

Original Research Article

A STUDY ON THE FETOMATERNAL OUTCOME OF REFERRED CASES OF PRETERM LABOUR BEYOND 30 WEEKS

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Abstract

OBJECTIVES: To study the various fetomaternal outcomes of referred cases of preterm labour beyond 30 weeks

To study the clinical profile of referred cases of preterm labour beyond 30 weeks

METHODS: A cross-sectional study was done on all cases of preterm labour, referred to SAT Hospital beyond 30 weeks for a period of 1 year after institutional ethical committee clearance.

SAMPLE SIZE: As per an internal audit conducted from November 15, 2019 to December 15, 2019

Total number of patients referred beyond 30 weeks as preterm labour was 86

Total number of patients referred beyond 30 weeks who had preterm delivery (vaginal or Caesarean) was 28

This was used for sample size calculation

$SAMPLE\ SIZE\ N = (Z^2 \cdot 1-a/2 \cdot P (1-P)) / (eP)^2$

P= anticipated population proportion

e= relative precision

(minimum 10% to maximum 20%)

From the pilot study: expected proportion = 0.28 relative precision(%) = 20

desired confidence level (1-a) = 95 required sample size = 233

Anticipating 10% dropout rates final sample size =260

RESULTS: Of the total study subjects, 63.1% had preterm deliveries. 40.4 % of the patients delivered immediately. The preterm perinatal mortality rate was 5.8%.

CONCLUSION: The independent risk factors identified, which may result in preterm birth from this study are a previous history of preterm birth, if the mother is diabetic, if mother is anemic and exposure to tobacco. The independent risk factors identified for immediate birth were history of previous preterm birth, mother being a multigravidae, hypertension in the mother and bronchial asthma in mother. The use of progesterone supplements was found to be protective against both preterm birth and immediate birth.

The independent factors supporting favourable neonatal outcome was a maternal age of 25 years or less, progesterone supplementation and administration of antenatal corticosteroids. The factors hindering a favourable neonatal outcome included hypertension and stress. The independent risk factors identified, which may result in perinatal mortality are mother being hypertensive, exposure to tobacco and periodontal infections in the mother. Maternal age of 25 years or less was found to be a protective factor.

ABBREVIATIONS

1. ACOG – American College of Obstetricians and Gynaecology

2. ANC – antenatal checkup
3. CDSCO – The Central Drugs Standard Control Organisation
4. CI – confidence interval
5. ELISA – enzyme linked immunosorbent assay
6. FFN – fetal fibronectin
7. FIGO – International Federation of Gynaecology and Obstetrics
8. FOGSI – The Federation of Obstetric and Gynaecological Societies of India
9. ICU – intensive care unit
10. IM - intramuscular
11. IV - intravenous
12. IVF – in vitro fertilisation
13. LEEP – loop electrosurgical excision procedure
14. LMP – last menstrual period
15. MgSO₄ – magnesium sulphate
16. NICE – The National Institute for Health and Care Excellence
17. NICU – neonatal intensive care unit
18. NRP – neonatal resuscitation program
19. PGI – post graduate institute
20. PPROM – preterm premature rupture of membranes
21. RCOG - Royal College of Obstetricians and Gynaecology
22. RR – relative risk
23. RSUTH – Rivers State University Teaching Hospital
24. SMFM – society for maternal and fetal medicine
25. STD – sexually transmitted diseases
26. TVS – transvaginal ultrasound
27. UTI – urinary tract infection
28. WHO – World Health Organisation

INTRODUCTION

“The usual period of a woman’s going with child is nine calendar months but there is very commonly a difference of one, two or three weeks. A child may be born alive at any time from three months: but we see none born with powers of coming to manhood, or of being reared, before seven calendar months or near that time. At six months it cannot be.”

William Hunter c.1760

Cited by Thomas Denmann in Introduction to Practice of Midwifery,
New York: E. Bliss and E. White, 1825, p253

Preterm labour is defined as onset of uterine contractions before 37 weeks (20 to 36+6 weeks) of gestation that causes the cervix to get thinned out (effacement) and subsequently open up (dilatation) (ACOG 2017 guidelines)[1]. Every year an estimated 15 million babies are born preterm globally and the complications of preterm birth are the leading cause of under- 5 mortality, disability and ill health later on in life (NICE 2016)[2]. Of the total preterm births, 84% occur between 34 – 36 weeks, 10% from 28 – 32 weeks and the last 5% at less than 28 weeks. Births occurring at less than 28 weeks is termed extreme preterm, from 28 – 32 weeks, they come under very preterm and finally from 32-37 weeks they are labelled as moderate to late preterm.

As per various studies by WHO and other international agencies, developing countries face the major wrath of preterm labour – varying from 5% to as high as 30% in the African countries[4]. Most of the times in these regions, the patient reaches the facility of health care late into labour, when favourable interventions are limited. The role of antenatal corticosteroids for lung maturity,

MgSO₄ for neuroprotection and tocolytics as may be the indication has to be suitably considered or offered to reduce adverse neonatal and future outcomes.

Most of the referrals in view of preterm labour are aimed at the provision of better neonatal care. It may range from the intrauterine period – need for antenatal corticosteroids, neuroprotection MgSO₄ as indicated, prophylactic antibiotics in cases of anticipated maternal sepsis and the occasional use of tocolytics, emergency theatre facilities, a well established blood bank availability and a decent ICU care for both maternal and neonatal sake plays a pivotal role in deciding referrals from the periphery.

In addition to the above mentioned fetal factors, a host of maternal factors may also pave way for the referral to the tertiary care centres. These include maternal pyrexia following prolonged periods of PPRM, sepsis, massive blood loss, need for ICU care and maternal resuscitation in probable abruption. In the light of the present Covid – 19 era, referrals were also based on the mothers' covid status and often post covid sequelae. Several of the peripheral centres getting closed down or being declared as covid care line centres have also contributed to this situation. Referrals on the request of the patients themselves and their caretakers are also not uncommon.

Analysing the spectrum of the referred patients, patients may be categorised into 3 broad groups : first comes those who actually end up in preterm birth, second group includes those who are in threatened preterm labour but which later becomes quiescent and the last group who have some suspicious features of preterm labour and were referred on a high index of suspicion more than clinical diagnosis. The point to be highlighted is the fact that the last group encompasses maximum number of the referred patients. Hence a proper triage of the referred patients is necessary both for reducing the burden on an already strained workforce as well as to prevent undue untimely interventions.

DATA COLLECTION TOOLS:

Data was collected using structured questionnaire. A thorough history was taken from the antenatal patients satisfying inclusion criteria admitted in SAT hospital. Complete physical and obstetric examination was done. All basic investigations and case-specific investigations were done as mandated by the patient's clinical condition.

PLAN OF ANALYSIS

Data was coded and entered in excel sheet. Analysis was done using SPSS software trial version 21.

ETHICAL CONSIDERATIONS

The study commenced after receiving approval from the Institutional Research Committee and the Institutional Ethics Committee. Patient at any time could withdraw from the study and this in no way affected the further standard of care the patient required/received. Strict confidentiality was ensured and maintained throughout the study.

RESULTS

TABLE: TABLE SHOWING DISTRIBUTION OF MATERNAL OUTCOMES

MATERNAL OUTCOMES	Frequency	Percent %
MATERNAL SEPSIS	45	17.3
ICU ADMISSION FOR MOTHER	32	12.3
TRANSFUSION FOR MOTHER	29	11.2

TABLE : TABLE SHOWING BINARY LOGISTIC REGRESSION OF PRETERM BIRTH

FACTORS IDENTIFIED	p	OR	95% C.I.for OR	
			Lower	Upper
HISTORY OF PRETERM BIRTH	0.024	2.48	1.13	5.44
TOBACCO EXPOSURE	0.048	2.25	1.01	5.04
PROGESTERONE SUPPLEMENTATION – GIVEN	<0.001	0.07	0.03	0.18
DIABETES	<0.001	10.00	3.72	26.86
ANEMIA	0.045	1.52	1.27	2.98

TABLE : TABLE SHOWING BINARY LOGISTIC REGRESSION FOR PERINATAL MORTALITY

FACTORS IDENTIFIED	P	OR	95% C.I.for OR	
			Lower	Upper
EXPOSURE TO TOBACCO	0.001	6.094	4.866	7.44
HYPERTENSION	0.008	4.096	2.579	3.277
PERIODONTAL INFECTIONS	0.037	3.871	1.249	2.736
MATERNAL AGE – 25 OR LESS	0.001	0.006	0.001	0.121

DISCUSSION

In my study a total of 260 study subjects were taken into account out of which 105 had immediate deliveries while 155 did not deliver immediately. 164 patients among the study subjects had preterm birth at any point of time before 37 completed weeks while the remaining 96 went onto deliver at or after 37 completed weeks.

Majority of the patients were in the age group of between 20 and 25 years of age. This is in line with the patient profile at SAT Hospital. Among the study population, 40.4% were primigravidae whereas majority of the patients were multigravidae – 59.6%. Majority of the patients were referred from government hospitals (68.5%) with the rest 31.5% being referred from private hospitals. Majority of the patients were from rural areas – 69.2% while the rest were from urban areas – 30.8%. More than half of the patients were from lower middle socioeconomic status – 54.2% followed by upper lower – 29.6%. 56.5% of the patients had the recommended 4 antenatal visits with 3.5% having no antenatal visits. All patients in the upper and upper middle classes had 4 or more ANC visits. 46.5% of the population were underweight, 22.7% were of normal BMI and 16.9% were obese. These findings are comparable with the study by Norman et al 2004. These findings also fall in line with the general patient profile at the study centre.

46.2% of the patients were referred between gestational age of 34 weeks and 35 weeks + 6 days with 34.2% of the patients being referred between 30 weeks and 33 weeks + 6 days and the rest (19.6%) were referred between 36 weeks and 36 weeks + 6 days. The most common indication for preterm referral beyond 30 weeks was preterm pain (43.1%) followed by PPRM (33.1%). These findings are also corroborative with the results of the study on trends of preterm births by MacDorman M, Callaghan W in 2006.

Analysis of the collected data was done. Multivariable analysis was done. On the variables with significance, bivariable analysis was done to identify independent risk factors of important study outcomes – preterm birth, immediate birth, favourable neonatal outcome and perinatal mortality.

Binary logistic regression of the various factors associated with preterm delivery was done. The independent risk factors identified, which may result in preterm birth from this study are a previous history of preterm birth (p value – 0.024, OR 2.48[95% CI 1.13 – 5.44]), if the mother is diabetic (p value <0.001, OR 10.00[95% CI 3.72 – 26.86]), if mother is anemic (p value – 0.045, OR 1.52[95% CI 1.27 – 2.98]), and exposure to tobacco (p value – 0.048, OR 2.25[95% CI 1.01 – 5.04]). On the other hand progesterone supplementation (p value <0.001, OR 0.07[95% CI 0.03 – 0.18]), was found

to be protective against preterm birth. Therefore any referred patient referred as preterm labour beyond 30 weeks has one or more of the above mentioned risk factors, has a high chance to deliver preterm. A similar significant conclusion has been drawn in the series of three papers on epidemiology, risk factors and preventive measures of preterm birth by Goldenberg, Culhane and Romero that the causes for spontaneous preterm birth is multifactorial. The likelihood of preterm birth seen at smaller gestational age is in concordance with the study by Usher R, Allen A in 1971 that the incidence of preterm related complications is inversely proportional to the gestational age at birth. The higher likelihood of preterm births if there is a previous history of preterm birth has already been proposed in the study by Goldenberg R, Iams J published in *The Lancet* 2008. Presence of diabetes (whether gestational or otherwise effectively reduces the length of gestation and thereby increases the incidence of spontaneous preterm birth was proven in the study by Kock and Klein in 2010. There is a dose-related impact of smoking on risk of preterm birth. The fact that the smoking-related risk of spontaneous preterm birth is more pronounced than that of induced preterm birth suggests that smoking including passive smoking, is associated with spontaneous preterm labor as is concluded in the study by Blomberg and Kyrkund, 1998.

Stress was associated with spontaneous preterm birth and low birth weight even after adjustment for maternal demographic and behavioral characteristics as per the study by Copper et al in 1996 published in *American Journal of Obstetrics and Gynaecology*. Vaginal progesterone was associated with reduced risk of preterm birth and composite neonatal outcomes but had no long-term benefit or harm as per the study by Fonseca and Bittar. Anemia in mother being a risk factor for preterm birth could be explained on the fact that anemia could be a pointer of the poor general nutritional status, sub optimal antenatal care and socio economic disposition of the patient.

Binary logistic regression of the various factors associated with immediate birth was done and the independent risk factors identified were history of preterm birth (p value < 0.001, OR 4.54 [95% CI 2.01 – 10.24]), mother being a multigravidae (p value – 0.003, OR 3.12 [95% CI 1.47 – 6.63]), hypertension in the mother (p value – 0.042, OR 2.29 [95% CI 1.03 – 5.11]), and bronchial asthma in mother (p value < 0.001, OR 4.62 [95% CI 2.23 – 9.59]). The use of progesterone supplements (p value – 0.002, OR 0.29 [95% CI 0.13 – 0.63]) was found to be protective against immediate birth as well. The spectrum of evidence for most of these factors being favourable for not delivering preterm has already been discussed at length before. The higher likelihood of immediate preterm delivery has been already substantiated in the study by Georgio and Quinzio. [4].

Following binary logistic regression, the independent factors in favour of favourable neonatal outcome was a maternal age of 25 years or less (p value – 0.021, OR 2.35 [95% CI 1.14 – 4.87]), progesterone supplementation (p value < 0.001, OR 7.41 [95% CI 2.88 – 19.02]) and administration of antenatal corticosteroids (p value – 0.032, OR 2.27 [95% CI 1.07– 4.81]). The factors which might hinder a favourable neonatal outcome included hypertension (p value – 0.001, OR 0.14 [95% CI 0.04 – 0.45]) and stress (p value < 0.001, OR 0.07 [95% CI 0.03 – 0.19]). Evidence pertaining to the positive effects of maternal age at or below 25 years and progesterone and suboptimal effects of hypertension and stress has already been enumerated before. The favourable profile of antenatal corticosteroids has been already proposed at length in the study by Roberts and Dalziel.

Binary logistic regression of the various factors associated with perinatal mortality was done. The independent risk factors identified, which may result in perinatal mortality are mother being hypertensive (p value – 0.008, OR 4.09 [95% CI 2.57 – 3.27]), exposure to tobacco (p value – 0.001, OR 6.09 [95% CI 4.86 – 7.44]) and periodontal infections (p value – 0.037, OR 3.87 [95% CI 1.24– 2.73]), in the mother. Maternal age of 25 years or less (p value – 0.001, OR .006 [95% CI 0.001 – 0.121]) was found to be a protective factor. Therefore, any referred patient referred as preterm labour beyond 30 weeks has one or more of the above mentioned risk factors, has a high chance to develop perinatal mortality. These findings are in sync with the risk factor profile which was found to be significant in the study by A Moser, K Macfarlane on gestation specific infant mortality rates in Wales and New England, published in the NHS Statistics, London 2007. The decreased

likelihood of preterm births and thereby perinatal mortality in young mothers may be attributable to the allied factors of less comorbid medical conditions, better embryo quality and vitality of the younger age. The higher likelihood of perinatal mortality in mothers with hypertension may be due to the complications such as abruptio placentae and pre-eclampsia which triggers a preterm birth with limited time for interventions to optimize neonatal outcome. Tobacco exposure contributing to increased likelihood of perinatal mortality maybe due to long standing chronic hypoxia in the mother as is postulated in the study by Blomberg and Kyrkud,1998.

In the presence of periodontal disease, oral opportunistic pathogens and/or their inflammatory products also may have a role in prematurity and thereby perinatal mortality via a hematogenous route since the species and subspecies of fusobacteria identified from amniotic fluid of such mothers most closely match those reported from healthy and diseased subgingival sites, namely *F. nucleatum* subspecies *vincentii* and *F. nucleatum* subspecies *nucleatum* as is concluded in the study by McDonald HM and O'Loughlin in 1998. In this context, regular dental examination of antenatal patients, especially those with multiple factors which may predispose to preterm births, may be considered in health care centres so that periodontal disease contributing to preterm birth can be controlled.

Various risk factors which can contribute to spontaneous preterm births have been enumerated. Timely detection and their modification holds the key to a positive foeto - maternal outcome and even positive pregnancy and motherhood experience. Early detection and necessary amendments to curb or alter those factors may go a long way in reducing preterm births and thereby perinatal mortality. This in turn may lead to significant improvement in the realms of neonatal, infant and under 5 mortality. They may also substantially reduce neonatal morbidity and long term sequelae including early onset cardiovascular disease, obesity and metabolic complications.

Ours being a referral based healthcare system, triaging becomes even more significant since the burden can be effectively reduced/ altered. This needs no further emphasis that such an approach would definitely positively modify an already burdened health care system. Adequate and thorough initial assessment of those referred cases of preterm labour may help us in both ways – immediate and optimum measures to ensure better perinatal and maternal outcome or to refer back/send home those patients who may be conservatively managed or kept under follow - up.

CONCLUSION

A cross sectional study was done among 260 antenatal women who were referred to SAT hospital as cases of preterm labour after 30 weeks of gestation over a period of 1 year. Of the total study subjects, 63.1% had preterm deliveries while 36.9% went on to deliver at or after 37 completed weeks. 40.4 % of the patients delivered immediately, 36.9% were managed conservatively and delivered at or after 37 weeks, 14.6% delivered at a later point but before 37 weeks and the rest 8.1% delivered at a later point but less at than 34 weeks. The perinatal mortality rate was 5.8%.

The need for triaging the patients also needs to be stressed here so that those in need of immediate and definite care may not be missed while those who can wait can be reassured, reassessed and sent home/wards which may provide relief for both the patients and caretakers as well as the health care personnels.

Considering their significant share in the infant and under 5 mortality, any measure to identify or prevent preterm birth and perinatal mortality has a pivotal role in bettering health care outcomes. They may also pave a better track in achieving the United Nations Sustainable Development Goal 3 target #3.2, aiming to end all preventable deaths of newborns and children aged under 5 by the year 2030[3].

RECOMMENDATIONS

1. In the above context, since periodontal disease is a risk factor, antenatal dental clinics may be established to prevent/alter the outcome of preterm birth/perinatal mortality.

2. In those patients at risk of preterm birth, favourable outcomes may be brought about progesterone supplementation for those indicated and timely administration of antenatal steroids.
3. Tobacco exposure – almost always passive smoking, has been identified as a risk factor for preterm birth as well as perinatal mortality. Hence community awareness programs on the harmful effects of tobacco exposure with emphasis on the need for its cessation may be conducted.
4. Future analytical studies may be undertaken to further establish the roles of the independent risk factors identified for preterm birth and perinatal mortality.

LIMITATIONS

1. The Covid – 19 pandemic may have altered the profile of antenatal patients seeking antenatal care in tertiary care centres.
2. The patient status before referral could only be ascertained from the referral letter and history divulged by the patient as original treatment records, laboratory and imaging reports were not available with some subjects.

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