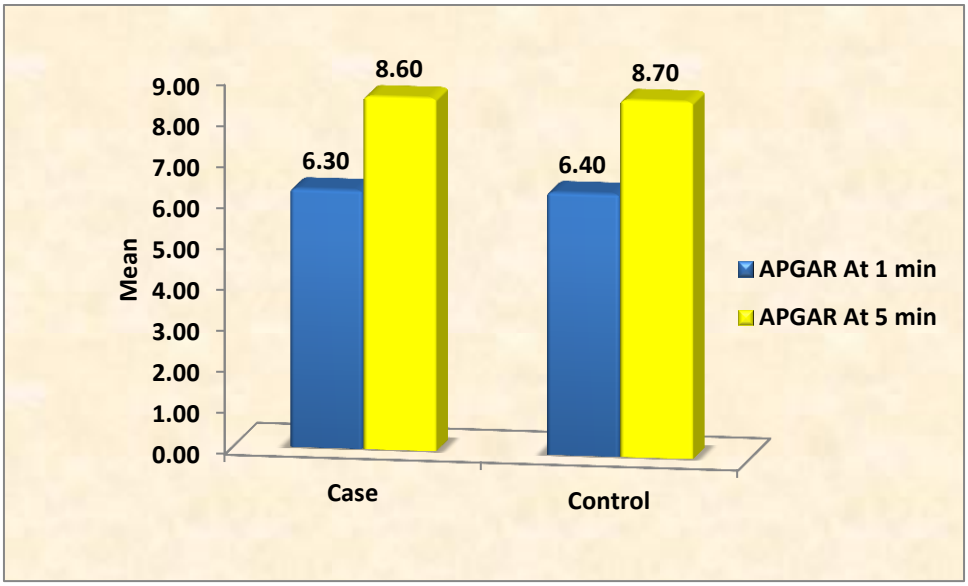


Most of the neonates admitted with MAS in our study was associated with thin meconium stained liquor 73.5% in case group and 69.4% in control group.

Table 8: Apgar score

Parameters (Mean ± SD)	Case	Control	p value
Apgar At 1 min	6.3±0.9	6.4±1.1	0.867
Apgar At 5 min	8.6±0.7	8.7±0.7	0.915

Figure 8: Apgar score



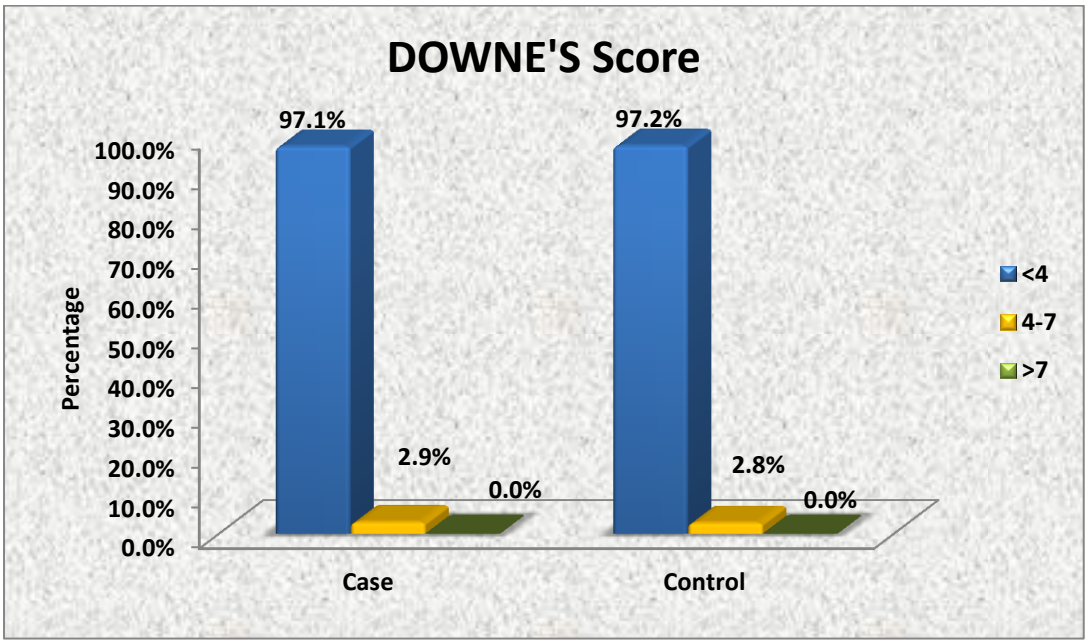
Mean Apgar score at 1 minute in case and control group were 6.3 ± 0.9 and 6.4 ± 1.1 respectively suggesting there was mild intrapartum depression.

Mean APGAR score at 5 minute in the case group was 8.6 ± 0.7 and in the control group was 8.7 ± 0.7. This suggest that there was minimal need for resuscitation in both the groups.

Table 9: Downe's score

Downe's score	Cases		Controls		p value
	N	%	N	%	
<4	33	97.1%	35	97.2%	0.967
4-7	1	2.9%	1	2.8%	
>7	0	0.0%	0	0.0%	
Total	34	100.0%	36	100.0%	

Figure 9: Downe's score

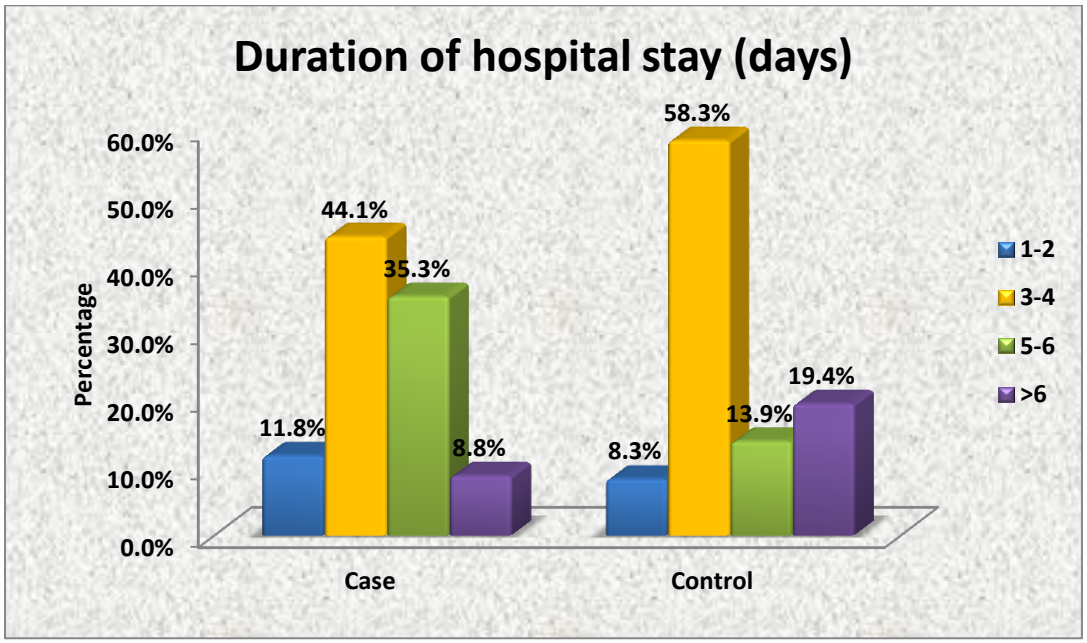


In our study we found that 97% of the neonates have mild/ no respiratory distress and only 3% has respiratory distress. None of the neonates in our study has impending respiratory failure.

Table 10: Duration of hospital stay (days)

Duration of hospital stay (days)	Case		Control		p value
	n	%	n	%	
1-2	4	11.8%	3	8.3%	0.134
3-4	15	44.1%	21	58.3%	
5-6	12	35.3%	5	13.9%	
>6	3	8.8%	7	19.4%	
Total	34	100.0%	36	100.0%	

Figure 10: Duration of hospital stay (days)

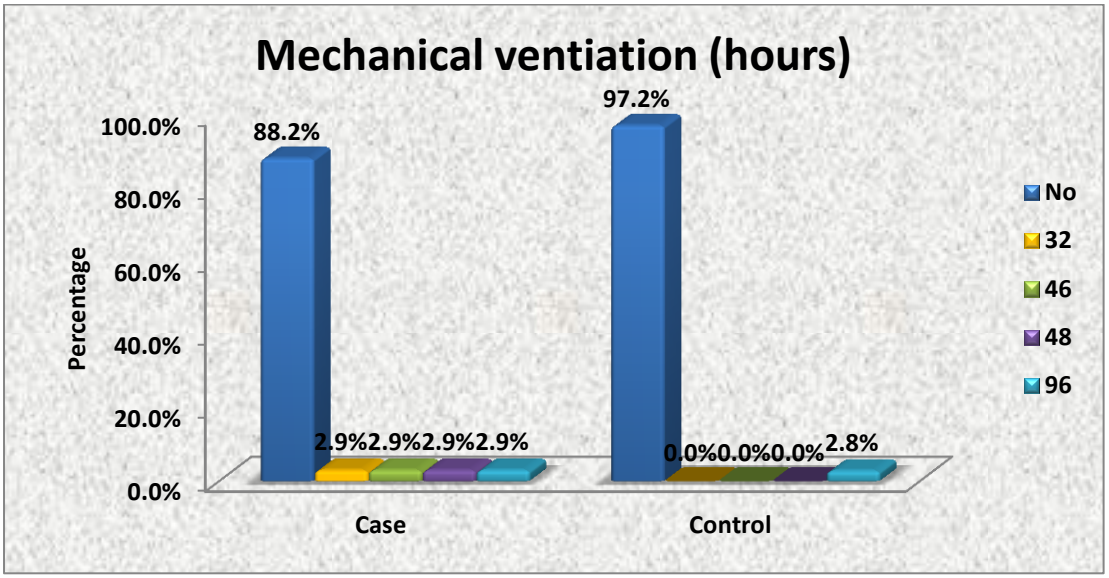


In our study, mean duration of hospital stay was 4.2 ± 1.6 days in case group and 4.3 ± 1.7 days in the control group.

Table 11: Duration of mechanical ventilation (hours)

Mechanical ventilation (hours)	Case		Control		p value
	n	%	n	%	
No	30	88.2%	35	97.2%	0.504
32	1	2.9%	0	0.0%	
46	1	2.9%	0	0.0%	
48	1	2.9%	0	0.0%	
96	1	2.9%	1	2.8%	
Total	34	100.0%	36	100.0%	

Figure 11: Duration of mechanical ventilation (hours)

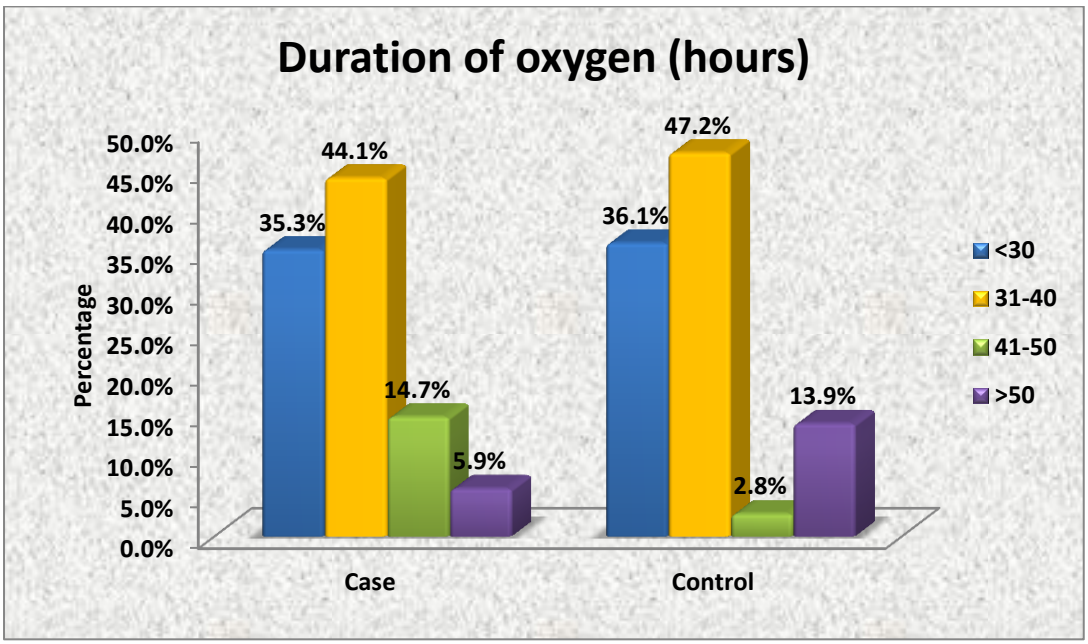


In our study, need for mechanical ventilation was more in the case group i.e., 4 neonates , with maximum need for 96 hours and minimum need for 32 hours and only 1 neonates in the control group with a duration of 96 hours.

Table 12: Duration of oxygen dependency (hours)

Oxygen (hours)	Case		Control		p value
	N	%	N	%	
<30	12	35.3%	13	36.1%	0.255
31-40	15	44.1%	17	47.2%	
41-50	5	14.7%	1	2.8%	
>50	2	5.9%	5	13.9%	
Total	34	100.0%	36	100.0%	

Figure 12: Duration of oxygen dependency (hours)

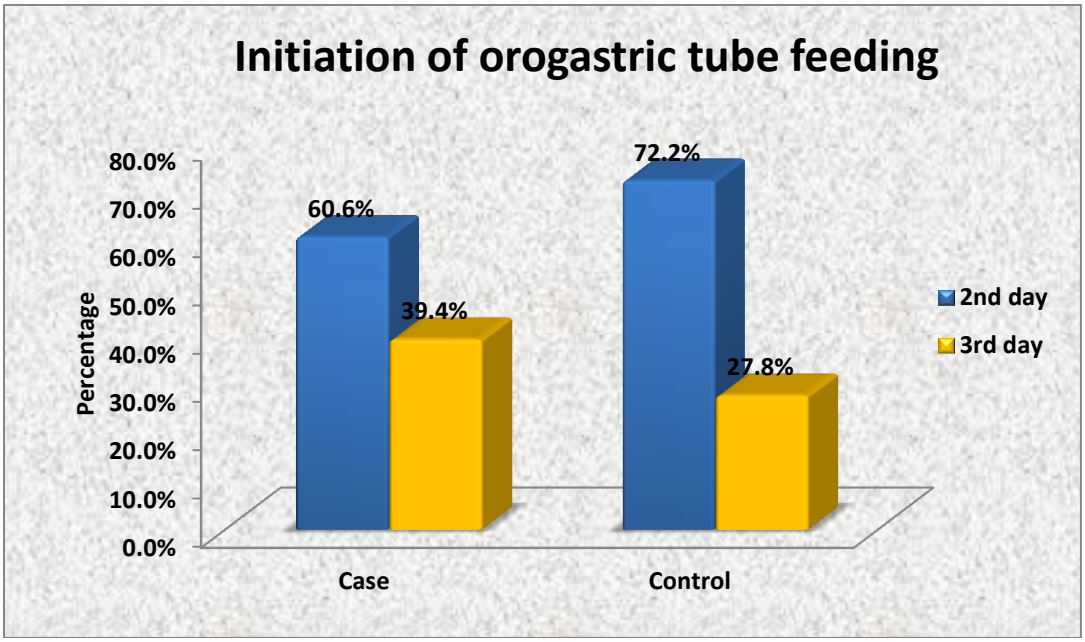


In our study we found that maximum number of neonates in both the groups needed 31 to 40 hours of oxygen supplementation i.e., 44.1% in the case group and 47.2% in the control group. It was not statistically significant.

Table 13: Initiation of orogastric tube feeding

Orogastric tube feeding	Case		Control		p value
	n	%	n	%	
2nd day of life	20	60.6%	26	72.2%	0.307
3rd day of life	13	39.4%	10	27.8%	
Total	33	100.0%	36	100.0%	

Figure 13: Initiation of orogastric tube feeding

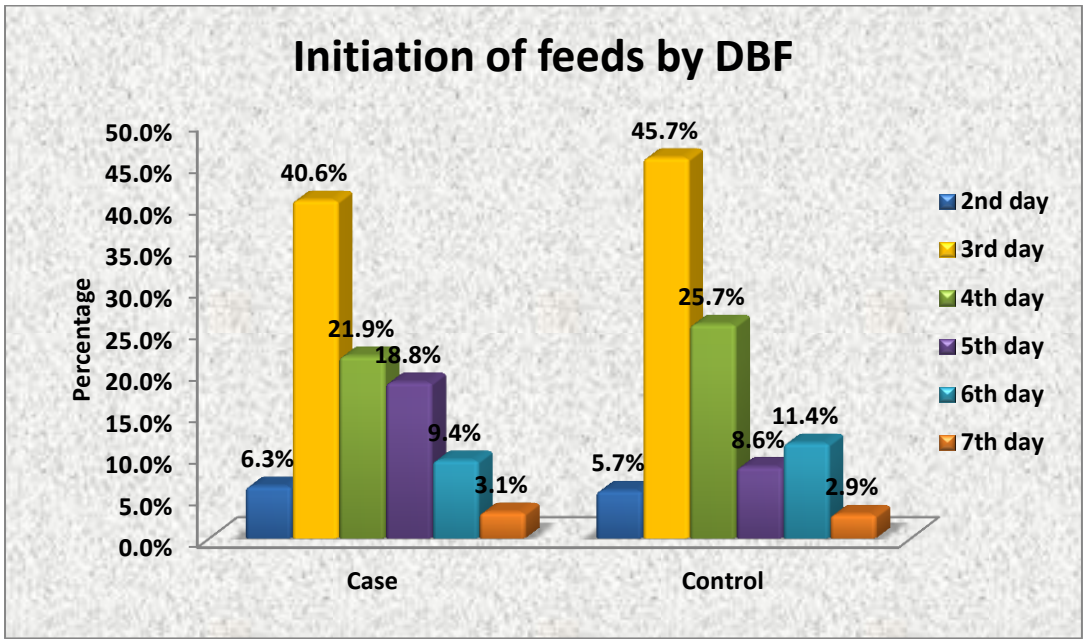


Orogastric tube feeding was started in 60.6% in the case group and 72.2 % in the control group on the second day of life. This shows that initiation of feeding was same in both the groups.

Table 14: Initiation of feeds by direct breast feeding (DBF)

DBF	Case		Control		p value
	N	%	N	%	
2nd day	2	6.3%	2	5.7%	0.905
3rd day	13	40.6%	16	45.7%	
4th day	7	21.9%	9	25.7%	
5th day	6	18.8%	3	8.6%	
6th day	3	9.4%	4	11.4%	
7th day	1	3.1%	1	2.9%	
Total	32	100.0%	35	100.0%	

Figure 14: Initiation of feeds by direct breast feeding (DBF)

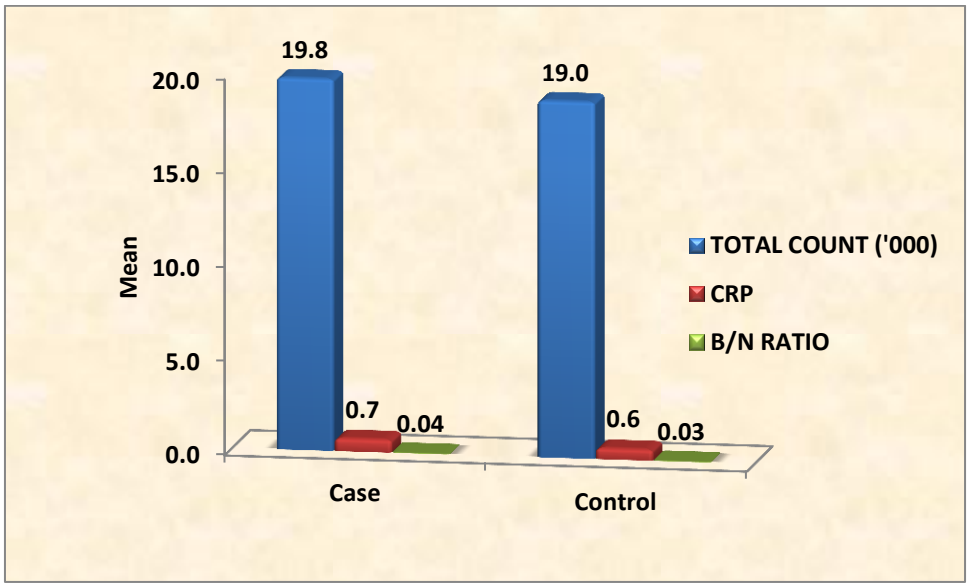


There was no significant difference in the achievement of direct breast feeding in between the two groups. Most of them achieved direct breast feeding (40.6% in case group and 45.7% in control group) by third day of life.

Table 15: Sepsis parameters

Parameters (Mean±SD)	Case	Control	p value
Total Leucocyte Count (‘000) [cells/mm$^{3]}$	19.8±6.1	19±6.6	0.596
C- Reactive Protein (CRP) [mg/dl]	0.7±0.8	0.6±0.9	0.678
Band Neutrophil Ratio (B/N Ratio)	0.04±0.1	0.03±0.15	0.512

Figure 15: Sepsis parameters

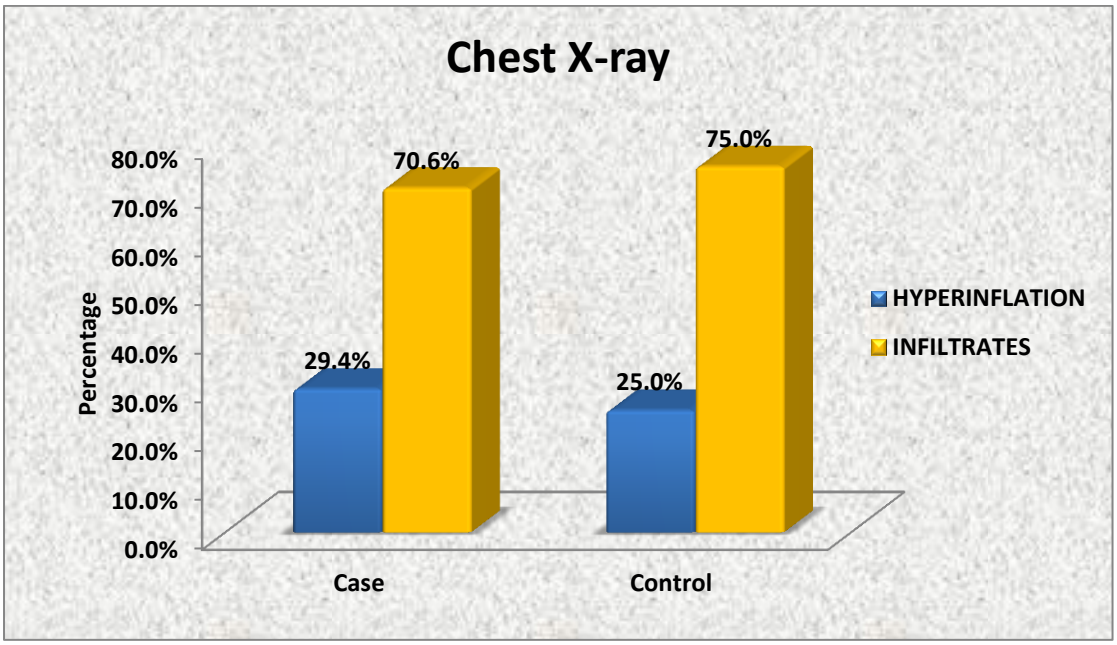


The above table shows that there was no sepsis screen positive either in the case or control group. Mean total leucocyte count 19000 cells/mm^3 both in case and control, mean CRP in case group is 0.7± 0.8 mg/dl and in control group is 0.6± 0.9.

Table 16: Chest X- ray

Chest X-ray	Case		Control		p value
	N	%	N	%	
Hyperinflation	10	29.4%	9	25.0%	0.678
Infiltrates	24	70.6%	27	75.0%	
Total	34	100.0%	36	100.0%	

Figure 16: Chest X- ray



The above table shows that 70.6% in the case group and 75% in the control group shows parenchymal infiltrates. 29.4% in the case group and 25% in the control group shows hyperinflation.

Table 17: Distribution of neonates according to the diagnosis

Diagnosis	Case (n = 34)	Control (n = 36)
Term AGA male baby with MAS	13	11
Term AGA female baby with MAS	5	7
Term AGA male baby with MAS with hyperbilirubinemia	1	0
Term SGA male baby with MAS	4	5
Term SGA female baby with MAS	1	3
Term AGA female baby with MAS with HIE stage I	1	2
Term SGA male baby with MAS with HIE stage I	0	2
Term SGA female baby with MAS with HIE stage I	1	0
Term AGA male baby with MAS with HIE stage II	3	2
Term AGA female baby with MAS with HIE stage II	4	2
Term SGA female baby with MAS with HIE stage II	0	1
Term AGA male baby with MAS with HIE stage II with hyperbilirubinemia	0	1
Term AGA female baby with MAS with HIE stage II with hyperbilirubinemia	1	0

The above table shows the distribution of neonates according to the diagnosis which was almost similar in between the groups. Majority of the neonates were diagnosed with only meconium aspiration syndrome (49 neonates) followed by meconium aspiration with hypoxic ischemic encephalopathy (HIE) stage II (12 neonates) and HIE stage I (6 neonates), and hyperbilirubinemia in 3 neonates out of which two are associated with HIE stage II.

Table 18: Clinical profile of the neonates

Parameters	**Case (n = 34)**	**Control (n = 36)**
Age of mothers (years) [mean ± SD]	25.3 ± 2.3	24.9 ± 2.0
Antenatal registration [no (%)]	26 (76.5)	27 (75.0)
Gravida [mean ± SD]	1.9 ± 1.6	1.8 ± 1
Mode of delivery		
NVD [no (%)]	26 (76.5)	26 (72.2)
Caesarean [no (%)]	8 (23.5)	10 (27.8)
Gestational age (weeks) [mean ± SD]	38.9 ± 1.2	38.8 ± 1.1
Birth weight (kg) [mean ± SD]	2.7 ± 0.3	2.7 ± 0.4
Male : Female	20 : 14	21 : 15
Apgar score (mean ± SD)		
At birth	6.5 ± 1.0	6.3 ± 1.3
1 min	8.5 ± 1.0	8.3 ± 1.3
5 min	8.5 ± 0.5	8.7 ± 0.5
MSAF		
Thick [no (%)]	9 (26.5)	11 (30.6)
Thin [no (%)]	25 (73.5)	25 (69.4)
Downe's score at admission (mean ± SD)	1.6 ± 1.2	1.5 ± 1.1

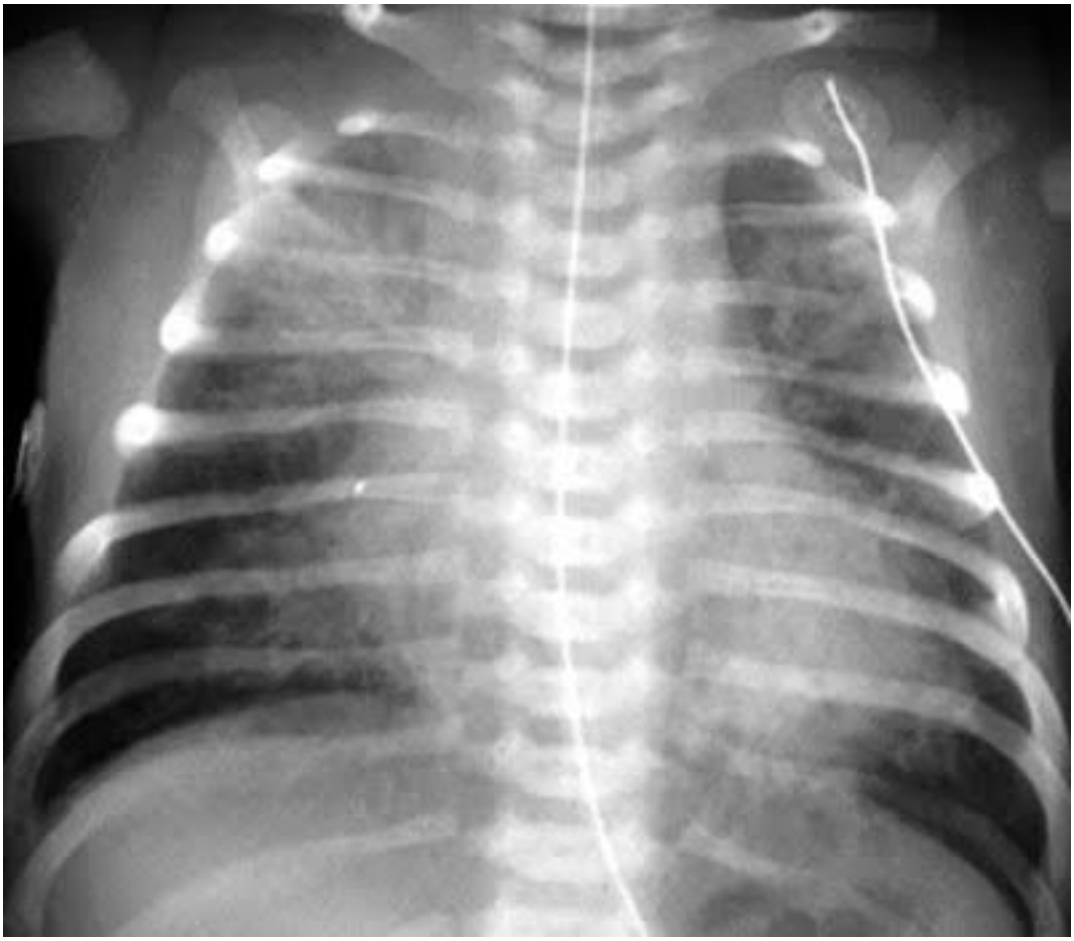
The above table shows the summary of the clinical profiles of the neonates. There is no statistical significant in the clinical profile in between the case and control groups.

Table 19: Progress of neonates during hospital stay

Parameters	**Case (n = 34)**	**Control (n = 36)**
Duration of hospital stay (days) (mean ± SD)	4.2 ± 1.6	4.3 ± 1.7
Initiation of orogastric feeds (days) (mean ± SD)	2.4 ± 0.5	2.3 ± 0.5
Initiation of feeds by direct breast feeding (days) (mean ± SD)	3.9 ± 1.2	3.8 ± 1.2

The above table shows the progress of neonates during the hospital stay. Duration of hospital stay, initiation of orogastric tube feeding and initiation of direct breast feeding (DBF) were similar in between the two groups.

Picture 4: Neonate with meconium aspiration syndrome on mechanical ventilation.



Picture 5: Chest X- Ray of neonate with meconium aspiration syndrome with bilateral parenchymal infiltrate with right upper lobe consolidation.

DISCUSSION

Despite improvement in obstetrical and neonatal care, MAS continues to be a major cause of respiratory distress in term and post term infants especially in the developing country. Extensive research on prevention and intervention has been performed; still only supportive treatment is generally used.

Among preventive strategies, elective induction of labour for pregnancies at or beyond 41 weeks is associated with significant reduction in the incidence of MAS.

The pathophysiology is still poorly understood, especially the prenatal events leading to meconium aspiration and the fact that some neonates may aspirate meconium without the development of severe symptoms or complications.

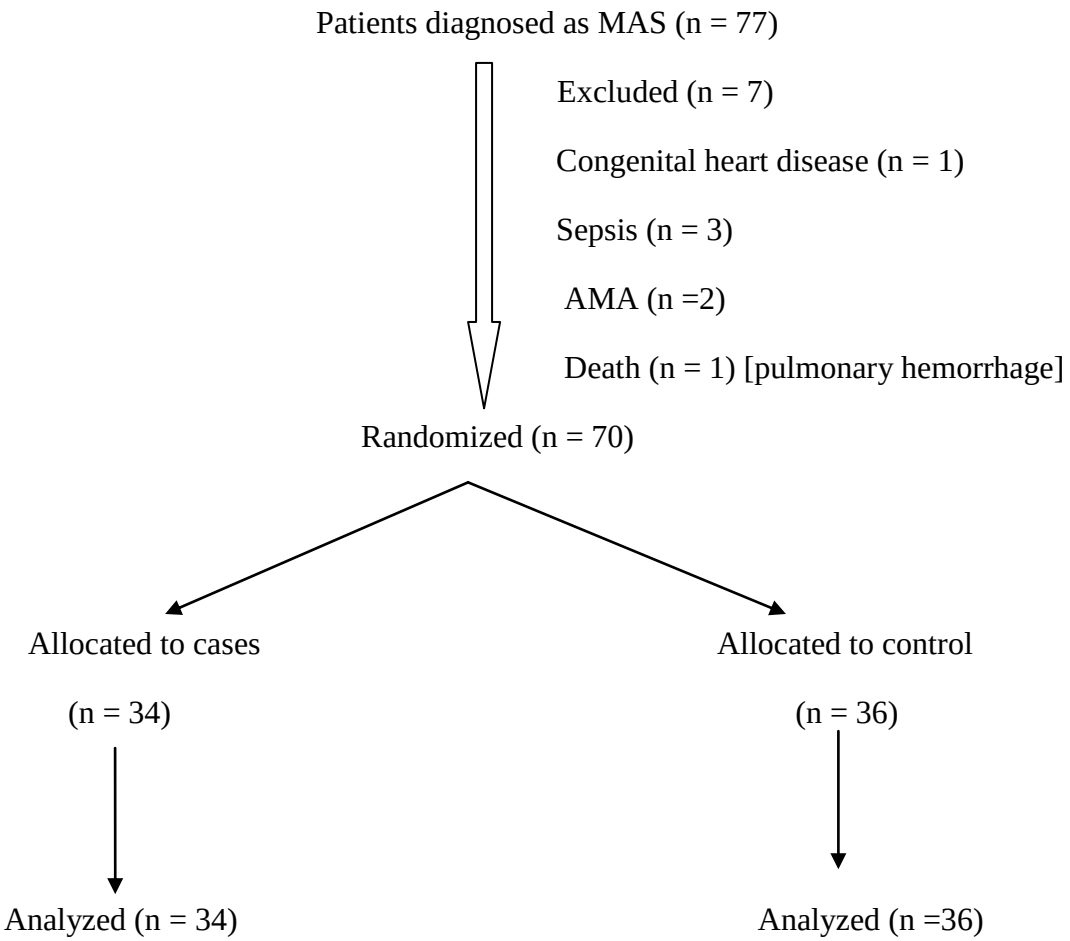
The role of steroids and other adjuvant pharmacotherapies like magnesium sulfate, free radical scavengers, and protease inhibitors is still experimental.

Since inflammation plays an important role in the pathophysiology of MAS, suppression of inflammation by corticosteroids appears to be of potential benefit

Steroids were used for the treatment of MAS since 1977 by Frantz et.al[6], they showed promising results of clinical improvement but mortality was high. Hydrocortisone was used by Yeh et al[63] and he found that it was ineffective as it prolongs the duration of stay, oxygen requirement and respiratory distress.

In the present study we have used injection dexamethasone intravenously starting after 24 hours of life for three days (0.5mg/kg/day)[4]. The rationale behind starting dexamethasone after 24 hours was to exclude the neonates in whom the respiratory distress got settled by 24 hours and were considered to be due to transient

tachypnea of newborn[2]. Dexamethasone was used as it is 30 times more potent than hydrocortisone and five times stronger than prednisolone[4] and longer duration of action (18 – 24 hrs) and lesser side effects.



Flowchart showing the participants through each stage

A total of 77 babies diagnosed with MAS and admitted to the neonatal intensive unit were studied, of which 7 were excluded from the study because of various reason as shown in the above flowchart. A total of 70 neonates were finally included in the study, 34 neonates in the case group and 36 neonates in the control group.

PROFILE OF THE NEONATES

In our study we found that there was no significant difference in the anthropometric indices, clinical profile of both the groups were comparable including APGAR score, Downe's score and MSAF which was comparable to the study conducted by Sriparna Basu et al in 2007[2]. Another study by Suresh R et al in 2015 also shows that clinical profile were comparable in both the groups[71].

DURATION OF HOSPITAL STAY AND PERIOD OF OXYGEN DEPENDENCY

Our study shows that duration of hospital stay in the case group was 4.2 ± 1.6 days and in the control group 4.3 ± 1.7 days. 44.1% in the case group and 47.2% in the control group had oxygen dependency of 31 to 40 hours. There was no significant difference in the duration of hospital stay and period of oxygen dependency in both the groups.

However in a study by Yeh TF et al in 1977 found that the infants in the treated groups took significantly longer period of time to wean to room air than those in the control group[77]. In a study by Sriparna Basu et al in 2007 found that duration of the hospital stay and oxygen dependency was longer in the control group as compared to steroid treated group[2].

MECHANICAL VENTILATION

Need for mechanical ventilation was more in the case group that is 4 neonates and only 1 neonate in the control group needed mechanical ventilation of 96 hrs. This shows that neonates in case group were more sick but was not statistically significant. In a study by Wu (1999) also concluded the same that there was no significant difference in the duration of mechanical ventilation[5].

INITIATION OF FEEDING

In our study we found that there was no statistical difference in the start of the orogastric tube and achievement of direct breast feeding. Orogastric tube feeding was started in 60.6% in the case group and 72.2 % in the control group on the second day of life. This shows that initiation of feeding was same in both the groups. There was also no significant difference in the achievement of direct breast feeding in between the two groups. However in a study by Sriparna basu et al in 2007 concluded that full enteral feeding was achieved earlier in case group as compared to control group. This was because neonates in the control were sicker and oxygen dependent for loner time as a result feeding was delayed[2]. In another study by Suresh R et al (2015) found that full enteral feeds was much earlier in budesonide treated group as compared to the control group[71].

OTHERS

In our study we found that the commonest chest X-ray findings were parenchymal infiltrates in 70.6% in the case group and 75% in the control group followed by hyperinflation in 29.4% in the case group and 25% in the control group. Sriparna basu et also found that the commonest chest X-ray changes were parenchymal infiltrates followed by hyperinflation and atelectasis which is similar to our study. Air leak was seen only in one neonate in the control group[2].

We found that there was no increased incidence of adverse effects associated with the use of intravenous steroids. We did not find any significant difference in the incidence of complication like sepsis, hypoglycemia, hyperglycemia, hypocalcemia. Sriparna basu et al found that there was no significant difference in the incidence of complication in between the groups[2].

LIMITATION OF OUR STUDY

- First the study was not blinded to the doctors.
- Long term follow-up for complications such as neurodevelopmental outcome was not done.
- Neonates enrolled in our study were not very sick as evidenced by the fact that only one death in our study. So, it is difficult to comment the effect of dexamethasone on very sick neonates.
- Sample size was not large and larger studies are necessary to recommend the effect of steroid (dexamethasone) in the routine management of MAS.

CONCLUSION

In our study we found that there was no significant difference in terms of oxygen dependency, duration of hospital stay and morbidity and mortality in between the steroid treated group and the control group. A further large randomised control trial is needed to study the effect of steroid in the outcome of meconium aspiration syndrome.

SUMMARY

A prospective study of 70 neonates with MAS admitted in Neonatal intensive care unit of Shri B. M Patil Medical College, Hospital and Research Centre, Vijayapur; was done from October 2014 to April 2016, was done with objectives to evaluate the effect of dexamethasone in MAS and to compare the oxygen dependency, duration of hospital stay and any other morbidity and mortality in between the groups.

All neonates admitted with MAS whose parents gave consent were included in the study. A porforma was used to collect data from the day of admission. Injection dexamethasone (0.5mg/kg/day) was given intravenously in the case group starting from 2nd day of life for three days along with the routine treatment of MAS and in the control group only routine treatment of MAS was given.

During this study we observed that clinical profile, period of oxygen dependency, hospital stay and initiation of feeds were similar in both the groups. No serious adverse effects were noted in steroid treated group (case group). We concluded that there was no significant difference in terms of oxygen dependency, duration of hospital stay and morbidity and mortality in between the steroid treated group and the control group. A further large randomised control trial is needed to study the effect of steroid in the outcome of meconium aspiration syndrome.

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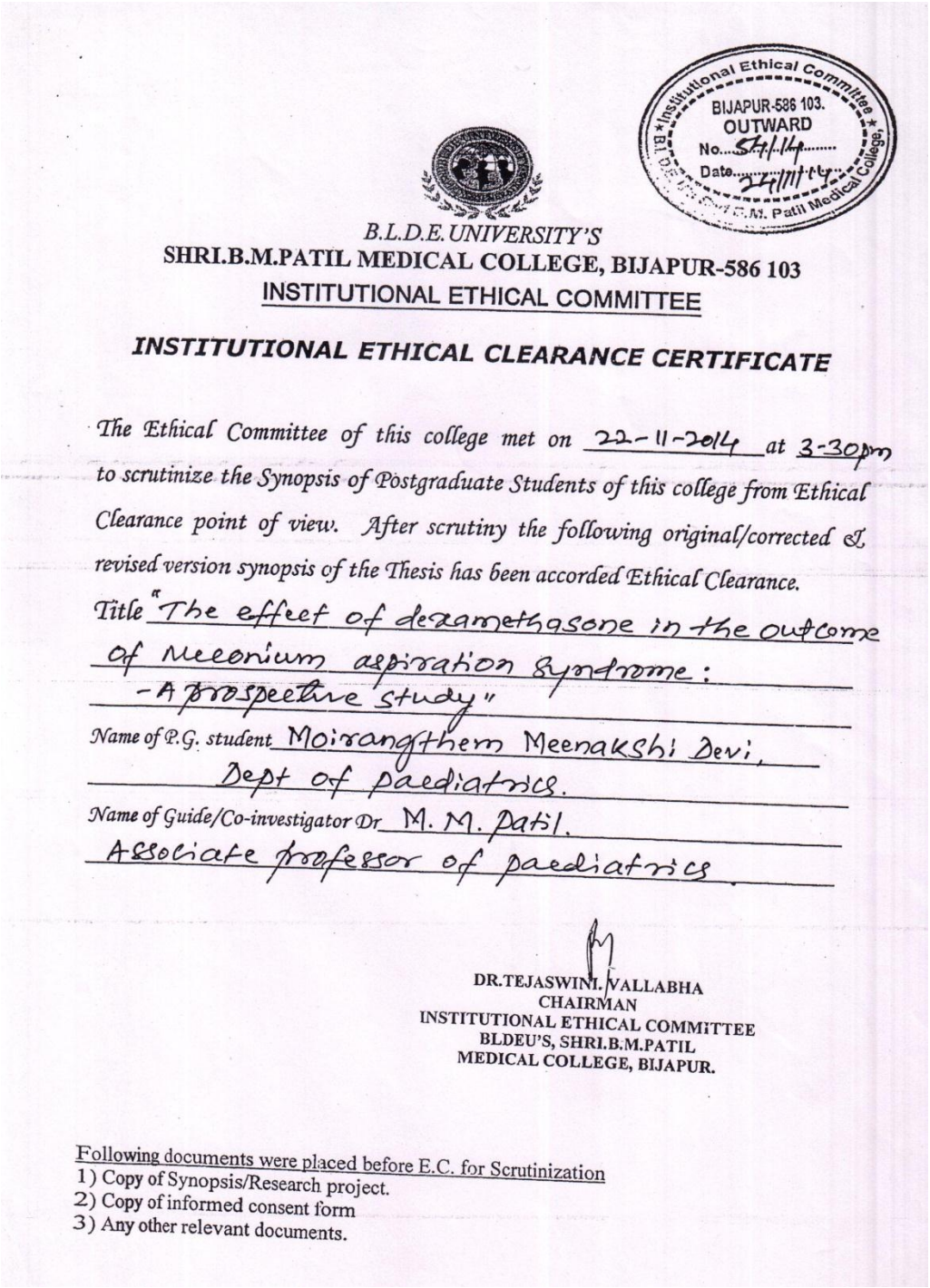
ANNEXURES

ETHICAL CLEARANCE CERTIFICATE



Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 571/14
Date 24/11/14
B.L.D.E. Shri B.M. Patil Medical College

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 22-11-2014 at 3-30pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "The effect of dexamethasone in the outcome of Meconium aspiration Syndrome: -A prospective study"

Name of P.G. student Moirangthem Meenakshi Devi, Dept of paediatrics.

Name of Guide/Co-investigator Dr M. M. Patil. Associate professor of paediatrics.

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

CONSENT FORM

PARENTS / GUARDIAN CONSENT STATEMENT:

We confirm that Dr. Moirangthem Meenakshi Devi is doing a study on THE EFFECT OF DEXAMETHASONE IN THE OUTCOME OF MECONIUM ASPIRATION SYNDROME. Dr. Moirangthem Meenakshi Devi has explained to us the purpose of research and the study procedure. We are willing to allow our baby to undergo investigations and the possible discomforts as well as benefits. We have been explained all the above in detail in our own language and we understand the same. Therefore we agree to give consent to participate as a subject in this research project.

_____ _____

(Parents / Guardian) Date

_____ _____

(Witness to signature) Date

PROFORMA

SCHEME OF CASE TAKING :

Name :

Sex : IP NO :

Religion : DOA :

Postal address: DOD :

Age of the mother :

Antenatal registration(Yes/No):

Gravida :

Gestational age :

Mode of delivery (NVD/Caesarean/Forceps):

Meconium stained amniotic fluid (Thick/Thin):

APGAR score :

Maternal obstetric history :

OTHER HISTORY:

1. Oxygen dependency (Yes/No) :
   - If yes then period of oxygen dependency:
2. History of development of sepsis (Yes/No) :
3. Need for mechanical ventilation :
4. Full enteral feeding :

GENERAL PHYSICAL EXAMINATION:

EGA : by dates …… weeks : by examination …… weeks ;

Length……..cms ; HC ……cms

Birth weight ……. Kgs . CC…….cms

SYSTEMIC EXAMINATION

- Cardiovascular System :

- Respiratory System:

- Gastro-intestinal system:

- Central Nervous System:

INVESTIGATION :

1) Complete hemogram :

PARAMETERS	
Total count	
Neutrophils	
Lymphocytes	
Eosinophils	
Basophils	
Monocytes	
Hb	
MCH	
MCHC	
PCV	
Platelet count	
B:N Ratio	
Peipheral Smear	

2) C-reactive protein :

3) RBS:

4) Serum Electrolyte:

- Sodium -
- Potassium -
- Calcium -
- Chloride -

5) Arterial blood gas:

- pH -
- pCO_2 -
- HCO_3 -

6) Serum bilrirubin:

- Total bilirubin –
- Unconjugate bilirubin –
- Conjugate bilirubin -

7) ECHO :

8) X- Ray chest :

9) Blood culture:

MONITORING CHART:

Date	Time	Heart rate	Respiratory rate	SpO_2	CFT	Downe's score	Weight	RBS

KEY TO MASTERCHART

Sl. No. : Serial number

IP No. : In patient number

M : Male

F : Female

DOA : Date of admission

DOD : Date of discharge

Y : Yes

N : No

P : Primigravida

M : Multigravida

NO : Normal vaginal delivery

LS : Lower segmental Caesarean

TN : Thin meconium stained amniotic fluid

TH : Thick meconium stained amniotic fluid

OGT : Orogastric tube

DBF : Direct breast feeding

Hb : Hemoglobin

CRP : C-reactive protein

B/N Ratio : Band neutrophil ratio

RBS : Random blood sugar

I : Parenchymal infiltrates

H : Hyperinflation

S : Sterile SPO_2