"A ONE YEAR CROSS SECTIONAL STUDY OF PRETERM BIRTHS IN A TERTIARY CARE CENTRE IN SOUTH INDIA"

By

REG. NO. BJ0120006

Dissertation

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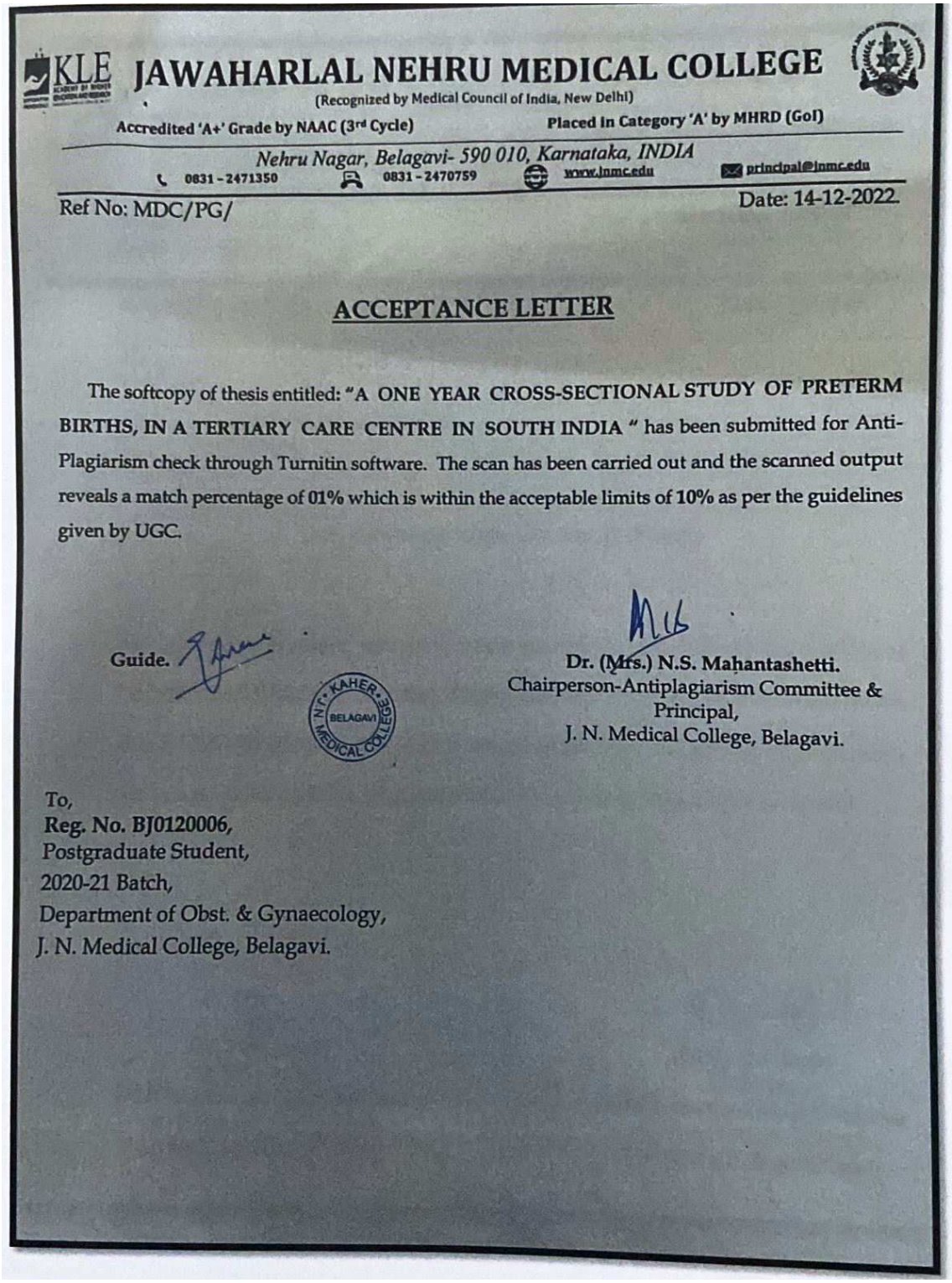

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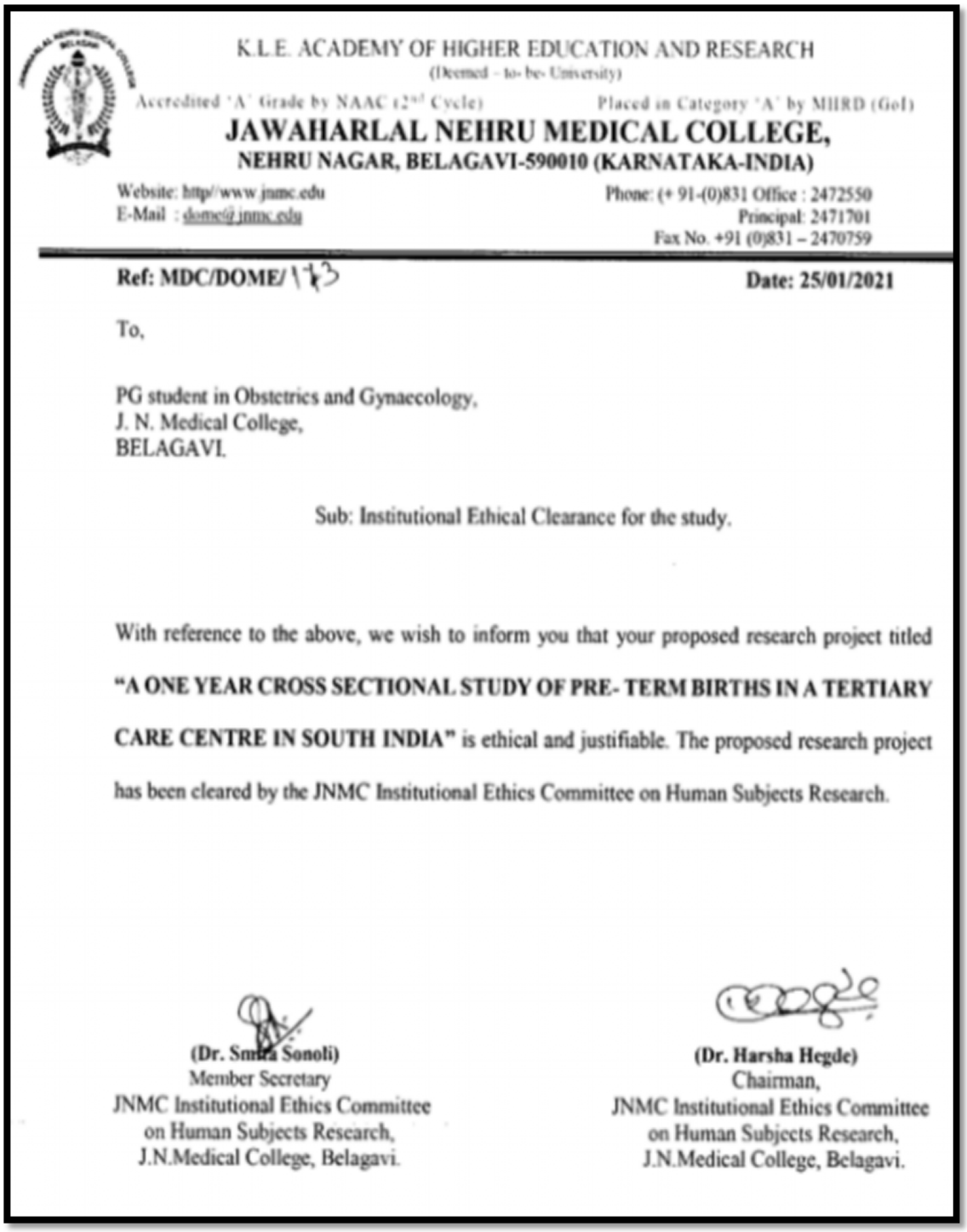

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To,

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Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"A ONE YEAR CROSS SECTIONAL STUDY OF PRE- TERM BIRTHS IN A TERTIARY CARE CENTRE IN SOUTH INDIA"** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

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LIST OF ABBREVIATIONS

ACOG	American College of Obstetrics and Gynaecology
AFI	Amniotic Fluid Index
ARDS	Acute Respiratory Distress Syndrome
Damps	Damage-Associated Molecular Patterns
DIC	Disseminated Intravascular Coagulation
FGR	Fetal Growth Restriction
GAA	Global Action Agenda
GDM	Gestational Diabetes Mellitus
HELLP	Hemolysis, Elevated Liver Enzymes, and Low Platelets count
IBP4	Insulin-like Growth Factor-Binding Protein 4
HIV	Human Immunodeficiency Virus
ICD	International Classification of Diseases
IMA	Indian Medical Association
KMC	Kangaroo Mother Care
LMIC	Low Middle Income Countries
LPS	Lipopolysaccharides
LTA	Lipoteichoic Acid
LSCS	Lower Segment Cesarean Section
LMP	Last Menstrual Period
MITS	Minimally Invasive Tissue Sampling
MNCH	Maternal, Newborn and Child Health
NEC	Necrotising enterocolitis
NICU	Neonatal Intensive Care Unit
Pamps	Pathogen-Associated Molecular Patterns

PGN	Peptidoglycan
PRR	Pattern Recognition Receptors
POG	Period of Gestation
RCOG	Royal College of Obstetrics and Gynaecology
PROM	Prelabour Rupture of membranes
PPROM	Preterm Prelabour Rupture of membranes
RDS	Respiratory distress syndrome
SCFA	Short Chain Fatty Acid
SHBG	Sex hormone binding globulin
TLR	Toll- Like Receptors
TVUS	Trans Vaginal Ultrasonography
USG	Ultrasonography
WHO	World Health Organisation

ABSTRACT

"A one year cross sectional study of preterm births in a tertiary care centre in South India"

Background*:* Preterm birth is defined as delivery before 37 completed weeks of gestation, or 259 days, from the commencement of the previous menstrual cycle. It is significantly linked with under 5 mortality, LSCS rates, morbidity over the long term, financial burden. This study is an effort to determine the incidence of total preterm births, including the incidence under the different categories, risk factors, and neonatal outcomes of preterm deliveries in our study setting, taking into account the increased incidence of preterm delivery in India, as highlighted by WHO and the previous studies conducted in our hospital settings.

Methods: It is a prospective observational study conducted in KAHER'S Dr Prabhakar Kore charitable hospital over a period of 12 months in women who delivered in less than 37 weeks of pregnancy in the Labour Room as per inclusion and exclusion criteria. Maternal and perinatal outcome were studied.

Results: In this study, the incidence of preterm births was 17.67%, majority – 79.93% of them falling in the moderate to late preterm category. Around 56% of the preterm births were iatrogenic preterm births in our study. 39.6% of the participants had maternal medical risk factor. The most common maternal medical risk factor was Hypothyroidism. While significant obstetric risk factors included PPROM (26.02%), Pre-eclampsia (10.2%), fetal risk factors such as FGR contributed to 22.10%. 15.64% of the neonates were still born. FGR contributed to 34.27% of iatrogenic preterm births. 61% of the patients in the study received atleast a single dose of steroid. The

most common mode of delivery was by LSCS (65.99%) out of which Previous one or more LSCS was the most common indication for LSCS. Mean birth weight was 1.9 kg. 298 babies were admitted to NICU for complications or observation. 84% of the neonates were stable at the time of discharge.

Conclusions: The incidence of total preterm births is 17.67%. Moderate to late preterm and iatrogenic preterm births contributed maximum to the overall preterm birth rates. The commonest mode of delivery was Emergency LSCS. Approximately a quarter of preterm births have contributed to perinatal mortality. Thus, early detection of medical risk factors in the mothers and pre-conceptional control of diseases like Hypothyroidism, Hypertension, Type 2 Diabetes Mellitus is recommended for prevention of preterm births and to achieve better maternal and neonatal outcomes.

Further research should focus on reducing the iatrogenic preterm

Key words: Preterm Births, Maternal, Fetal, Outcome

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INTRODUCTION

Preterm birth is defined as delivery before 37 completed weeks of gestation, or 259 days, from the commencement of the previous menstrual cycle. It is divided into three categories: extremely preterm (less than 28 weeks), very preterm (between 28 and 32 weeks), and moderate to late preterm (between 32 and 36 weeks plus 6 days) [1]. According to the WHO, the expected rate of live preterm births worldwide in 2014 was 14 84 million (12 65 million-16 73 million), or 10 % (confidence interval 9 0-12 0). 12,000,000 (81%) of these preterm births are concentrated over sub-Saharan Africa and Asia. Bangladesh had the highest projected national rate for 2022 at 19% (UI 13-26-2).

India, China, Nigeria, Bangladesh, and Indonesia, the top five countries for preterm births, are expected to account for 5,79,45,623 (41%) of 13,99,45,950 livebirths and 66,22,621 (44%) of 1,48,35,606 preterm births globally in 2022 [2]. Preterm births account for over 80% of all births, with South-East Asia and sub-Saharan Africa having the highest rates. In KLE, Dr. Prabhakar Kore Hospital, Belagavi, Karnataka, the prevalence of LSCS was 44.61%, according to earlier studies, of which preterm contributed up to 4.4%, which was a statically important contributor to the overall LSCS rates [3].

The preterm newborns do survive, but they also have to deal with problems that have an impact on their family and healthcare facilities. In low- and middle-income nations, where misinterpretations cause delays in care and prevention, more attention is required [1]. Preterm birth increases the risk of dying from other causes, especially neonatal infections, in addition to carrying the burden of several developmental complications like motor and behavioral disturbances leading to

impairment in academic performances, and be the leading direct cause of neonatal deaths [4,5]. In 2022, it will be the biggest global cause of mortality for children under the age of five, according to WHO. There are 2.6 million newborn fatalities each year, of which nearly a third are due to premature births [6].

Pre-eclampsia, inadequate spacing between births, gestational diabetes mellitus, polyhydramnios, multiple pregnancies, maternal infections, foetal deformities, and chromosomal abnormalities are among the most frequent risk factors [7,8]. A substantial sum of money has been spent on the birth and care of foetuses who are delivered prematurely, and the cost is negatively correlated with the gestational weeks [9]. Extreme and very preterm newborns have been linked to severe neurodevelopmental problems [10]. Preterm is regarded as the single biggest condition leading to the high mortality and permanent damage, per the WHO's 2008 Global Burden of Disease analysis.

Previous studies conducted in our hospital settings have highlighted that preterm birth is contributing significantly to our overall Cesarean Section rates and still birth [9,11]. This study is an effort to determine the incidence of total preterm births, including the incidence under the different categories, risk factors, and neonatal outcomes of preterm deliveries in our study setting, taking into account the increased incidence of preterm delivery in India, as highlighted by WHO and the previous studies conducted in our hospital settings.

OBJECTIVES

PRIMARY OBJECTIVE

- To find out the incidence of total preterm births and incidence in different categories of preterm.

SECONDARY OBJECTIVES

- To assess the risk factors leading to preterm delivery.
- To assess the mode of delivery in preterm birth.
- To know the neonatal outcome in preterm deliveries.

REVIEW OF LITERATURE

Background and Incidence

Preterm delivery is a leading global health problem remarkably contributed to neonatal mortality and morbidity with high healthcare costs. In 1967, J Yerushalmy [12] had suggested a classification for newborn according to Birth weight and the Gestational age at birth.

For a number of nations, a systemic analysis through 1990 to 2010 was done. According to the study's findings, there are 1,65,800 extremely preterm births each year, roughly 80,700 preterm survivors, 3,61,600 preterm fatalities, and 3,65,800 preterm births (babies delivered at less than 28 weeks).

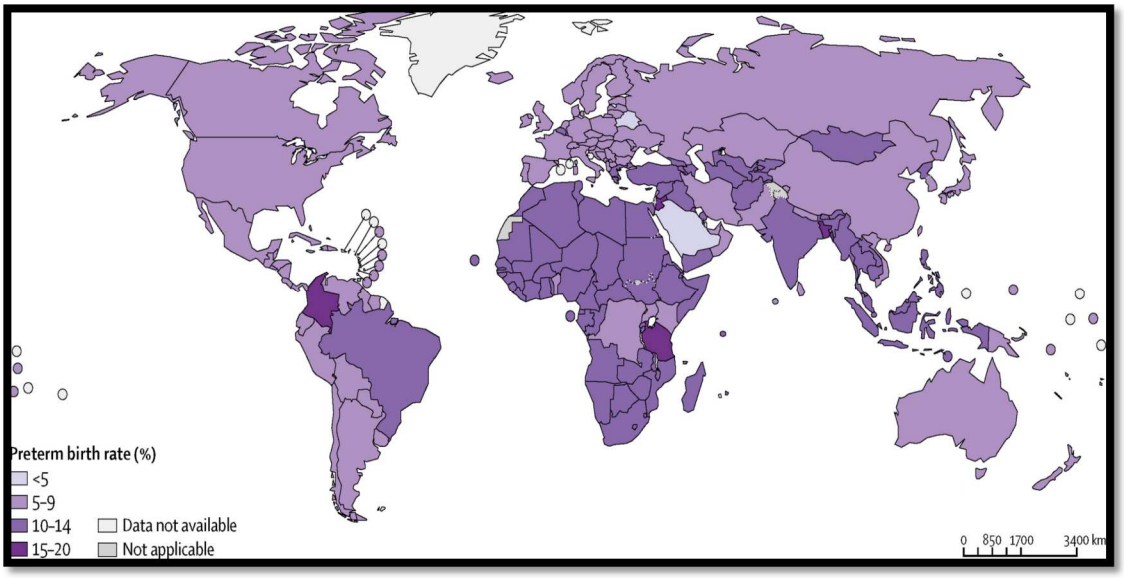
An epidemiology report published by Janet Tucker in 2004 states that for the past 20-30 years the incidence of preterm birth has been 5-7% in most developed countries.

In the United States the rate of preterm birth increased in the late 20th century form 9.5% in 198 to 12.8% in 2006. By the year 2014 there was decline in rate of 9.57%. However, again there was a slight increase in the rate of preterm birth rate as 9.62% in 2015. Furthermore, most of the preterm deliveries were in the late preterm subgroup increasing up to 25% from 1990(7.3%) to 2005(9.1%) [13]. According to a study done in India in May 2019, the prevalence of preterm is estimated to be around 35,19,100 in 2019 - 13% (10-15%);

The predominant risk factors of preterm birth involves increased births among women >34 years, births as a result of assisted reproductive therapy and induction of

ovulation for multiple births. At the same time due to substantial improvements in neonatal care for the past 5 years the survival of preterm babies have increased (Lumley et al., 2013) [14].

Premature births are more common in multiple foetal gestations than in single births. Each year, there are a few more single preterm births. Preterm birth rates were much lower among live births than among all births. Furthermore, countries with low Human Development Index countries had significantly higher rates of stillbirths among preterm deliveries in 2017 [15]. 2.97% of stillbirths with a stillbirth rate of 29.71/1000 were seen in pregnant women who had stillbirths after 20 weeks of gestation in a prospective observational research. The significant risk factors of stillbirths include preterm delivery, congenital malformation, anemia, oligohydraminos, abruption, and hypertensive disorder. Anemia and prematurity show the highest prevalence with stillbirth. The study concluded the need for specialized antenatal care for pregnant women to manage the risk factors of stillbirths (2021) [16]. Recently, a retrospective case-control study at Telangana in a rural tertiary teaching hospital study showed a 10.86% prevalence of preterm birth. Overall, the rate of premature babies keep rising, especially due to the large number of multiple births in recent years.



Estimated preterm deliveries in 2022

Dating of pregnancy

Accurate assessment of gestational age is essential for the calculation and categorization. The most commonly used and reliable methods are: This also ensures obstetric intervention and treatment provision timely and reduces the complications of pregnancy and preterm. Pregnancy dating precisely helps to diagnose preterm labor and delivery.

The commonly used method and one of the earliest known ones for estimating the duration of pregnancy is calculating from last menstrual period (1967, J Yerushalmy) [12]. Another method was calculating from the date of quickening – a study done in 1970 by Rawlings et al., found that 2 inaccurate methods can be combined to get a more reliable expected delivery date or period of gestation [17]. Methods were later devised to hear the first Fetal Heart Sounds (Hertz et al.,1978) [18].

With the advent of Ultrasonography, the accuracy of calculation of the gestational age had improved. Biovicelli et al., in 1981 opined that use of USG with

first trimester CRL and BPD showed promising results [19]. Since clinical methods were all based on menstrual cycle regularity and correct memory of the last menstrual period, they are unreliable (Michael Kramer et al., 1988) [20]. Clinical estimation can be used, but may not always be reliable due to Multifetal gestations, Fetal growth restriction, uterine anomalies and diseases and maternal obesity.

Thus, Hadlock et al, in 1991, studied and opined the standard ultrasound of fetal biometric measurements at 14 to 20 weeks and after 20 weeks of gestation will give an accurate gestation age [21].

Currently, the gold standard method for estimating the duration is by measuring the fetal crown-rump length at the first trimester.

(1) Calculating the date of delivery expected from the last reliable menstrual period (LMP).
(2) Ultrasound parameters – First and Second trimester

A study done by Jehan et al., in Pakistan in 2010 state that the symphysio - fundal height examination in late pregnancy after 20 weeks gives an estimation of gestational age similar to that of calculated by last menstrual period [22] but is not always reliable. Along with standard biometry measurements, Adeyukun et al., in 2014 have found that the cerebellum and femur length assessment will also provide an accurate gestational age estimation [23].

There is an overestimation of duration in high income settings and extended in low-and-middle income countries, as was studied by Savitz et al., and Fulcher et al., in 2001 and 2021 [24,25]. However, standard guidelines for Ultrasound practices (2016)

state that ultrasound is not available universally especially in low-and-middle income countries which result late present of the pregnant women for antenatal care [26].

Definition of preterm birth

Gruenwarld was one of the firsts to suggest in 1950, that babies called pre-mature in terms of birth weight were infact Intra-uterine Growth retarded term infants [27]. Thus, it was important to provide a universal standard for analysis of prematurity and preterm. **WHO, in 1969**, came up with the definition of preterm based on Gestational age of less than 37 weeks rather than the weight of the babies. It is defined as the delivery of the baby prior completion of 37 weeks of gestation or 259 days from the last recorded Menstrual Period – (WHO 1977) [12]. This is widely accepted and is currently in use.

The location of a premature baby's delivery (less than or equal to 27 weeks gestation) may affect the classification and, consequently, the perinatal mortality statistics. Additionally, the fact that the burden of classification and viability assessment is frequently placed on inexperienced staff, which may have an impact on the perinatal mortality statistics. It would be beneficial to implement a uniform recording system for all neonates weighing more than 500 gms, as suggested by WHO in 1977. International Classification of Diseases, in 1991, had included all live births under preterm but there is no fixed lower boundary implemented. Due to high rates of misclassification of live and stillbirth worldwide, there is no official lower margin of the gestational age specified [29].

Global definition includes stillbirth as births >1000 gms or over 28 weeks POG (Counsens et al., 2011 and Lawn et al., 2011). Chiefly attributed to the limited

accuracy of gestational age calculation, 37 weeks is considered the upper limit – as a standard. [30]

Different facilities and countries have a different lower limit set – varies from 20 weeks to 28 weeks – chiefly dependent on the support for neonatal resuscitation.

Threatened preterm labour refers to regular uterine contractions without the progression of cervical dilatation and cervical ripening occurring before 37 weeks of pregnancy - this may result in preterm birth.

Classification of preterm birth

For the ease of obstetric management and expected outcomes, there is a need for classification of the preterm. One of the earliest known classifications was done in 1967 by Yerushalmy et al., [12] where the Birth weight and Gestation were taken into account and were classified into Groups I to V. However, some infants with the same birthweight and longer gestational age were found to have lesser morbidity (Ghosh et al., 1967) [18].

The World Health Organisation in 1970 [31], has classified the live births into 4 groups.

Group I	< 20 weeks gestation
Group II	20 completed weeks but less than 28 weeks
Group III	28 completed weeks of gestation and over
Group IV	Not classifiable

This was for the ease of classification of the fetal death. The increase in preterm birth rates in Canada from 1992 to 1994 can be attributed to changes in the incidence of multiple gestations, ultrasound-based estimations of gestational age, and obstetrical intervention patterns.

Preterm birth rate was 6.8% from 1992 to 1994 and multiple births was 2.1% which was comparatively higher than the previous study conducted from 1981 to 1983. Upon adjusting the possibilities of the determinants, rate of preterm birth was reduced to 3% of all live births [32].

The prevalence in selected countries from a period of 1990 to 2010 was published in 2010 by Blencowe et al., and nearly 80-85% of the premature babies are moderate or late preterm groups (32 and 37 weeks of gestation). At the same time 5 and 10% of babies born at <28 weeks and between 28 to <32 weeks of gestation resulted in high fetal mortality particularly in low and middle income countries [33].

ACOG (2006) has classified preterm into different subcategories

- Extremely preterm with <28 weeks of gestation
- Very preterm between 28 to <32 weeks of gestation and
- Moderately preterm from 32 to < 34 weeks of gestation
- Late preterm from 34 to < 37 completed weeks of gestation

According to **WHO in 2013**, on the basis of gestational period, preterm delivery is classified into three different groups as

- Extremely preterm with <28 weeks of gestation
- Very preterm between 28 to <32 weeks of gestation and

- Moderately or late preterm from 32 to < 37 completed weeks of gestation[34,35].
- Moderate preterm can further be classified as late preterm – 34 to <37 completed weeks. [36]

This is the classification currently in use and is also applied in the current study.

Subtypes of preterm delivery

Preterm delivery is defined by two subtypes based on their cause as iatrogenic or spontaneous delivery.

Iatrogenic delivery – also called provider initiated delivery - referred by induction of labor or caesarean before 37 completed weeks of gestation accounting for almost 20% of preterm delivery cases. Both 'urgent' or 'discretionary' cases are included. [37]

Spontaneous preterm delivery occurs with the spontaneous onset of preterm labor causing cervical ripening and uterine contraction. This accounts for 50% of preterm delivery, in addition 30% of preterm delivery occurs due to premature rupture of fetal membrane [38].

Spontaneous preterm is a multiple – step requiring process, contributed by a plethora of factors.

One of the studies done in 1995 by Meis P.J. et al., postulated that spontaneous preterm were concerned due to various causes such as early pregnancy bleeding, maternal factors like low weight, young age, smoking and previous abortion. Whereas indicated preterm births were correlated to previous stillbirth, low weight

and older age [39]. The major reason for this type is either due to fetal or maternal complications like pre-eclampsia or intrauterine growth retardation [40].

Medically indicated preterm birth accounts for nearly 40% of overall preterm births. Surprisingly, a study done in 2006 by Ananth et al, shows that apart from the spontaneous preterm birth, medically indicated preterm birth is also correlated with the increased recurrence of spontaneous preterm delivery [41]. An observational study on epidemiology of preterm birth by Goldenberg et al in 2008 reports the frequency of preterm birth as 12-13% in USA and 5-9% in other developed countries. The primary predictor of spontaneous birth includes increased cervical-vaginal fetal fibronectin and short cervical length. The major risk factors for spontaneous preterm includes black race, periodontal disease, low maternal body-mass index and history of previous preterm birth [42].

A document was recommended by the International Federation of Gynecology and Obstetrics in 2021 for reducing the rate of iatrogenic preterm delivery. They encourage the healthcare team to identify and take preventive measures for the endowment of iatrogenic preterm delivery. Multiple pregnancies would also be a significant cause of iatrogenic preterm birth. Hence they recommend that the health authorities maintain single embryo transfer policies. [43].

Risk factors assessment

It is multifactorial, mostly related to lifestyle factors - including nutrition, habits such as smoking. Social factors are taken into account, as a risk and also to help ensure appropriate care and treatment access. Studies show that there is increased risk of PTB when mothers are extremes of age, black or African ethnicity or a lower body

mass index (BMI). Domestic abuse is an evidence-based risk factor of PTB. Women with a previous history of spontaneous PTB or mid-trimester miscarriage, particularly when this occurs before 32 weeks, are also at high risk of PTB. Other risk factors which identify high-risk women who must receive further assessment of risks and specific care include women who have had a previous caesarean section at full cervical dilatation and women with congenital uterine abnormalities as evidenced from prior studies.

Almost 80% of the preterm births occur in low-and middle income countries with increased prevalence in South-East Asia and sub-Saharan Africa. The primary areas to be concerned during pregnancy for preterm birth includes

- Demographic details and history of the patient
- Dating pregnancy
- Diet during pregnancy
- Infections
- Alcohol, tobacco, and substance abuse

Low socioeconomic status, low antenatal weight, inadequate weight gain during the pregnancy, a prior preterm birth, a history of infertility problems, an induced abortion ending the preceding pregnancy, vaginal spotting or light bleeding during the pregnancy, a lack of leisure-time physical activity during the pregnancy, antepartum haemorrhage, abnormal placental implantation, and alcohol consumption were all associated with preterm birth. Obstetric, maternal, or foetal problems have been linked to nearly half of all preterm births. [44] (Jean-Marie et al., 2003).

A data analyses in six low and middle-income countries, namely the Democratic Republic of India, Pakistan, Congo, Guatemala, Kenya, and Zambia conducted in 2020 collected the data of all the pregnant women during delivery and followed up after 42 days of delivery. Among 272,192 live births, 12.6% of the overall preterm birth rate. Low birth weight was found to be overall 13.6%. The correlated risk factors for preterm birth and low birth weight includes antenatal hemorrhage, nulliparity, hypertensive disorders, and maternal age below 20. All these factors were found to be analogous across the sites [45].

Demographic and Genetic characteristics

Preterm birth is associated with demographic features of the women like young or old age, low body weight and ethnicity particularly black mothers. Women with poor gain of weight in pregnancy, lower BMI are at increased risk.

Eastman et al., in 1968 suggested that there was a linear relationship between the maternal weight gain during pregnancy and the weight of the baby [47]. Some early studies done in 1988 [46] by AD McDonald, took into consideration 11 non-occupational confounding factors, the frequency of low birth weight (less than or equal to 2500 g) and preterm birth (less than 37 weeks) in 22,761 single live births was examined in relation to maternal employment. In all types of prematurity, there was a small but statistically significant increase in both the service and manufacturing sectors of the economy. Women working in the hospitality industry, psychiatric nursing, food and beverage service, chambermaids and cleaners, the production of metal and electrical, and some other occupations all had a significant excess of preterm births [48].

Nulliparous women below 18 years are at highest risk of preterm birth (Kozuki et al., 2013) [49]. Extremes in maternal age defining women over 40 years, and between 13-19 years have an increased risk of preterm and extremely preterm delivery (Marvin et al., 2018; Fuchs et al., 2018) [50] [51].

Preterm birth is four times more likely to occur in Black women in the United States than in White women. According to Donovan et al. (2016) [53, 52], societal issues like domestic violence have an impact on both the prevalence of low birth weight and preterm birth rates. According to a study comparing singleton preterm delivery rates from 2014 to 2019 and from 2019 to 2020, the rate of preterm birth grew from 2014 to 2019 (8.47%), whereas the rate of preterm birth decreased by less than 1% from 2019 to 2020. (8.42). The non-Hispanic white preterm maternity rates fell by 1%, but the rates for non-Hispanic black, non-Hispanic hispanic, non-Hispanic american indian, and non-Hispanic Alaskan mothers did not change much. The singleton preterm birth rate rose in two states in 2019 and 2020 while falling in four states [54].

An observational study in 2022 in Odisha, India investigated the socio-demographic characteristics and etiological factors accompanying preterm birth. The study revealed a 5.52% incidence of preterm birth in the study population [55]. The majority of the women belonged to lower socioeconomic strata and rural backgrounds.

The mechanisms by which the maternal demographic characteristics are related to preterm birth are unknown. Whether differences in demographic, social, or economic risks, frequent absence of health insurance, and absence of a strong supportive economic and social safety net contribute to the disparity in preterm birth rates between the USA and other developed countries is unknown [56]. Although the cytokines appear to be the final common mechanism leading to premature labour, the

aberrant inflammatory response to infection that causes preterm labour is likely hereditary or genetic, since the response to the same pathogen differs in different persons.

Psycho-social factors

Psychological aspect of pregnant women has a major impact on preterm birth. Women in preterm labour have been shown to experience higher levels of maternal stress (Newton et al. 1979). It is likely that single teenagers would encounter more stressful life events than married women, according to research done by these researchers using a modified version of the Life Events Inventory. [57].

Stress can affect immunological response, which increases vulnerability to inflammation or infection within the womb (Wadhwa et al., 2001). In addition, stress can lead to high-risk activities as a coping mechanism (Whitehead et al., 2003) [58].

The primary psychological factors affected includes pregnancy-related anxiety, life events depicting in the negative impact weight and incisiveness on race, according to Dole et al, 2003 [59]. Domestic violence and abuse also played a contributory role as per Hogue et al., in 2005 [60].

Preterm uterine contractions can be triggered by PGs generated during coitus and from those found in the seminal fluid. When the pregnancy was unplanned and unwanted, poor antenatal care, nutrition may lead to preterm birth. Increased levels of catecholamines and cortisol can be released during times of maternal stress, which may induce the placental corticotropin-releasing hormone to activate early. This could trigger preterm labour. [58]

Alcohol, tobacco and substance abuse

Meyer (1977) conducted a thorough examination of the effects of smoking during pregnancy. According to her analysis, smoking increases the probability of delivering at an earlier gestational age and the hazards were correlated with daily cigarette consumption. These might be connected to hypoxia in the mother and foetus brought on by carboxyhemoglobin [61] .

Use of alcohol, tobacco, and other psychoactive substances during pregnancy increases the risk of birth abnormalities like preterm birth, stillbirth, low birth weight, spontaneous abortion, and other health issues for both the mother and the unborn child. In conclusion, Quesada et al., in 2012, stated that combining the use of these drugs with additional psychosocial risk factors raises the likelihood of unfavorable outcomes across all contexts [62].

Similarly, a meta-analysis done in India in 2016 showed that pregnancy-related substance use disorders are a serious public health issue. Tobacco, alcohol, cannabis, opiates, and cocaine are the most commonly utilized substances during pregnancy worldwide, but other illegal substances may also be used [63].

Past History of preterm birth

Kaltreider and Johnson in 1976, indicated that the incidence of Preterm Low birth weight had an impact on the subsequent pregnancies being Preterm [64]. Earlier studies (Hoffman et al.., 1984 and Mercer et al., 1999) have reiterated that a previous history of preterm birth has 15-50% of recurrence risk. Similarly, Edlow et al., in 2007 stated that the history of preterm twin pregnancy has 57% recurrence; mid-

trimester miscarriage; singleton preterm birth has 10% absolute recurrence risk after a previous history of term twin [65-67].

Previous history of premature rupture of membranes, a prior stillbirth, interpregnancy interval <6 months and caesarean section delivery at full cervical dilatation increases the risk of preterm delivery according to Lee, T., et al., 2003 Getahun, D., et al., 2009; Smith, G.C. et al., 2003 [68-70]. Past history of multiple pregnancy accounts for 15-20% of all preterm births. Several other factors include past history of cervical surgery, cold knife conisation and large loop excision of transformation zone [71-73].

Diet during pregnancy

Nutrient deficiencies and both high and low BMI can have an impact on PTB risk as well as overall pregnancy outcomes.

Some of the earliest studies conducted in 1992 by Michelle A Williams et al., stated that in comparison to women who drank two or fewer cups of coffee, those who drank three or more cups daily during the first trimester had a 2.2-fold higher risk of preterm PROM (95% Cl 1.5-3.3). There was limited evidence of a linear relationship in the risk of preterm PROM among coffee consumers as coffee consumption increased. Three or more than three cups per day were not as substantially linked to the development of preterm NONPROM. However, there was no correlation between daily cigarette consumption and the incidence of preterm PROM. Similar outcomes for premature NONPROM were noted. Pregnant women in LMICs may face difficulties accessing a balanced diet. In general, prenatal vitamins

like iron and folic acid and calcium are essential, and they may also reduce the incidence of PTB in specific situations [73-77].

Some studies on micronutrient deficiencies were done in 2005 spanning to 2020. Additional nutritional deficiencies, such as a zinc deficiency, have been linked to PTB outcomes with low certainty, but the usefulness of routine supplementation over and above a balanced diet is debatable. Nevertheless, supplementation may be beneficial in certain Low and Middle Income countries with low dietary zinc intake [73].

Infections

Maternal infection, either intrauterine or extrauterine, may predispose to preterm labour – especially spontaneous preterm type (Naeye & Peters 1978) [57]. An important amount of idiopathic preterm labour is related to infection, which may help with premature birth prediction and prevention (Lamont et al., 1980) [78].

Several studies from 2001 to 2007 state that bacteria and viruses are recognized by Toll-Like Receptors and activate the immune system, activating NF-κB and other pro-inflammatory factors, resulting in release of cytokines, chemokines, prostaglandins, proteases [79-82]. These result in contractions, cervical ripening, detachment of placenta, rupture of membranes.

Numerous pathogenic mechanisms are active when there is an ascending urogenital infection, and these mechanisms may cause premature labour to start [83,84]. Proteases are produced by a number of organisms, including the bacteroides species and Group B streptococcus (GBS), which may weaken the chorioamniotic membrane. Additionally, GBS and E. coli lower the in vitro bursting pressure of membranes.

High levels of phospholipase A2 are produced by Gardnerella vaginalis, anaerobic streptococci, and Bacteroides species. A precursor of prostaglandins, phospholipase A2 may contribute to the start of uterine activity. Several pathogens have been investigated for their potential role in the aetiology of preterm labour, including the hemolytic streptococcus (Group B), ureaplasma urealyticum, mycoplasma hominis, Chlamydia trachomatis, trichomonas vaginalis, and Neisseria gonorrhoeae, but none have been proven to be causal. [85,86]

The bio-creation of short-chain fatty acids (SCFAs) or alcohol from fermenting sugars or fibres is the first fundamental process that contributes to the formation of microbial PBM, and the bio-conversion of derivative molecules is the second (Tan et al., 2014 and Martinez et al., 2017) [87,88] Pathogen-associated molecular patterns (PAMPs) are produced by pathogenic bacteria, such as peptidoglycan (PGN), lipopolysaccharides (LPS), and lipoteichoic acid (LTA), whereas damage-associated molecular patterns (DAMPs) are produced by dietary components. Thus, Kawasaki et al., in 2014 postulated that infection and inflammation trigger the production of these PAMPs and DAMPs [89].

Through the use of pattern-recognition receptors that are programmed in the germline, the innate immune system can detect these two microbe-specific chemical signatures (PRRs).

Toll-like receptors (TLRs), among the primary PRR families in the mammalian system, were the first to be discovered and are the most thoroughly studied molecules. The activation of transcription factors NF-B and IRFs or MAP kinases to control the expression of pro-inflammatory cytokines, chemokines, and type I IFNs results from the recruitment of Toll/IL1 receptor (IL1R) domain-

containing adaptor proteins by TLRs after they recognise PAMPs and DAMPs. These proteins include MyD88 and TRIF. These occurrences control how innate immune reactions shield the host from microbial infections (Tan et al., 2014 and Martinez et al., 2017) [87,88]. Group – B Streptococci have been identified as one of the contributors (Nancy et al., 2022) [90].

Recently, in 2022 Weinberg et al., studied the incidence of preterm among the SARS-Cov-2 infected mothers have concluded that Covid is one of the important contributors of spontaneous preterm births – especially in the moderate preterm category [91]. A significant causative role in the aetiology of PPROM and the accompanying maternal and newborn morbidity has been identified as subclinical intrauterine infection.

Congenital uterine anomalies and cervical changes

The female progeny of women who had taken DES Diethylstilboestrol showed an increased risk of Uterine Anomalies [92]. Loop Excision Surgery, Cone Biopsy, Laser cervical ablation, Trachelectomy prior cervical manipulation of any kind have been strongly associated with preterm birth. [93,94,95]. There is a higher chance of cervical insufficiency if there have been two or more prior dilatation and evacuations, especially for late pregnancy termination [96].

Obstetric Risk factors

- **Ante-partum Hemorrhage**: Hemorrhage occurring in the antepartum period in the form of Placenta previa, abruptio placenta are one of the most important causes of preterm deliveries – both spontaneous and iatrogenic. According to Meyer (1977), smoking increases the probability of delivering

at an earlier gestational age where the placentas are smaller, placenta previa is more common and there are chances of abruption [61]. One of the studies conducted in 1989 by James H Harger et al., opined that preterm labour was significantly correlated with third-trimester haemorrhage [97]

- **Preterm Premature Rupture of Membranes**: If chorioamnionitis, vaginal haemorrhage early in pregnancy, or a urinary tract infection were present in a case that had preterm labour following premature rupture of membranes, the chance of preterm labour increased significantly (1989, James H Harger et al.,) [97-100].
- **Cervical Incompetence:** Risk assessment for preterm birth is still challenging, especially for women without a history of preterm birth. According to a study in 1986 [101] by Thomas et al., the relative risk of preterm labour increased if the cervix was dilated by more than 1 cm or effaced by more than 30%. According to Frank H. et al., in 1990, preterm deliveries were diagnosed in 76% of cases when the endovaginal ultrasonographic cervical measurement was 39 mm or lesser, which was linked to a significantly higher chance of delivery (25.0% versus 6.7%). 71% of preterm births were discovered with manual cervical effacement examination [48]. Cervical shortening, which can be seen even weeks before the start of active labour, is one of the early changes that accompany sPTB (Robert L Goldenberg et al., 1996) and cervical incompetence was common especially at 24-28 weeks [102, 103]
- **Pregnancy Induced Hypertension:** The preterm birth prevalence among the study population by Anto et al in Ghana in 2022 was 37.3%. Preeclampsia and HELLP (hemolysis, elevated liver enzymes, and low platelet count) among other factors are found to be most significant. The study concludes that early detection

of signs of adverse pregnancy outcomes can prevent a higher prevalence of preterm births [104].

- **Multiple Pregnancies:** There is a strong association between Multifetal pregnancy and preterm delivery. This is attributed to uterine overdistension. (Crowther et al., 1987) [64]. Increasing levels of CX-43 expression in response to mechanical strain have been seen in in vivo investigations, suggesting that mechanical and endocrine signals interact during myometrial activation (Ou et al., 1998). A study done in 2004 by Kurdi et al., was 7 times greater than singletons. Almost half of the deliveries were through Cesarean section. Children born as multifetal gestation may suffer complications including cerebral palsy and hearing disabilities [105]. There is a lack of knowledge on the methods by which uterine overdistension could cause preterm labour. Gap junction proteins including CX-43 and CX-26, as well as other contraction-associated proteins such oxytocin receptors, are expressed during uterine stretch (Ou et al., 1997) (Terzidoo et al., 2005).
- In vitro stretching of myometrial strips also results in an increase in PGHS-2 and PGE (Sooranna et al., 2004). Stretching the lower uterine segment's muscles has been shown to boost IL-8 and collagenase synthesis, which encourages cervical ripening (Loudon et al., 2004; Maradny et al., 1996). Uterine stretch seems to activate the MAPK pathway, increasing the expression of PGHS-2 and Interleukins in the myometrium (Sooranna et al., 2005). In 2018, Murray et al. confirmed that multiple pregnancies are also more likely to experience a high number of obstetric problems [106].
- **Oligohydramnios:** Reduced AFI between 24 and 34 weeks of pregnancy, including borderline AFI and oligohydramnios, was considerably more likely to

be linked to major foetal abnormalities and, in the absence of deformities, to be compounded by foetal growth restriction and preterm birth (Petrozella et al., 2011) [107]

- According to an observational research in Odisha, India, done in 2022, the most common unfavourable pregnancy disorders, particularly in the Eastern Indian population, were anaemia, eclampsia, preeclampsia, preterm rupture of membranes, and fetal growth restriction [55].

Maternal Medical Risk factors

- **Overt Diabetes:** A clear potential risk for preterm birth is overt diabetes. From the Norwegian Medical Birth Registry, Eidem and colleagues (2011) examined 1307 newborns in women who had pregestational type 1 diabetes. Compared to 6.8% of the overall obstetric population, more than 26% of births were preterm. Additionally, almost 60% of those births were induced preterm. [108].
- **HIV and HAART:** The association of HIV and HAART with preterm was studied in 2012 by Lopez M et al,. has demonstrated that early HIV detection and treatment minimize mother-to-child transmission as well as horizontal transfer to unaffected sexual partners (Lopez et al., 2012) [109]. Similarly, study at Gondar town health institutions in Northwest Ethiopia, in 2016, reports that the study participants had 4.4% of preterm births. The substantial cause and factors corresponding the preterm births mainly involve hypertension induced by pregnancy and HIV-positive pregnancy (Gebreslasie et al., 2016) [110].
- **Anemia:** A case-control study in tertiary care in 2021 reported independent risk factors for preterm delivery, especially in the South Indian population anemia and

other systemic diseases were one among the important factors (Sureshbabu et al., 2021) [111].

- **Maternal Connective Tissue Disorders:** Approximately 40 and 50% of preterm birth is caused by several maternal infections. Compared to high-income settings, LMIC settings are found to have higher incidence of maternal bacterial and viral illnesses (Nadeau et al., 2016) [112]. Preterm birth has been linked to connective tissue disorders such as Ehlers-Danlos syndrome and Marfan syndrome. Disorganised collagen fibrils in the cervix inturn lead to cervical incompetence (Vyas et al., 2006 ; Anum et al., 2009) [95,113].

Fetal risk factors

Intra uterine Growth restriction, Unstable fetal conditions, Fetal anomalies, Multifetal gestations are some of the known causes of preterm delivery – spontaneous and iatrogenic. (Jean-Marie et al., 2003) [44]

Diagnosis

The diagnosis for preterm birth is not predefined as there is no specific screening method available to identify the women at risk. Due to the lack of diagnostic evidence, a significant challenge arises to prevent high-cost treatment and inessential interventions (Krupa et al., 2006) [114].

As existing clinical practice measures, cervical length remains the best, most cost-effective method. [194] Ultrasound and other markers like fetal fibronectin, interleukin-6, placental alpha-macroglobulin-1, and insulin-like growth factor binding protein are also used for diagnosis (Oskovi et al., 2018) [115].

Predictors

Cervical Length

Regardless of parity or obstetric history, endovaginal ultrasonographic cervical measurement predicted increased preterm birth risk. Thus, Frank H. et al., in 1990, predicted that one procedure that promises prediction of the likelihood of a preterm birth is endovaginal ultrasonography [48]. Cervical length screening by transvaginal ultrasound is a beneficial predictor for preterm birth risk. The cervical length measure of 25 mm at 24 gestational weeks has 37.3% sensitivity and 92.2% specificity risk for preterm birth. Shortening cervical length by <10% over three weeks increases the risk of preterm birth (1997) [116].

The gold standard, currently, for predicting spontaneous Pre Term Birth is mid-trimester transvaginal ultrasound (TVUS) cervical length (CL) evaluation (Skentou et al., 2006) [117]. As the predictive accuracy of first and early second-trimester CL testing for PTB is limited, especially in asymptomatic women without a history of PTB, it should not be regularly assessed before 16 weeks of gestation (Mella et al., 2009) [61].

For asymptomatic women with a history of PTB, the majority of clinical guidelines addressing this issue advise doing cervical length screening between 16 and 24 weeks of pregnancy (ACOG, 2012) [47].

The risk is negatively correlated with cervical length regardless of obstetric history (Melamend et al., 2013) [117], with women who have both a history of a PTB and a short cervix being at the highest risk.

The assessment of cervical length among women at risk of preterm labor reports that women with short cervical lengths are independently associated with preterm birth. The measure of cervical length ≤15 mm has 81% specificity and 83% positive predictive value for preterm labor [118].

Fetal fibronectin

A study conducted by Robert L Goldenberg et al., in 1996 concluded that fetal fibronecin was a significant predictor of preterm birth <32 weeks [102]. Fetal fibronection exists between chorion and decidua at the maternal-fetal interface. It is an extracellular matrix protein found at deficient levels of <50 ng/ml in cervicovaginal secretions during mid-pregnancy (Peaceman et al., 1997) [119].

Goldenberg et al., in 2001, conducted a preterm prediction study – and found that one of the most potent marker for preterm was cervical-vaginal fetal fibronectin test, along with other combined inflammatory markers[120]. Honest et al [121], in 2009 published a study, which showed a similar co-relation. The fetal fibronectin levels would increase at standard conditions during 22 and 35 weeks of gestation. Increased levels >50 ng/ml during 22 weeks of gestation intensify the risk for spontaneous preterm birth (Son et al., 2017) [122].

Inflammatory biomarkers.

The biomarkers have received more concern in screening for the identification of preterm birth. An inflammatory response specifically intervenes in the inflammatory and infection biomarkers (Coussons-Read, et al., 2012) [123].

The pro-inflammatory cytokines, namely tumor necrosis factor (TNF- α), interleukins (IL-6, 8, 1α), and C-reactive protein get stimulated upon infection at the maternal-fetal interface and release prostaglandins and metalloproteinase. They cause uterine contractility and cervical ripening for induction labor. Hence, these biomarkers are vital in screening for preterm birth (Bastek et al., 2013) [124].

Serum proteomics

The recent approach to proteomics has become one of the non-invasive testing methods for identifying women who are at risk of preterm birth. Along with this, for the best clinical practice, the authors analysed the predictor levels of maternal serum insulin-like growth factor-binding protein 4 (IBP4): sex hormone binding globulin (SHBG) in women with body mass index range >22 and ≤37 kg/m^2 at 19-20 weeks of gestation. This ratio helps to identify women who deliver less than 37 weeks (Glover et al., 2018) [125].

Use of biomarkers:

Along with serum alpha feto protein, Granulocyte colony stimulating factor and alkaline phosphatase along with cervical length will enhance the predictive value. (Goldenberg et al., in 2001) [120] .

Management of preterm

Preterm birth is frequently the unanticipated result of unforeseen maternal or foetal discomfort, even though pregnancy problems can manifest early in gestation. Modern obstetric practises and in-hospital antenatal care for high-risk pregnancies have improved preterm overall survival rate (Skrablin et al. 2002) [126]. Prenatal care, antenatal corticosteroids, and hospitalisation in a tertiary care facility with on-site

neonatal specialists are some of the factors that significantly reduce complications, but not all at-risk pregnant women have access to them (O'Shea 2008) [127] .

The ultimate aim in the management of preterm labor involves maintaining the pregnancy for at least up to 34 weeks.

Prevention of Preterm Labor

Despite significant improvement in the survival due to medical advancements, it is still believed that the long-term negative effects of preterm delivery cannot be mitigated (Tyson and Saigal 2005; Tommiska et al., 2007) [128]

However, recent births have started to get reports of more ideal outcomes. After 2000, the survival rates for extremely preterm babies have continued to rise, alo ng with varying reports of medical problems and related long-term morbidities.

However, morbidity was reduced for infants born at 22 to 27 weeks gestational age in 1999–2000 (Markestad et al. 2005), and in 1990- 2000 (O'Shea et al. 2002; Riley et al. 2008) [129,130].

Increasing survival rates has not always been correlated with a decrease in un favourable neurodevelopmental outcomes (Washburn et al. 2007). Young survivors have made improvement even if extremely preterm babies after 2000 haven't yet considerably changed the expectation of a bad result (Tyson and Saigal 2005; De Groote et al. 2007) [128] . It is still crucial to identify the factors that are most important for producing positive long-term outcomes. There are few documented standards, therefore judgments about when to vigorously revive the barely alive newborn are still center-specific and individual (Kaempf et al. 2006; Batton 2009). [131, 132]

Between 1988 and 2001, a multicenter cohort of newborns with extremely low birth weight who made it out of the NICU alive had 27% of their outcomes at 18 to 22 months unchanged (Gargus et al. 2009) [133] .

Progesterone and quitting smoking are the main preventative measures for premature deliveries. Eight common interventions, including caesarean sections for breech babies, immediate obstetric care, elective induction for post-term deliveries, insecticide-treated mosquito nets, malaria and syphilis treatment during pregnancy, a healthy diet and supplementation, and birth preparation, are suggested to prevent stillbirth.

Preterm labour preventive steroids, adequate resuscitation, an introduction antibiotic course, thermal care, and therapy for respiratory distress syndrome may all be necessary for improving the survival of preterm infants (Barros et al., 2010) [134].

Due to a lack of funding, a shortage of healthcare personnel with the necessary training, poor governance, societal limitations, and political instability, a number of obstacles were put in the way of implementing these treatments. Strong healthcare system support and wise strategy selection based on the right channels for high coverage and reach are required for intervention diversification. Scaling up has been suggested for a number of concerns, such as syphilis diagnosis and treatment, neonatal resuscitation, care for kangaroo mothers, and emergency caesarean sections. To achieve better results in preterm and stillbirth interventions and to prioritise the needs, a comprehensive framework should be established. Victoria and others [135].

With regard to cultural and moral views, the interventions based on these concerns must be better understood. Interventions should be made to balance the short

and long-term effects in order to address the ethical concerns, such as providing care to the preterm newborn despite prevention, choosing the best intervention to balance both maternal and newborn outcomes, and comprehending the cross-cultural context of preterm and stillbirth among women. As a result, offering therapies, financing for research, and support for preterm and stillbirth present ethical dilemmas (Kelley et al., 2010) [136].

The Global Action Agenda (GAA) lists specific objectives for preventing stillbirths and premature births. The GAA suggests the following themes: cutting-edge research on the cause, importance, and novel solutions; effective intervention at low cost; bringing awareness that preterm birth as well as stillbirth are a major burden on global health; increasing resource, funding for research and its enforcement; and taking into account ethical and social justice. All of these recommendations were created by stakeholders for the Global Action Agenda (Rubens et al., 2010) [137].

Megan et al. focused on the potential opportunities and barriers for raising worldwide knowledge of maternal, newborn, and child health (MNCH). The three main issues with preterm birth and stillbirth that were mentioned in the interview were as follows: inadequate knowledge and understanding, a lack of appropriate interventions, and a lack of information regarding the impact and relevance of the issue. As a result, promoting the inclusion of preterm and stillbirth in MNCH targets may help to minimise the negative effects (Sather et al., 2010) [138].

Some methods which are in use are listed below:

Cervical cerclage

Cervical cerclage is a surgical procedure in which a suture is made around the neck of the cervix in order to provide mechanical support and maintain the cervix closed during the pregnancy (M.S. yet al., 2004) [139].

Women with a previous history of frequent spontaneous mid-trimester losses or ultrasound revealing a short cervix can instinctively reduce the risk for preterm through the positioning of the cervix by mechanical support (Alfirevic et al., 2017) [140].

Progesterone

The progesterone hormone is naturally secreted in the body by the corpus luteum and placenta during pregnancy. It is secreted at a concentration of 10-40 ng/ml during the first trimester and 100-200 ng/ml towards the last trimester of the pregnancy (Dodd et al., 2008) [141].

The uterus continues to be in the quiescent stage during pregnancy due to the progesterone hormone. There is a consent that in women with a short cervix of <25 mm and no previous history of spontaneous preterm birth, the addition of progesterone proves to be efficacious in reducing the risk of preterm birth (Sykes et al., 2018) [142].

Antenatal corticosteroids

Liggins discovered that lambs born at gestations when the lungs should have been airless, had some expansion of the lungs while studying the effects of the steroid dexamethasone on preterm parturition in foetal sheep in 1969. The first human randomised controlled trial was published in 1972 by Liggins and Howie, and many more followed. [143]

The first ever Cochrane review comprising of 18 trials which evaluated the effects of corticosteroids to enhance fetal lung maturity before preterm delivery was in 1996 by Crowley et al., They had concluded that corticosteroids are effective in respiratory distress syndrome and neonatal mortality. However, sufficient evidences regarding the repeated doses of corticosteroids in women at risk of preterm were not studied [144].

Nearly 1-2% of the infants born before 32 weeks suffer from serious problems. Tucker et al., in 2004, postulated that the available perinatal care and interventions like exogenous surfactants and prophylactic antenatal steroids has improved the outcomes of preterm infants [145]

The majority of preterm babies die or have respiratory problems. In order to prevent the death and suffering of neonates from breathing problems in the early labor stage, women are treated with corticosteroids. The corticosteroids help in the maturation of the lungs; hence, they are given to women with spontaneous preterm labor or ruptured membranes according to Roberts et al, 2017 [146].

Preterm babies born early suffer from breathing difficulties and various health problems during birth and in the later stage of life. The babies born too early cannot

tolerate these difficulties and are unable to survive. While those neonates who survive face developmental difficulties like learning or movement (Briceno-Perez et al., 2019) [147].

Steroids used are commonly Betamethasone and Dexamethasone. In preterm labor both dexamethasone and betamethasone show similar effectiveness. It has been reported that dexamethasone shows a decreased incidence of intraventricular hemorrhage, while betamethasone improves neurological outcomes (Battarbee et al, 2020) [148].

The glucocorticoids prove to be effective in lung maturation and cause a significant impact on neonatal survival in women whose delivery is delayed at least 24 hours upon initiation of steroids (Gulsern et al, 2021) [149].

The prevailing regimen insists on one course of glucocorticoids, either two doses of 12mg each 24 hours apart of betamethasone or four doses 12^{th} hourly of 6 mg dexamethasone. According to the National Institute of Excellence (NICE) guidelines, a single dose of antenatal steroids to women between 34+0 and 36+6 weeks of gestation is recommended if the delivery is expected within seven days (Ciapponi et al, 2021) [150].

Some evidence shows that repeated administration of antenatal corticosteroids results in an increased incidence of cerebral palsy. An analysis of patients who received steroids as a complete course shows no differences in morbidity and mortality (Zahedi et al, 2022) [151].

Tocolytics

Tocolytic drugs recently used include beta-agonists and oxytocin, receptor antagonists. At present, prostaglandin synthetase inhibitors are not recommended. There is no substantial evidence available in comparison to the effectiveness of tocolytic drugs as well as persistent prescribing advice (Gyetvai, 1999) [152].

Though used, Tocolytics show no improvement in perinatal income; they are recommended to acquire time for the corticosteroids to act and shift the women to hospitals provided with NICU and intensive care units (Haas et al., 2012) [153].

Tocolytics are recommended at 22 to 33 weeks of gestation, with regular contractions being not less than 4 per 20 minutes. They are also indicated in conditions where changes in the cervix increase speed of dilation, shortening, and effacement (Berkman et al., 2003) [154].

Beta-agonists

The prevailing evidence suggests that using beta-agonists causes life-threatening risks such as hyperglycemia, hypotension, tachycardia, cardiac failure, myocardial ischemia, pulmonary edema, and death. Therefore, at favorable conditions under the monitoring of essential parameters, ritodrine and terbutaline were used during preterm labor (Lamont et al., 2019) [155].

Oxytocin receptor antagonists

Atosiban, an oxytocin receptor antagonist, suppresses vasopressin effects without affecting the cardiovascular system. Atosiban should be started immediately after the onset of labor and given in three stages. At first, the initial dose of the drug

should be given without dilution (1 vial of 0.9 ml, initial dose 6.75 for 1 minute). Next, the infusion of Atosiban 18 mg/hour should be given for 3 hours at a dose of 300 g/ min with a 24 ml/h rate of administration after the initial dose. Following this regimen, an Atosiban infusion of 6 mg/hour should be given for 45 hours at a dose of 100 g with a rate of administration at 8 ml/hour (Romero et al., 2000)[156].

These drugs can inhibit oxytocin receptors, reducing uterine contractility and myometrial tonus without any severe side effects .

These tocolytics are safe for both mother and fetus as they are helpful in outpatients and in transferring women to obstetrical units and provide intensive care to newborns (Papatsonis, 2005) [157].

Calcium channel blockers

Calcium channel blockers are used as a tocolytic as they are more effective than beta-agonists. Nifedipine, a calcium channel blocker, shows a better tocolytic effect than beta-adrenergic agonists with fewer side effects [158].

Nifedipine is given in three doses orally, 20 mg every 30 minutes. After initiation of the therapy, 20-40 mg is given sublingually every 4 hours for two days. During nifedipine therapy, continuous monitoring of the mother's heart rate and blood pressure every hour for the first 24 hours and fetal heart rate during uterine contractions is recommended [159].

Mode of delivery

For patients with Hypertensive disorders in preterm pregnancy, Everett et al., in 1994, concluded the prevalence of caesarean delivery was 76.2% (primary rate: 72.4%). 87% of pregnancies under 30 weeks' gestation were delivered via caesarean section, compared to 68% pregnancies under 30 weeks but more than 34 weeks gestation. The most common reasons for caesarean sections were failure to progress (11%), nonvertex foetal presentation (11.5%), and poor maternal status (50%). [160] A study done by Ment et al., in 1995 [161], stated that Cesarean rates helped in lowering the occurrence of Intraventricular Hemorrhage in preterm babies. Following the finding by Bejar et al. in 1999 [162] that preterm infants frequently experienced germinal matrix bleeding, which could progress to more serious intraventricular haemorrhage (IVH), there was speculation that caesarean delivery, which avoids the trauma of labour and delivery, could avoid these complications.

Studies done in 2007 in Sweden, also suggested that Cesarean Section lowered the complications of preterm. [163] The cohort study by Elina et al, 2021 shows that moderately and late preterm gestational age groups had no significant difference between the trial of labor and cesarean section groups. Among the women in the trial of labor, 85.4% of them delivered vaginally. Pregnant women who had planned for cesarean section had surgical complications and puerperal infection [164].

Cesarean section during preterm labour: The preterm foetus may suffer the most during labour and delivery than from the consequences of prematurity itself. Two fundamental findings—that preterm newborns survive hypoxia less well than infants at term, and that the stress of labour and the trauma of birth passage are

harmful to preterm infants—led to the concept that caesarean delivery was a safe alternative approach for delivering young infants.

The following factors have lead to an increase in the frequency of Cesarean sections, according to studies done from 1988 to 2021 [165-167]

As preterm babies are more susceptible to hypoxia, severe harm could be avoi ded by prompt action at the first indication of foetal distress.

- One of the major reasons of preterm labour is multiple pregnancies.
- Cesarean sections for twin deliveries have dramatically increased in frequency since the mid-1970s.
- When the first twin or both twins are mispresented in higher order pregnancie, a caesarean section is advised.
- A third of premature births are caused by placental haemorrhages and hyperte nsive disorders, according to Meis' study.
- If another acute or chronic sickness is present in an ongoing premature labour that cannot be treated conservatively, the pregnancy must be terminated right away. The illnesses include sickle cell disease, hyperthyroidism, chronic hypertension, chronic renal disease, systemic lupus, or any other connective tissue ailment. They also include heart diseases that cause moderate to severe functional impairment. However, a C section is not usually required in these circumstances.
- A foetus with growth retardation who has a good chance of survival should be delivered by caesarean section right away.
- An intriguing finding about the function of caesarean delivery in the prevention of cerebral haemorrhage in preterm infants weighing less than

1500g is that the active period of labour, not the delivery, is the primary cause of brain bleeding. In very preterm neonates, a caesarean birth was carried out in accordance with the usual obstetrical criteria. With an adjusted risk ratio of 0.18, caesarean deliveries have a lower chance of death, either in the delivery room or within 24 hours of the procedure.

Neonatal outcomes

Possible Known Complications: [168-172]

Respiratory: Interstitial emphysema, Respiratory distress syndrome (RDS), Pulmonary Hemorrhage, Apnea, Pneumomediastinum, Bronchopulmonary dysplasia, Pneumothorax, Pulmonary hypoplasia, Congenital pneumonia

Gastrointestinal: Necrotising enterocolitis (NEC), Poor intestinal motility

Cardiovascular: Patent ductus arteriosus, Congenital cardiac malformations, Bradycardia, Hypotension.

Central Nervous System: Intraventricular hemorrhage, Retinopathy of prematurity, Periventricular leukomalacia, Kernicterus, Hypoxic ischemic encephalopathy, Sensory and neuronal hearing loss

Renal: Renal glycosuria, Hypernatremia, Hyponatremia, Hyperkalemia, Renal tubular acidosis

Endocrine: Hypocalcemia, Hyperglycemia, Hypoglycemia, Hypothermia, Metabolic acidosis

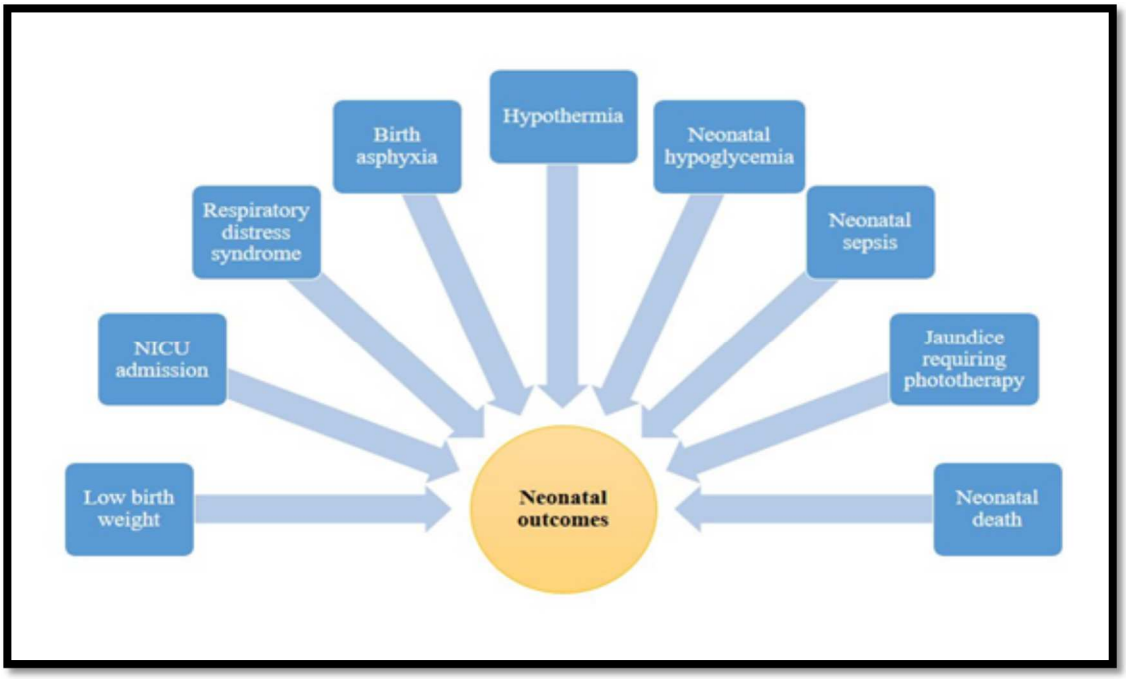
Hematological: Anemia, Vit. K deficiency, Hyperbilirubinemia, Fetal Hydrops, Disseminated Intravascular Coagulation (DIC)

Birth characteristics:

Preterm babies who survive after delivery face severe health complications for both long-term and short-term periods. Preterm babies are born with low birth weight in significant cases. This might be a concern due to preeclampsia, anemia, and intrauterine growth restriction - Wen et al., (2004) [173].

After birth, most preterm babies suffer from birth asphyxia.

The very-low-birth-weight neonates account for nearly 4-5 % of all live births reporting increased neonatal deaths. Furthermore, 20.5% of the study population enrolled in a year died from very-low-birth-weight neonates. The most common risk factors for mortality comprise respiratory distress syndrome, hyperglycemia, extremely low birth weight, and intraventricular hemorrhage. In addition, the mortality rates were higher among NICU-admitted preterm very-low-birth-weight neonates (Chawla et al., 2013) [174].



Neonatal outcomes of preterm birth

Nearly 76.9% of neonates require NICU admission because of asphyxia, jaundice, respiratory distress syndrome, and neonatal sepsis. According to a study conducted by Mohapatra V et al., in 2022, neonatal deaths occur in 9.21%, the most common cause being birth asphyxia. The fall in APGAR scores helps highly predict neonatal death [175].

Neonatal Mortality and Morbidity

Close to a million babies die due to preterm, shortly post delivery. Several long term impacts on preterm survivors have been studied – including Visual, hearing, cognitive and social impairment, Chronic lung diseases, Cardio-vascular involvement and other Non-Communicable diseases. Stein and Pomerance in 1950 stated that regardless of the birth weight, the fetal maturity in terms of gestational age had an impact on the fatality or mortality rate.

Preterm birth remains the foremost cause for the neonatal mortality and morbidity in the United States complicating 12.5% of the deliveries (Ananth 2006) [41].

According to WHO 2008 Global Burden of Disease analysis, preterm is considered a single largest condition in contributing to the high mortality and lifelong impairment and found to be a direct cause of almost 35% of neonatal deaths . A global estimation on preterm births shows 13 million births annually, with the highest rate in low and middle-income countries. Preterm birth is the foremost cause of 27% of neonatal deaths, with more than 1 million annually. However, the global estimates based on the surveys and vital registration accounted for only 2% of stillbirths. Thus, tracking stillbirths globally remains crucial due to intricate classification systems and global policies [176].

The major killers identified were congenital or hospital – acquired infections followed by birth asphyxia. Almost 40% of the mortality was contributed by the extremely preterm and late preterm groups combined; Majority of the babies died between 24-72 hours of life (Gravett, 2010) [176].

Almost 61.50% of perinatal deaths have occurred in preterm deliveries. Low birth weight, respiratory distress syndrome, birth asphyxia, and intra-uterine growth restriction were significant reasons for perinatal morbidity. Birth asphyxia (26%), septicemia (22.5%), and Respiratory distress syndrome (18.32%) were found to be the most significantly associated risk factors for perinatal mortality according to Asalkar et al., in a study conducted in 2014 [177].

Globally, the leading cause of death is prematurity, in children under 5 years of age. According to WHO, 2014, there is a vast difference in the survival – almost

90% of extremely preterm babies have very less chances of survival even within the first few days.

PURPOSe study (2018) - *The project to understand and research preterm pregnancy outcomes and stillbirths in South Asia - a* prospective cohort study at hospitals in India and Pakistan reveals that the most common cause of stillbirths was asphyxia. The higher mortality rates of neonates in South Asia can be reduced if the primary reasons for the death are identified [177].

PURPOSe concluded that nearly 30% of preterm births cause fetal or maternal complications like fetal growth restriction or maternal illness. Some conventionally approved pathways causing preterm birth involve stress, decidual hemorrhage provoked by uteroplacental thrombosis, infection-induced inflammation, and uterine overdistension due to multiple fetuses. However, the predominant cause of stillbirths was intrapartum asphyxia in low- and middle-income countries.

However, a study conducted by Chawla et al., in India, 2021 - opined that the most common risk factors for mortality comprise respiratory distress syndrome, hyperglycemia, extremely low birth weight, and intraventricular hemorrhage. In addition, the mortality rates were higher among NICU-admitted preterm very-low-birth-weight neonates [178].

The interrelation of preterm birth with early neonatal death, late neonatal death, and post-neonatal death was examined in a cross-sectional study in India. Among all births, preterm birth causes 4.2 times early neonatal, 3.8 times late neonatal, and 1.7 times post-neonatal deaths in full-term births. The most recent and second most recent births were associated with early, late, and post-neonatal deaths. In contrast, the third

most recent births were associated only with the risk of early and late neonatal deaths (Kannaujiya et al., 2022) [180].

Especially in low income countries, almost half the preterm babies die due to lack of facilities. Almost all preterm babies survive, in high income countries. According to WHO – 12th November 2022, middle income countries increase the burden of physically and mentally challenged children, due to suboptimal technological and resource usage. In addition, 31.21 % of preterm deliveries required neonatal intensive care unit admissions, with 9.21% of neonatal death in preterm infants. Most common neonatal complications involve neonatal sepsis, jaundice, and respiratory distress syndrome, whereas birth asphyxia is the leading cause of neonatal death.

The morbidity and mortality largely depends on the Gestational age at birth. According to Zahedi et al 2022, who conducted a study on very preterm neonates, [151] 74.5 % of deliveries had neonatal morbidity, and 9.59% had mortality.

Surprisingly, Respiratory Distress Syndrome contributed to less than 10% of the deaths – especially among the extreme preterm category.

Maternal cause - The chief maternal cause identified according to a few studies – was hypertensive disorders in pregnancy, almost one-third of the deaths among preterm.

Placental cause - Placental malperfusion was found to be contributing to almost 30% of the preterm neonatal deaths.

Neonatal cause – Congenital and Neonatal infections were identified to contribute significantly, alongside Intrauterine (birth) hypoxia – identified as the primary non-infectious cause of preterm infant death.

A thorough examination including determining the correct gestational age, History, maternal investigations, MITS, autopsy was warranted for further accurate conclusions.

METHODOLOGY

Type of study: Observational Cross Sectional Study.

Study population: Pregnant women who are getting delivered, in less than 37 weeks of pregnancy at the Labour room of KAHER'S Dr. Prabhakar Kore, will be recruited as per inclusion and exclusion criteria in the study period.

Data Collection: February 2021 to January 2022

CTRI Reg No – CRTI/2021/05/033527

Approved by "Ethical and Research committee, KAHER's Jawaharlal Nehru Medical College" Belagavi, prior to its commencement. Ethical clearnce number

Inclusion Criteria:

- Pregnant women who come to labour room in established preterm and induced preterm and deliver in less than 37 weeks period of gestation.
- Patients who give consent during the study period.

Exclusion Criteria:

- Pregnant women without a proper dating scan or not possible to assign a gestational age at the time of delivery.

Sample Size: Universal

Operational Definitions: Preterm birth is defined as delivery which occurs in less than 37 weeks or less than 259 days of gestation, counted from the first day of the last menstrual period. It is classified as

- Extremely preterm (< 28 weeks)
- Very preterm (28 weeks - 32 weeks)
- Moderate and Late preterm (32 weeks - 36 weeks + 6 days).

(WHO, 2022, November 14)

Period of Viability in the different countries

- WHO - 20 weeks (2016)
- IMA - 28 weeks or 1 kg
- RCOG - 24 weeks (2014)
- ACOG - 24 weeks or 500gms (2001)

Data collection: All pregnant women who were in less than 37 weeks of pregnancy admitted at the Labour room of KAHER'S Dr. Prabhakar Kore, in established preterm, after confirmation of the gestational age – either from dating scan , after provision of a consent for the same, were enrolled, as per the inclusion and the exclusion criteria. All participants were assessed by a skilled obstetrician. Participants in the study had their baseline demographic information gathered. The antenatal history, current and past histories, the presence or absence of other maternal acute and chronic illnesses such hypertension, thyroid disorders, asthma, infections, obstetric and fetal risk factors were documented. Thorough general and obstetric examinations were done. Each participant was given a unique serial number and a data file that were used to record this information during the course of the hospital stay. Using a unique identification number, data was entered into the final electronic database (from data files and surveys). According to institutional protocol, the management of the enrolled cases were carried out. The course of labour - including induction of labour,

administration of steroids and Magnesium Sulphate, were documented. The pregnancy's outcome such as the mode of delivery and the indication, the absence or presence of complications throughout the intrapartum period – to both the mother and the fetus were noted.

Following delivery, a prospective study of the neonates was performed. All the neonatal resuscitation procedures and recording of the data was performed by a skilled paediatrician available at the time of the delivery. The birth characteristics such as weight, sex, APGAR score at the end of 5 minutes, need for NICU admission and the indication (if warranted) were recorded. Management of the complications were done following institutional protocols. A follow up was done on the neonatal complications and the condition of both the mother and the neonate during hospital stay and at discharge. At 28 days of life, a follow up on the condition of the neonates though routine checkup at the hospital or through telephonic conversation was done. The participants who were lost to follow up were excluded from the study.

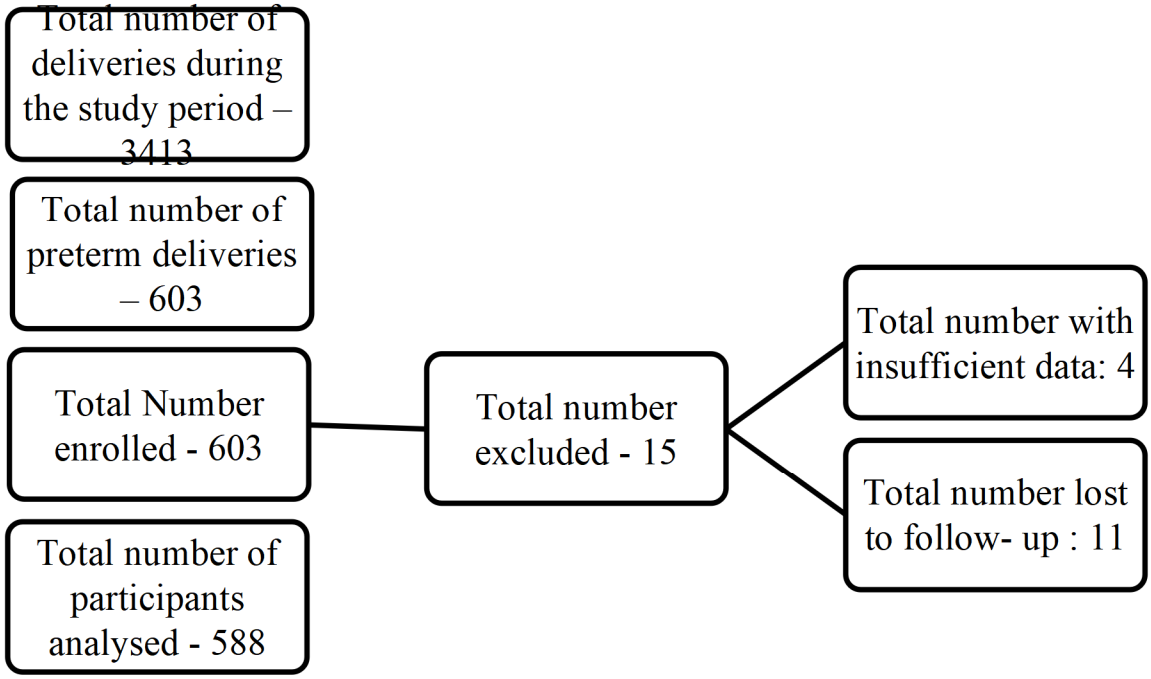
STATISTICAL ANALYSIS

Data is analyzed using statistical software R version 4.2.1. and Microsoft Excel. Categorical variables are represented by frequency and percentage. Continuous variables given in Mean ± SD / Median (Min, Max) form. Chi-square test/Fisher's exact test is used to check the dependency between categorical variables. Normality of variable is checked by Shapiro Wilk test and QQ plot. Kruskal Wallis test is used to compare the distribution of variables over type of preterm. Dunn's test is used as post hoc analysis. P-value less than or equal to 0.05 indicates statistical significance.

RESULTS

A prospective observational study was conducted in the labour room of KAHER'S Dr Prabhakar Kore hospital attached to JNMC during the period from February 2021 to January 2022 and the data on preterm birth was collected and analysed. A total of 588 women were analysed during the study period.

Flow chart



In this study, 3413 number of deliveries occurred during the study period, out of which 603 were preterm births. A total of 15 patients were excluded, out of which 4 patients had insufficient data and 11 patients were lost to follow-up.

Month	No. Of Deliveries	No. Of Preterm Deliveries	Percentage of Preterm Deliveries
February 2021	173	40	23.12 %
March 2021	190	41	21.57 %
April 2021	195	33	16.9 %
May 2021	248	53	21.37 %
June 2021	312	55	17.6 %
July 2021	307	64	20.84 %
August 2021	256	51	19.92 %
September 2021	349	64	18.3 %
October 2021	357	55	15.4 %
November 2021	357	51	14.28 %
December 2021	344	47	13.6 %
January 2022	325	49	15.07 %
Total	**3413**	**603**	**17.67 %**

Table 1. Distribution of deliveries and the incidence of Preterm births.

Incidence of total preterm birth was **17.67%** in this study.

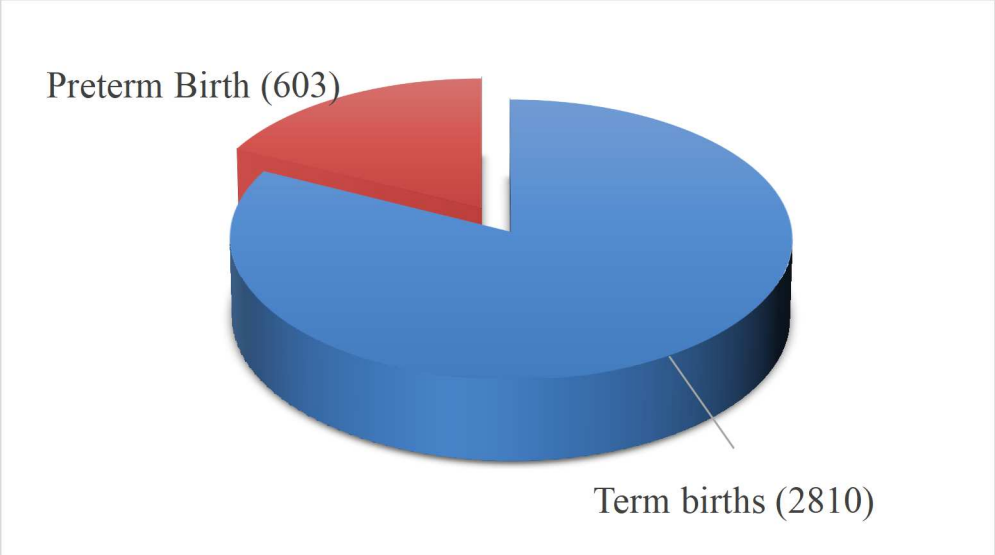


Figure 1: Incidence of total preterm birth during the study period.

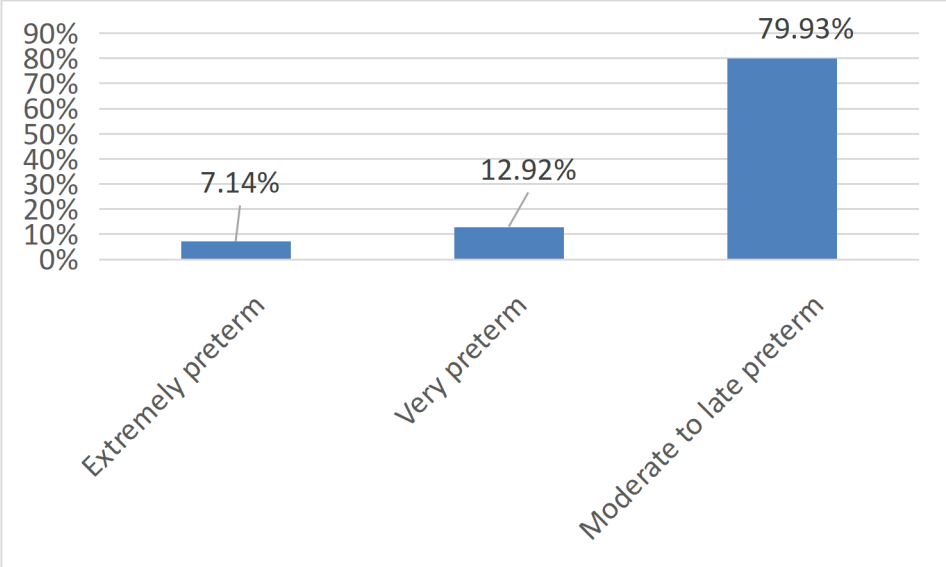


Figure 2: Distribution according to the type of preterm.

In our study, as expected, around 79.93 % of the total preterm births were falling in the category of moderate to late preterm. Considerable portions – 12.92% belong to the very

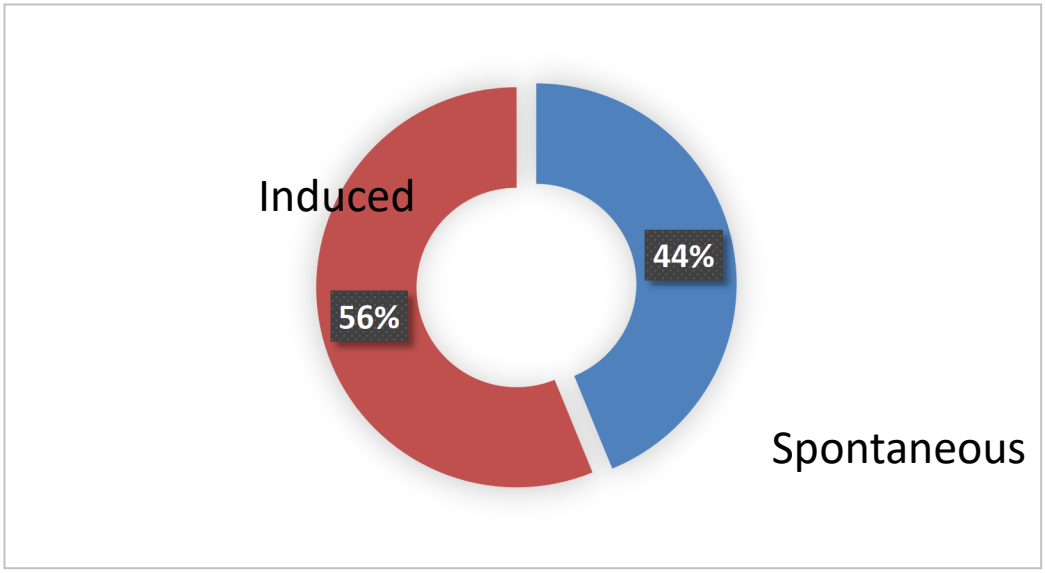


Figure 3: Distribution of subjects according to type of delivery.

Iatrogenic or Induced preterm was around 56% in our study, while Spontaneous Preterm birth was around 44% of the total preterm births.

Variables	Sub Category		Number (%) (n = 588)
Socio Economic Class – Modified Kuppusamy (Rural)	1		92 (15.6%)
	2		97 (16.4%)
	3		49 (8.3%)
	4		5 (0.85%)
	5		4 (0.85%)
Socio Economic Class – B.G.Prasad Classification (Urban)	1		138 (23.47%)
	2		163 (27.72%)
	3		34 (5.78%)
	4		4 (0.85%)
	5		2 (0.34%)
Residence	Rural		247 (42%)
	Urban		341 (58%)
Age (years)	≤ 20	34 (5.8%)	**0.002^{MC*}**
	21 - 30	454 (77.2%)	
	31 - 40	98 (16.7%)	
	> 40	2 (0.3%)	
BMI (WHO Asian Criteria)	Underweight (<18.5)	28 (4.83%)	0.712
	Normal (18.5 – 22.9)	32 (5.42%)	

	Overweight (23 – 24.9)	419 (71.25%)	
	Obese (>25)	109 (18.5%)	
	Mean ± SD	24.21 ± 4.58	
Gravidity	Multigravida	331 (56.3%)	
	Primigravida	257 (43.5%)	0.271
Bad Obstetric History		86 (14.6%)	0.441
Registered/ Unregistered	Unregistered	211 (59.94%)	
	Registered	141 (40.06%)	

Table 2: Distribution of subjects according to demographic details.

Both in the rural and the urban settings, most of the mothers who delivered preterm, belonged to the Socio Economic class 1. 341(58%) women were from urban areas. 419 (71.25%) subjects were overweight and 109 (18.5%) were obese. It was observed that 331 were Multigravida (56.3%). Bad obstetric history was observed on 86 (14.6%) subjects. Nearly 211(59.94%) of the patients were Unregistered cases

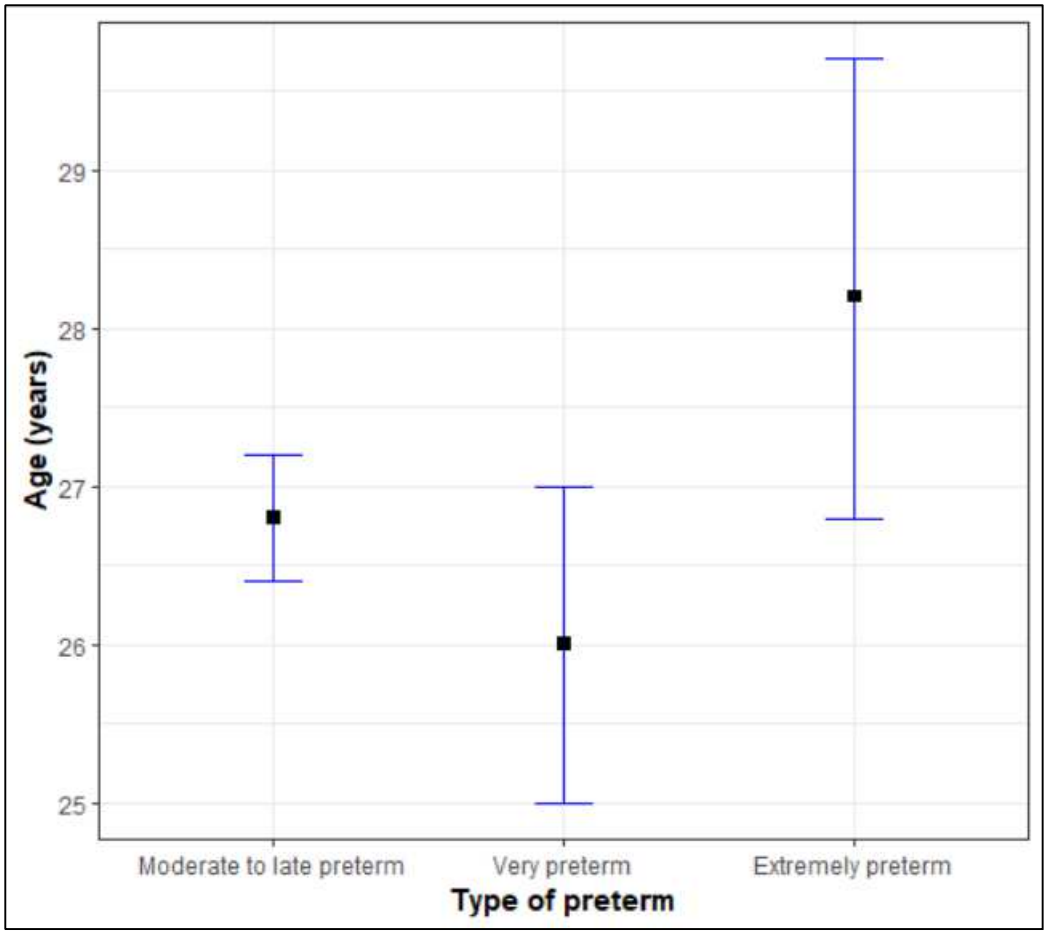


Figure 4: Mean plot of age over type of preterm.

Majority (77.2%) subjects who delivered preterm belonged to the age group 21-30 years.

Table 3: Distribution of participants according to different risk factors.

Variable	Number	Percentage
Maternal Medical Risk Factors	233	39.6 %
Obstetric Risk Factors	157	26.9 %
Fetal Risk Factors	154	26.19 %
No risk factors	64	10.88 %

Out of 588 mothers, 39.6% of them had maternal medical risk factors, 26.9% had obstetric risk factors, 26.19% had Fetal risk factors. **Only around 11% of the participants had no risk factor that was identified.**

Table 4: Distribution of participants according to acute maternal medical condition.

Acute medical condition	Number (%) (n =588)	p-value
Urinary Tract Infection	47 (8 %)	0.2798^{F}
Acute episode of fever	28 (4.76%)	0.0863^{F}
Gastero-enteritis	24 (4.08%)	0.0573^{F}
COVID Positive status	14 (2.38%)	$\mathbf{0.0033^{F}*}$
Vaginitis or cervicitis	13 (2.21%)	1^{F}

Out of 588 motehrs, acute episode of fever was observed in 28 (4.76%) subjects, urinary tract infection was observed in 25 (4.25%) subjects, history suggestive of acute gastero-enteritis was observed in 24 (4.08%) subjects.

Table 5: Distribution of participants according to chronic maternal medical condition.

Chronic medical condition		Number (%) (n=588)	p-value
Thyroid disorders (Hyperthyroidism - 2)		97 (16.5%)	**0.0036[F]***
Hypertension (Chronic)		21 (3.57%)	**0.0129[F]***
Diabetes Mellitus (Overt)		18 (3.06%)	0.13[F]
Anemia / Blood transfusions		16 (1.02%)	0.5197[F]
TORCH positive status		9 (1.9%)	0.1878[F]
Hepatitis B Infection		3 (0.51%)	1[F]
HIV Infection		2 (0.34%)	1[F]
H/O pulmonary Tuberculosis		1 (0.17%)	1[F]
Bronchitis		1 (0.17%)	1[F]
Diagnosed uterine anomalies	Subseptate uterus	3 (0.51%)	1[F]
	Bicornuate uterus		
Epilepsy		2 (0.34%)	1[F]
Psoriasis		1 (0.17%)	1[F]
Neurogenic Bladder		1 (0.17%)	1[F]
Pneumothorax		1 (0.17%)	1[F]
Bell's Palsy		1 (0.17%)	1[F]
Maternal single kidney		1 (0.17%)	1[F]

Out of 588 participants, Thyroid disorders were observed in 97 (16.5%) subjects, Chronic Hypertension was observed in 21 (3.57%) subjects, Overt Diabetes Mellitus was observed in 18 (3.06%) of the patients.

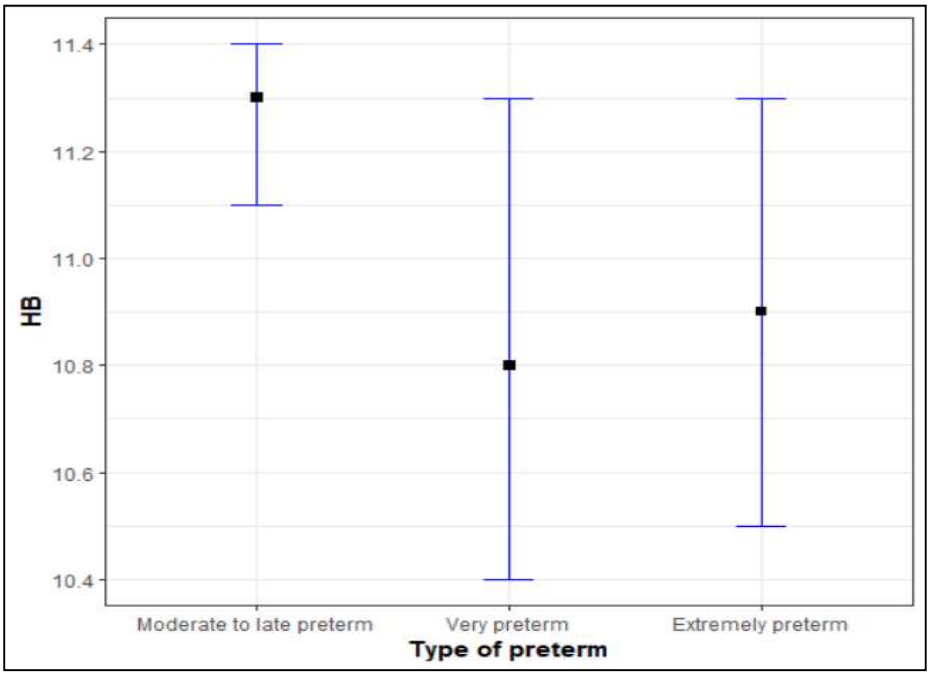


Figure 5: Distribution of HB over type of preterm.

Obstetric complication	Number (%) (n=588)		p-value
PPROM	153 (26.02%)		**0.0351[F]***
Hypertensive Disorders of Pregnancy	Total	118 (20.06%)	
	Gestational Hypertension	38 (6.46%)	0.6793[F]
	Eclampsia	14 (2.38%)	0.1028[F]
	Preeclampsia	60 (10.2%)	**0.0042[F]***
	HELLP	6 (1.02%)	0.1079[F]
Oligohydramnios	62 (10.54%)		1[F]
Rh Negative Pregnancy	28 (4.76%)		0.6861[F]
GDM	44 (7.48%)		**0.0011[F]***
Cervical Incompetence	18 (3.06%)		0.4386[F]
Polyhydramnios	16 (2.72%)		0.286[F]

Table 6: Distribution of participants according to obstetric complications leading to preterm delivery.

In our study setting, out of 588 participants, PPROM was observed in 153 (26.02%) , PIH was observed in 118 (20.06%) , oligohydramnios was observed in 62 (10.54%) and GDM was observed in 44 (7.48%) .

Fetal complication		Number (n=588)	p-value
Still Birth		92 (15.64%)	**0.0248[F]***
Multiple pregnancies		70 (11.9%)	0.4385[F]
Fetal macrosomia		12 (0.2%)	**0.0015[F]***
Fetal anomalies		13 (2.21%)	**0.0015[F]***
FGR [n = 130 (22.10%)]	Increased resistance on Doppler	88 (14.97%)	**0.0206[F]***
	AEDF or REDF	22 (3.74%)	**0.0129[F]***
	Without Doppler Changes	20 (3.40%)	0.7164[F]

Table 7: Distribution of participants according to Fetal complications leading to preterm delivery.

Out of 588 participants, still birth was observed in 92 (15.64%) mothers and Fetal Growth Restriction with increased resistance on Doppler was observed in 88 (14.97%) patients.

Risk Factor	Number (n=318)	Percentage
FGR	109	34.27%
Still Birth	66	20.7%
Pregnancy Inducted Hypertension	62	19.5%
Oligohydramnios	32	10.06%
Polyhydramnios	16	5.03%
Anamnios	16	5.03%
Fetal macrosomia	6	1.89%
Fetal anomalies	11	3.46%

Table 8: Distribution according to the indications for induction of labour.

Out of 318 patients who were induced, 109 (34.27%) had FGR, 66(20.7%) participants had still birth, 62 (19.5%) had Pregnancy Induced Hypertension and 32 (10.06%) had Oligohyramnios.

Variables	Sub Category	Type of preterm			p-value
		Moderate to late preterm	**Very preterm**	**Extremely preterm**	
Registration status	Registered	251 (52.4%)	30 (42.25%)	25 (65.79%)	0.05997[C]
	Unregistered	228 (47.6%)	41 (57.75%)	13 (34.21%)	
Residence	Rural	195 (40.71%)	38 (53.52%)	14 (36.84%)	0.0997[C]
	Urban	284 (59.29%)	33 (46.48%)	24 (63.16%)	
S.E.C.	1	190 (39.67%)	27 (38.03%)	13 (34.21%)	0.7687[C]
	2	227 (47.39%)	32 (45.07%)	21 (55.26%)	
	3	62 (12.94%)	12 (16.9%)	4 (10.53%)	
Age (years)	<20	10 (2.09%)	2 (2.82%)	0	**0.0449[F]***
	20-29	343 (71.61%)	57 (80.28%)	21 (55.26%)	
	30-39	124 (25.89%)	12 (16.9%)	16 (42.11%)	
	40-49	2 (0.42%)	0	1 (2.63%)	
	Mean ± SD Median (Min, Max)	26.75 ± 4.46 26 (19, 41)	25.96 ± 4.46 26 (19, 38)	28.18 ± 4.5 28 (21, 42)	**0.03495[K]***
Obstetric score	Multigravida	274 (57.2%)	41 (57.75%)	17 (44.74%)	0.3199[C]
	Primigravida	205 (42.8%)	30 (42.25%)	21 (55.26%)	
Bad Obstetric History	No	404 (84.34%)	62 (87.32%)	36 (94.74%)	0.1928[C]
	Yes	75 (15.66%)	9 (12.68%)	2 (5.26%)	
Addiction history	Father	44 (9.19%)	8 (11.27%)	6 (15.79%)	0.3299[F]
	No History	435 (90.81%)	63 (88.73%)	32 (84.21%)	
BMI	Mean ± SD Median (Min, Max)	28.55 ± 4.49 28 (18, 36)	28.77 ± 4.85 30 (18, 36)	28.53 ± 4.61 28 (18, 36)	0.8604[K]

Fetal distress	No	348 (72.65%)	46 (64.79%)	19 (50%)	**0.00997^{F*}**
	Yes	102 (21.29%)	17 (23.94%)	12 (31.58%)	
S. TSH	Mean ± SD	2.47 ± 1.43	2.63 ± 1.53	2.68 ± 1.49	0.4908^{K}
	Median (Min, Max)	2 (0.7, 8.2)	2.3 (0.98, 8.2)	2.4 (0.95, 6.87)	

Table 9 : Comparison of different variables with type of preterm.

*Abbreviation: C – Chi square test, F – Fisher's exact test, K – Kruskal Wallis test, * indicates statistical significance.*

From Fisher's exact test, it is observed that, there is significant difference in the distribution of age and Fetal distress over type of preterm. There is no significant difference in the distribution of addition history over type of preterm.

From Kruskal Wallis test, it is observed that, there is significant difference in the distribution of age over type of preterm. There is no significant difference in the distribution of Serum TSH and BMI over type of preterm. Further from post hoc analysis, it is observed that, there is significant difference in the distri bution of age between extremely preterm and Very preterm (p-value = 0.0294).

Drug History		Number (%) (n=588)
Betamethasone (n = 351)	Dose completed	128 (21.7 %)
	Dose not completed	223 (37.9 %)
Dexamethasone (n = 6)	Dose completed	5 (0.9 %)
	Dose not completed	1 (0.2 %)
Steroid not given		231 (39.28 %)
MgSO4 administration		61 (10.37 %)

Table 10 : Distribution of the different drugs administered

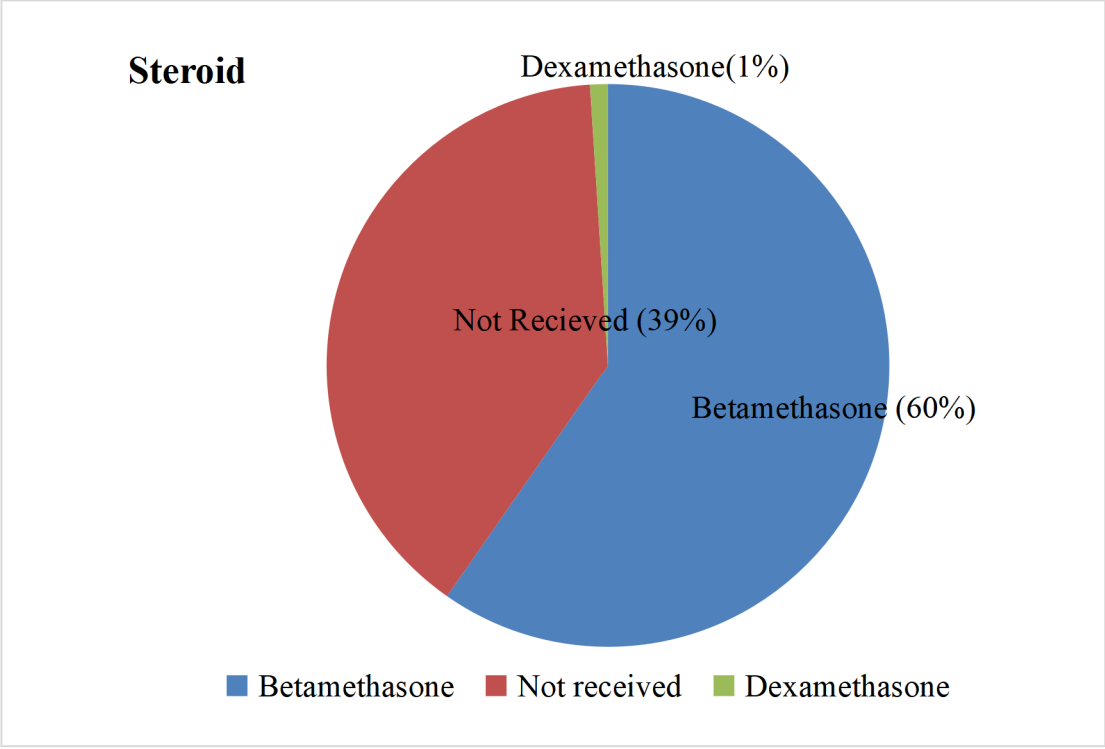


Figure 6: Distribution of participants according to the steroid received.

Around 60% of the mothers had received atleast 1 dose of Betamethasone. 39% of the mothers had not received any steroid and delivered preterm.

<table>
<tr><th colspan="2" rowspan="2">Mode of delivery</th><th colspan="3">Number (%) (n=588)</th><th rowspan="2">P value</th></tr>
<tr><th>Moderate to late preterm</th><th>Very preterm</th><th>Extremely preterm</th></tr>
<tr><td rowspan="4">Preterm Vaginal Deliveries</td><td rowspan="2">Total (n=198)</td><td>111 (28.6%)</td><td>49 (39.44%)</td><td>38 (100%)</td><td rowspan="6"><0.001^{MC}*</td></tr>
<tr><td colspan="3">88 (44.4%)</td></tr>
<tr><td rowspan="2">Spontaneous</td><td colspan="3" rowspan="2">110 (55.6%)</td></tr>
<tr><td>Induced</td></tr>
<tr><td>Vacuum Delivery</td><td>Total (n=2)</td><td>2 (0.42%)</td><td>0</td><td>0</td></tr>
<tr><td rowspan="3">Cesarean Section</td><td>Total (n=388)</td><td>366 (94.3%)</td><td>22 (5.67%)</td><td>0</td></tr>
<tr><td>Emergency</td><td colspan="3">365 (94%)</td></tr>
<tr><td>Elective</td><td colspan="3">23 (5.9%)</td></tr>
</table>

Table 11 : Comparison of mode of delivery with type of preterm.

From Chi square test, it is observed that, there is significant difference in the distribution of mode of delivery with type of preterm. A total of 388 women delivered via Cesarean Section, 198 women delivered Vaginally and 2 delivered via Ventouse (Vacuum). Emergency LSCS contributed to about 365 (94%)

Indication		**Number (%) (n=385)**
Previous LSCS/ Previous 2 LSCS		90 (23.37%)
Fetal distress		37 (9.61%)
Multifetal Gestation		34 (8.83%)
Absent End Diastolic Flow with IUGR		21 (5.4%)
Anamnios		21 (5.4%)
Precious pregnancy		18 (4.67%)
Prolonged PPROM		17 (4.41%)
Severe Oligohydramnios		15 (3.9%)
Failed induction		15 (3.9%)
CDMR		13 (3.37%)
Non progression of labour		9 (2.33%)
PIH	Severe PE with Imminent signs	42 (10.9%)
	Eclampsia	7 (1.81%)
Antepartum Hemorrhage	Abruptio placenta	5 (1.3%)
	Placenta previa	9 (2.33%)
Breech presentation		8 (2.07%)
Cephalo-Pelvic Disproportion		6 (1.56%)
Uncontrolled GDM with macrosomia		4 (1.03%)
Transverse/ Oblique lie (2 twins and 1 singleton)		3 (0.78%)

Placenta accreta spectrum	3 (0.78%)
Fetal macrosomia	2 (0.52%)
Cord presentation	2 (0.52%)
Maternal Respiratory Distress **(1 Maternal Pulmonary TB and 1 Covid 19 positive)**	2 (0.52%)
Maternal Heart disease	2 (0.52%)
AFLP with Fulminant Hepatitis with DIC	1 (0.26%)

Table 12: Distribution according to indication for LSCS.

Out of 385 mothers, most common indication for LSCS was Previous LSCS/ Previous 2 LSCS in 90 (23.37%), fetal distress in 37 (9.61%) and multifetal gestation in 34 (8.83%) mothers.

Neonatal outcomes:

Variables	Sub Category	Number (%)
Gender (n=658)	Ambiguous (Amorphous)	2 (0.49%)
	Female	270 (40.94%)
	Male	386 (58.56%)
Still Births [n = 92] (13.98%)	FSB	45
	MSB	47
APGAR at the end of 5 mins [n = 566]	Severely Depressed (0-3)	15 (2.65%)
	Moderately Depressed (4-6)	107 (18.9%)
	Excellent (7-10)	444 (78.45%)
Level of Neonatal care (n=566)	NICU admission	298 (52.65%)
	Mother side	176 (31.1%)
	KMC admission	92 (16.25%)

Table 13: Birth Characteristics in Preterm Deliveries

Out of 658 babies, 386 (58.56%) were males and 270 (40.94%) were females. 92 still births were observed.

Birth Weight	Number (%) (n = 658)
< 1 kg	50 (7.57%)
1.01 kg to 1.5 kgs	124 (18.84%)
1.51 kg to 2 kg	149 (22.64%)
2.01 kgs to 2.5 kgs	199 (30.24%)
2.51 kgs to 3.0 kg	117 (17.78%)
> 3 kg	19 (2.89%)
Mean ± SD	1.93 ± 0.7 kg

Table 14: Distribution of neonates according to birth weight.

Out of 658 neonates, 199 (30.24%) had birthweight in the range 2.01kg to 2.5 kg, 149 (22.64%) had birthweight in the range 1.51kg to 2 kg and 124 (18.84%) had birthweight in the range 1.01kg to 1.5 kgs.

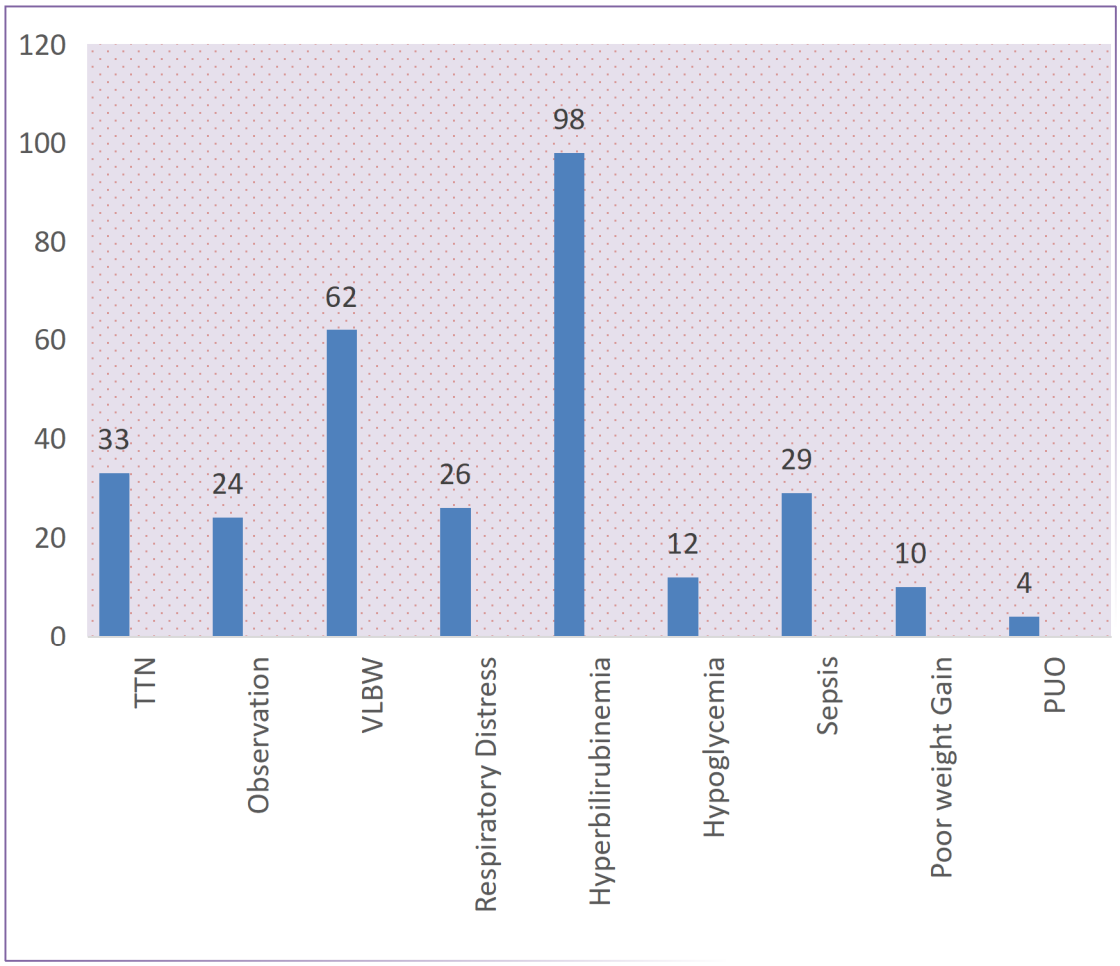


Figure 7: Indication for NICU admission.

During the course of the study, the total number of NICU admissions were 298. the commonest indication for NICU admission was identified as Hyperbilirubinemia – 98(32.8%), followed by Very low birth weight 62 (20.8%). The mean days of NICU admission was 8 days.

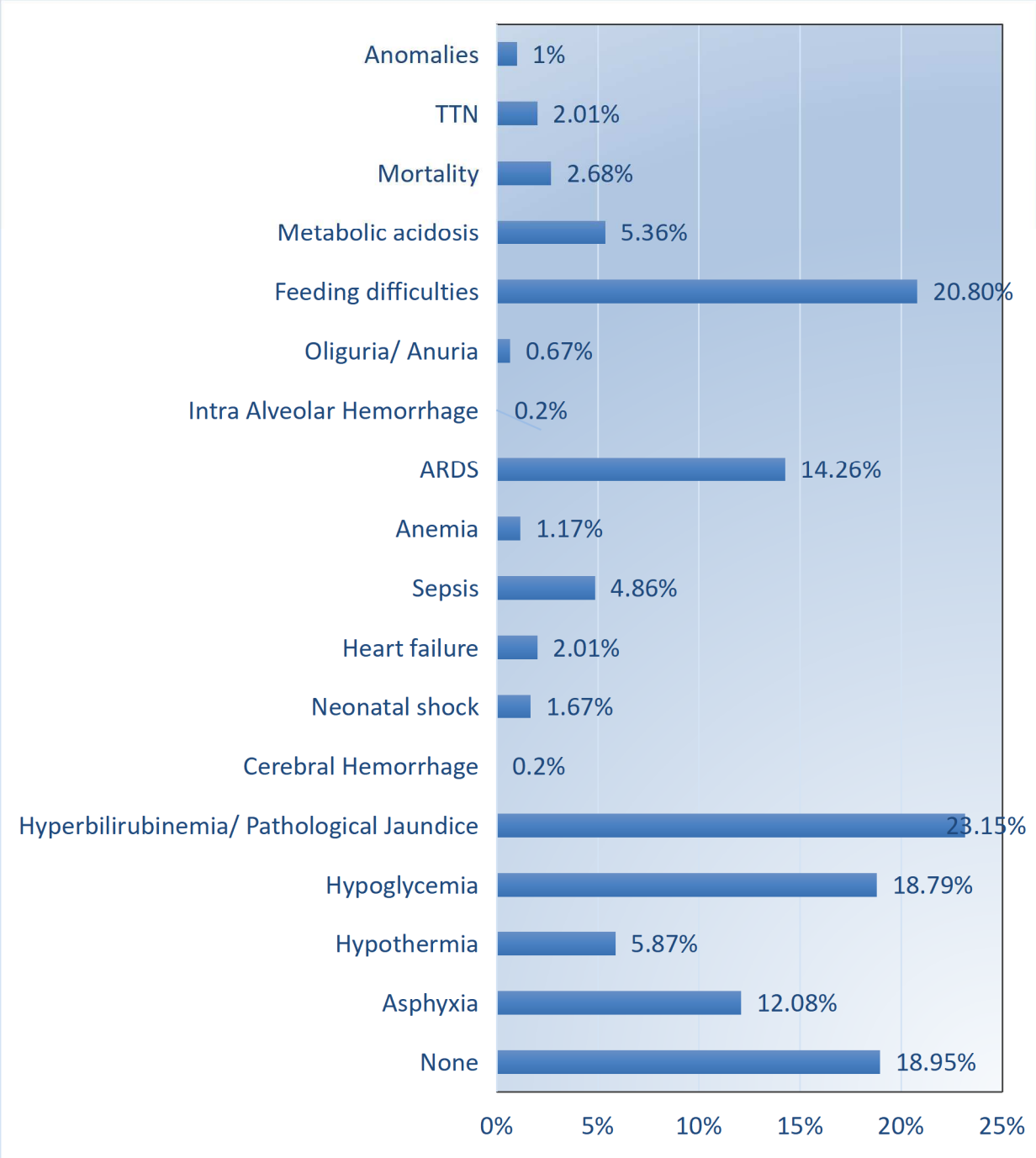


Figure 8: Distribution of neonates according to neonatal complications.

Neonatal complications were observed in 215 babies out of the 566 neonates. The commonest complication was Hyperbilirubinemia (23.15%), followed by feeding difficulties. About 18.95% neonates had no complications.

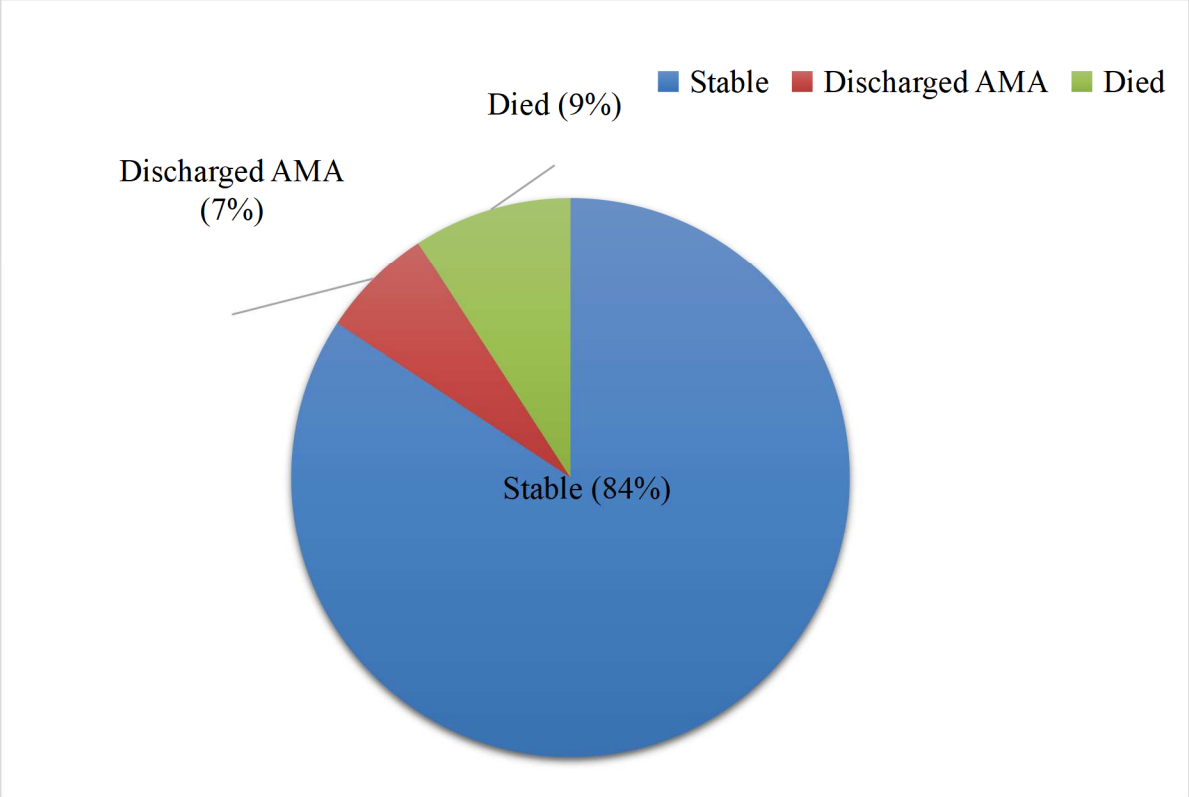


Figure 9: Distribution according to the condition of neonates at time of discharge.

477 (84%) of the live preterm neonates were stable at the time of discharge, and around 52 (9%) had expired.

Drug	Mean	Number	No. of	Complications	Mortality

	Gestational Age	**(n=588)**	**NICU Admissions (n=298)**	**(n=215)**	**(n=52)**
Betamethasone	32 weeks ± 3 days	128 (21.7 %)	92 (30.87%)	87 (40.4%)	14 (26.9%)
Dexamethasone	28 weeks ± 2 days	5 (0.9 %)	3 (1.0%)	3 (1.4%)	2 (3.8%)
MgSO4	30 weeks ± 3 days	61 (10.37 %)	68 (22.81%)	52 (24.18%)	14 (26.92%)

Table 15: Distribution of neonatal outcomes with drug administration.

Out of 588 subjects, betamethasone was administered for 128 (21.7 %) subjects, Dexamethasone was administered for 5 (0.9 %) and MgSO4 was administered for 61 (10.37 %) subjects.

Cause of neonatal mortality	Number (%) (n= 52)
Sepsis	16 (30%)
Shock	7 (13%)
Hypothermia	5 (10%)
Acute respiratory distress	5 (10%)
Congenital cardiac malformations	5 (10%)
Severe Anemia	3 (6%)
Intraventricular Hemorrhage	3 (6%)
Asphyxia	2 (4%)
Metabolic acidosis	2 (4%)
Ileal atresia	2 (4%)
Multiple anomalies not compatible with life	1 (2%)
Necrotising enterocolitis	1 (2%)

Table 16: Distribution of neonates according to cause of neonatal mortality.

Out of 52 neonates, the cause of mortality was sepsis in 16 (30%) neonates, shock in 7 (13%) neonates, Hypothermia in 5 (10%), Acute respiratory distress in 5 (10%) and Congenital cardiac malformations in 5 (10%).

The mean time of death was 11 days. The mean gestational age was 28 weeks + 6days.

Outcome		Number (n=46) %
Mortality (Total - 34)	**FSB**	17 (36.96%)
	MSB	3 (6.52%)
	Neonatal deaths (n=26 *)	14 (53.84%)
NICU Admissions (n=26)		26 (100%)
Complications (n=26)		26 (100%)
Number survived (n=26)		12 (46.15%)
Mean birth weight		0.712 ± 0.09

Table 17: Distribution of neonatal outcomes in extremely preterm cases.

Out of a total of 46 extremely preterm babies, 26 were live born. Out of them, 14 (53.84%) died at neonatal stage. All 26 of the extremely preterm babies required NICU admission. Mean birth weight was 0.712 ± 0.09 kgs. Most common complication was ARDS.

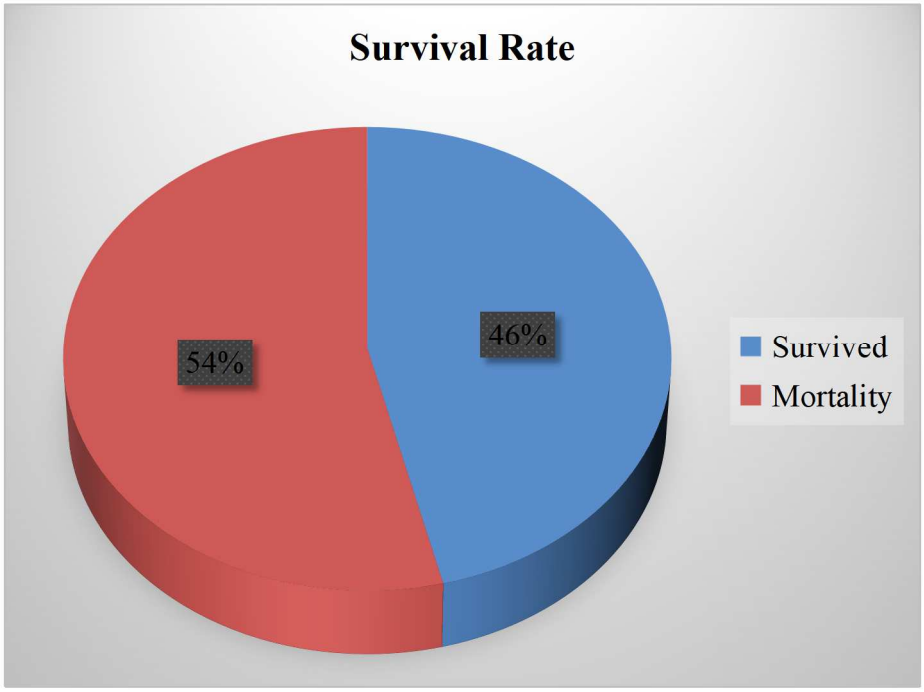


Figure 10: Distribution according to survival rate in extreme preterm cases.

Out of 46 extremely preterm births, 12 (46.15%) survived.

Outcome		Number (n=93) %
Mortality (Total - 35)	**FSB**	4 (4.30%)
	MSB	10 (10.7%)
	Neonatal deaths (n=79)	21 (26.58%)
NICU Admissions (n=79)		54 (68.3%)
Complications (n=79)		47 (59.49%)
Number survived (n=79)		58 (73.41%)

Table 18: Distribution of neonatal outcomes in very preterm cases.

Out of a total of 93 very preterm babies, 78 were live born. Out of them, 21 (26.58%) died at neonatal stage. 54(68.3%) of the very preterm babies required NICU admission. The most common complication was sepsis.

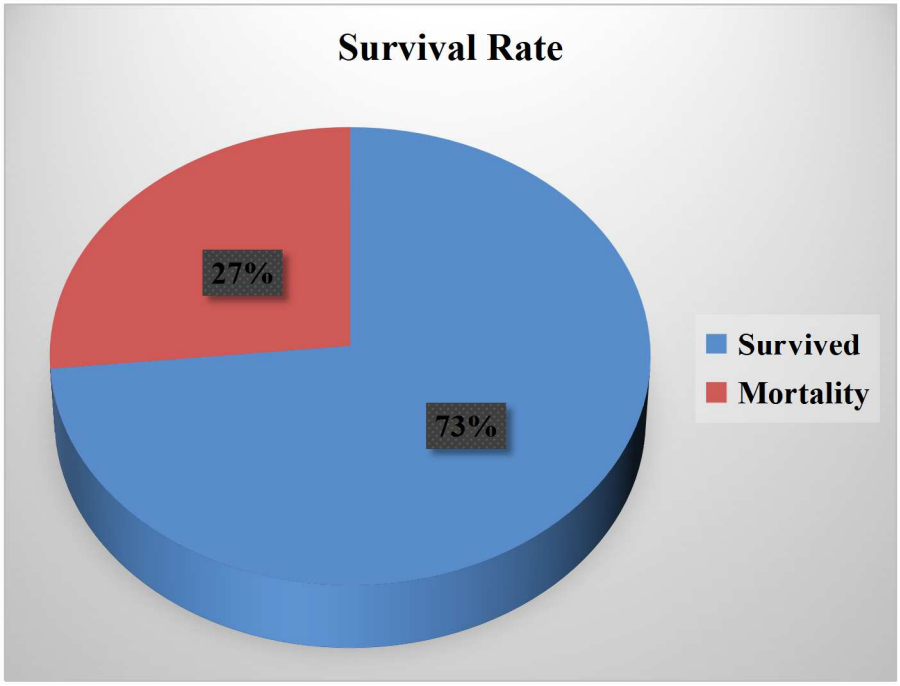


Figure 11: Distribution according to survival rate in very preterm cases.

Out of 93 subjects, 58 (73.41%) survived.

Outcome		Number (n=519) %
Mortality (Total - 75)	**FSB**	24 (4.62%)
	MSB	34 (6.55%)
	Neonatal deaths (n=461)	17 (3.69%)
NICU Admissions (n=461)		218 (47.28%)
Complications (n=461)		142 (30.8%)
Number survived (n=461)		444 (95.66%)

Table 19: Distribution of neonatal outcomes in moderate to late preterm cases.

Out of a total of 519 moderate to late preterm babies, 461 were live born. Out of them, 17 (3.69%)died at neonatal stage. 218 (47.28%) of the moderate to late preterm babies required NICU admission. Most common complication is Hyperbilirubinemia.

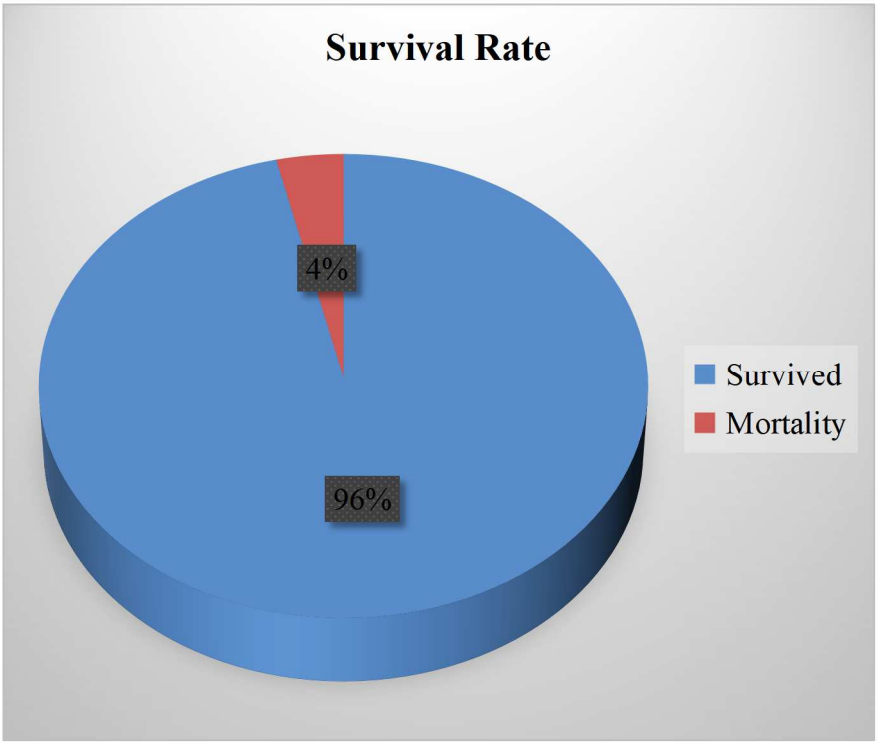


Figure 12: Distribution according to survival rate in moderate to late preterm cases.

Out of 519 neonates, 444 (95.66%) survived.

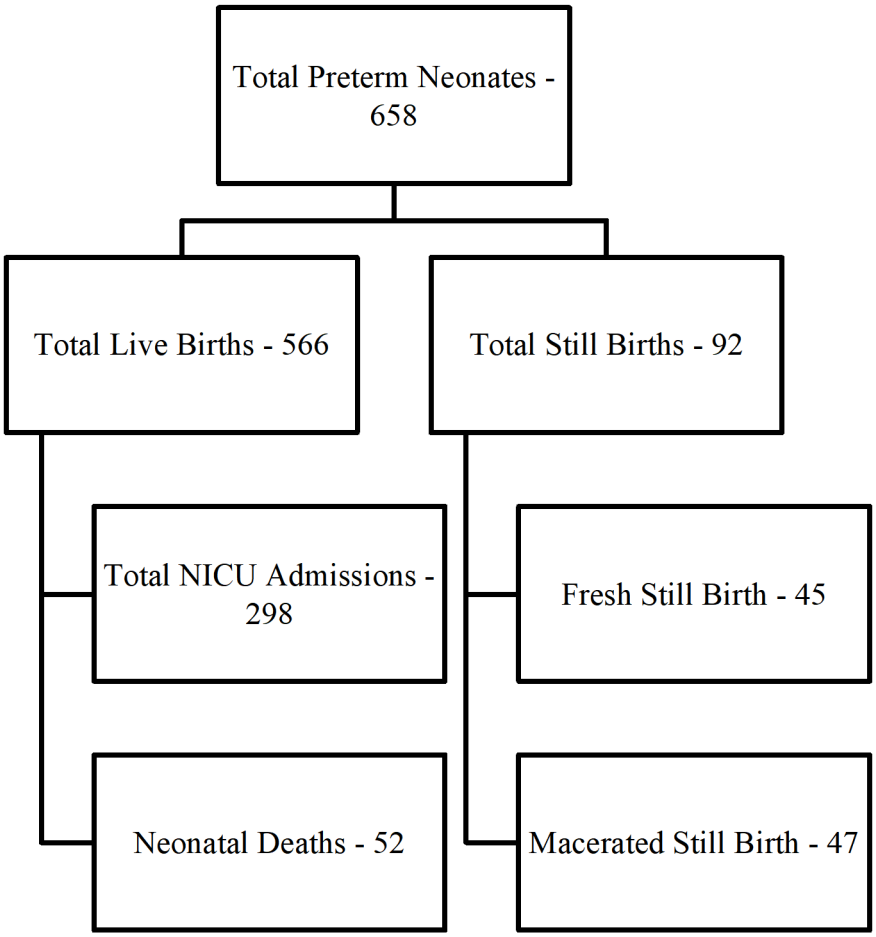


Figure 13: Summary of the total number of preterm births and their outcomes

DISCUSSION

The present study was a prospective observational study conducted in KAHER's Dr. Prabhakar Kore Hospital attached to JNMC, to know the incidence of Preterm Births in the centre, the mode of delivery in these preterm births, the risk factors associated and the outcomes in these neonates.

The incidence of preterm birth in this study setup was found to be 17.67%. which was much higher than the national average. According to WHO in 2022 – the global prevalence is 10.6%. Studies from 2010 – 2014 suggest that India has an incidence of nearly 13-17% (13·6% or around) and contributed to 23-24% preterm births globally[2]. This can be mainly attributed to the health facility being a tertiary care centre, high number of referrals for maternal complications, NICU care and institutional protocols leading to iatrogenic preterm deliveries. This data was similar to the results of a study done by Thangjam Devi et al., where the prevalence was found to be 15% [181]. Another study conducted by Begum et al., in 2003 showed an astonishing 23.3% incidence of preterm births [182].

According to the different categories of preterm, the incidence of Extremely preterm (<28 weeks) was 7.14%; Very preterm – gestational age between 28 weeks and 31 weeks 6 days - was found to be 12.92% and Moderate to late preterm was 79.93% . Roberta et al., in 2019 conducted a 7 year study and founf that majority of all the preterm births belonged to the late preterm category and only 1.72% belonged to extremely preterm [183]. As in comparison with the global standards, a study done in 2021, by Morgan et al., the incidence of extremely preterm is around 2-5 in every 1000 pregnancy [184]. According to an Indian study done by Vandana et al., from 2019

- 2020 , the incidence of moderate to late preterm was more, the mean Gestational Age of preterm births was 34.39 ± 1.92 weeks. [185].

The incidence of Induced (iatrogenic) preterm in this study was found to be around 56%. Owing to the routine, regular ANC practices, early detection of the high risk pregnancies, the employment of the institutional protocols for treatment of each such cases, increasing burden of referrals from outside for management of these high risk cases, and for NICU admission – there is a rise in the number of iatrogenic preterm when compared to the spontaneous preterm. Globally, the incidence of iatrogenic preterm is around 30-40 %. A study done by Xi Chen et al., in the United States in 2021, showed around 38.5% incidence of iatrogenic preterm and around 61.5% spontaneous preterm births [186]. However, in an Indian study done by Vandana et al., from 2019 - 2020, there was around 70.40% spontaneous preterm births. There is an increasing trend in the incidence of iatrogenic preterm observed, following which the FIGO recommendations to reduce the iatrogenic preterm incidence was released in 2021. Several modifiable causes such as a single embryo transfer and reduction of preterm cesarean section rates have been recommended.

Contrary to the studies done in other countries [41] and few Indian studies [187] in 2021 done over a period of 2 years, by Chhabra et al., where preterm was linked to extreme poverty, Low birth weight and Small for gestational age, here, the mothers belonging to Urban population and Middle Income Status were more prone to deliver preterm – about 16.4% and 27.52% women belonged to SEC 2 in the rural and urban areas respectively.

The present study shows that women belonging to 21-30 years of age significantly contributed to the preterm birth. Similarly, a positive association of

preterm with maternal age 20 years and above was given by Buyun et al., 2019 [188]. However, a mean maternal age >= 35 years according to Xun Li et al., 2018 [189] and advanced maternal age > 40 years according to Florent et al., 2018 [190] lead to preterm deliveries. However, since Indian and other Middle Income Countries' practices and cultural norms generally tend to begin families at an earlier age, along with lack of availability of facilities for Artificial Reproductive Techniques, these numbers may be biased.

419 (71.25%) mothers who had preterm deliveries, belonged to a BMI of 23-24.9 kg/m^2. Maternal obesity pre-pregnancy has been strongly associated with preterm birth, according to Buyun et al., 2019 [188]. However, the conclusion of obesity leading to preterm birth cannot be given as it involves inclusion of other maternal medical and obstetric risk factors.

Contrary to studies done priorly, 331 (56.2%) women who delivered preterm were multigravida. A study done on 8,02,199 pregnancies showed that nulliparous women and women with gravidity >5 had an increased risk of delivering preterm spontaneously (Koullali et al., 2020) [191]. Primiparous women had higher risk of obstetric complications and inturn had increased risk of delivering preterm [192,193].

Many adverse outcomes have been associated with women having a bad obstetric history. Congenital infections, cervical incompetence are some important factors for the same. Around 86 (14.6%) women had a bad obstetric history – either as recurrent pregnancy losses or a longer married life in the current study, consistent with prior studies [195,102,194]. The reverse also holds true - studies showed that women with bad obstetric history had 48.6% chances of delivering preterm [196]. Since women

with bad obstetric history have associated risk factors, isolated factors for the preterm delivery in these cases have also been looked into in this study.

More than half of the cases – 211 (59.94%) were unregistered in the study setting. This reiterates the fact that the incidence of unregisteredcases are more among tertiary care centres like our hospital. Mothers with antenatal visits - less that 4 throughout the pregnancy and unregistered cases were delivering preterm, according to Tekley et al,2018 [197]. In these cases, any high risk factors in the pregnancy are more likely to be missed.

Many studies on preterm have established prominent risk factors leading to the same. However, a clear distinction or classification of the different risk factors have not been made in a concise manner**.**

In this study, we have classified all the risk factors into different strata – such as Maternal medical factors, Obstetric factors, Fetal factors and studied the individual risk factors as a part of the group.

In the current study, maternal medical risk factors were contributing to 39.6% (233 women), overpowering the obstetric risk factors and making it the prime contributor for preterm births.

Among the maternal medical conditions, Urinary tract infection contributed to a total of 47 (8%). Around 14 (2.38%) Covid positive mothers also delivered preterm.

Approximately 38.46 % of women who have delivered preterm in our study, have a past history of preterm birth. Cobo et al., in 2020 women who have delivered a preterm priorly, have 4-6 times greater risk of delivering preterm in the current

pregnancy [198]. Shorter interpregnancy interval (<18 months) has been strongly associated with subsequent preterm births [49].

Anemia has been known to be an important cause of preterm births and low birth weight. There was a strong association of Anemia with preterm birth (O.R. 3.42) according to a study from North India, 2019 [199]. Severe anemia and history of blood transfusion was analysed in our study and around 1% of the patients were identified. The incidence among other types of anemia was not analysed in the current study.

Among the chronic maternal medical conditions, strikingly, hypothyroidism has proved to be a significant contributing factor – around 97 (16.5%). According to Casey et al., who did a study on subclinical hypothyroidism and the effect on the perinatal outcome, there was a 2 fold increase of preterm deliveries [200]. While there was a significant three fold increase among very preterm deliveries, the moderately preterm deliveries were unaffected, according to Alex et al., 2005 [201]. However, in our study – Hypothyroidism was associated with 15.66% of moderate to late preterm deliveries. Stringent monitoring by decreasing the threshold of S. TSH for the detection of hypothyroidism and better thyroid control can prevent further complications. Although it is a well-known risk factor for a plethora of diseases, this particular arena is a scope for further exploration.

Preeclampsia, caesarean delivery, cerebrovascular accidents, preterm birth, fetal growth restriction and maternal and perinatal death are only a few of the consequences that chronic hypertension in pregnancy is linked to, according to Ashley et al., 2020 [202]. In our study, 3.57 % of the chronic hypertensives have delivered preterm. According to Baha et al., 2000, about 33.1% of the women had hypertension of some form – either chronic or gestational [203].

Obstetric risk factors in the current pregnancy contributed to 26.9% of the preterm births in our study. This case-control study by Rahele et al. in 2014 at three maternal hospitals in Iran reports the prominent risk factors which are statistically significant and include obstetric risk factors like bleeding or spotting amidst pregnancy, oligohydramnios, hypertension, urinary tract infection and premature rupture of membranes [204].

Hypertensive disorders of pregnancy including Gestational Hypertension, Preeclampsia and Eclampsia, HELLP syndrome were contributing 118 (20.06%). Preeclampsia contributed 60 (10.2%) – which was statistically significant. One of the most recent meta-analysis with around 11 studies conducted in 2022 by Tsujimoto et al. [205], 11 studies with a combined 752 316 participants were found. Preterm birth, LBW, or SGA were linked to preeclampsia (pooled odds ratio (OR),1.35;) and gestational hypertension (pooled OR, 1.31;). Eclampsia was not assessed as a result in the study. A study conducted in Northern India by Pandan et al., [206] over a period of three years also found similar association of preterm among Hypertensive disorders of pregnancy - 102 (25.3%) had respiratory distress syndrome with preterm births, 33 (8.2%) had FGR with preterm births. Similar association was shown with Hypertensive disorders of pregnancy in an Indian study in 2021 [207].

PPROM contributed significantly – 26.02% in the current study. According to a study in India by Raveena et al., in 2021, [207] PPROM (O.R. – 10.27) was strongly associated with preterm. 04-047% pregnancies have been associated with PPROM [208]. Although the cases are multifactorial, as described in the article before, there is a strong association with infections – extra amniotic and intraamniotic.

4 (0.6%) women had diagnosed uterine anomalies were in our study. The risk differs with the type of uterine malformation. Uterine didelphys, unicornuate uterus, septate uterus and bicornuate uterus have different incidence of preterm birth – 56%, 43%, 31% and 39% respectively [209].

Prior studies conducted in our hospital settings [210], stated that around 9% of the PPROM was contributed by GDM. This was in concordance with our study, where 7.48% of the cases had GDM as a risk factor. Similar results (12.6%) have been obtained from studies made by Ostlund Ingrid et al., [211] Dittakaran et al., in their study concluded that around 7.4% was the incidence of preterm [212].

Around 10.54% of the cases of preterm had oligohydramnios, falling mostly under the moderate to late preterm birth category. A study by Jun Zhang et al., [213] in 2004 stated that adverse perinatal outcomes are not a result of isolated oligohydramnios. Alongside other fetal anomalies, Preterm Premature rupture of membranes, Diabetes, Hypertension, Fetal Growth Restriction, it is more likely to produce adverse outcomes. 3.06% of the preterm births were contributed by cervical incompetence.

Fetal risk factors contributed to around 26.19% of the total preterm births. 15.64% of the still births – delivered preterm - either induced or spontaneous.

One of the most important factor observed was multiple pregnancy – 11.9% of the total preterm births. Complications of the overdistension of uterus or along with several maternal obstetric risk factors due to the higher levels of pregnancy-related hormones may relate to the higher number of preterm pregnancies.

Among singleton live pregnancies, Fetal growth restriction with increased resistance on doppler caused 14.97% of the preterm births – which was statistically significant (p-value 0.0206).

Fetal malformations in general, contribute to preterm deliveries- either iatrogenic or spontaneous. The influence of malformations on the liquor status increases the risk of preterm deliveries. 2.21% of the preterm deliveries were due to Fetal malformations – the most common was fetal cardiac anomalies incompatible with life. This is largely due to early detection with advanced Ultrasound techniques and timely intervention done in our setup. Nearly 3% was the incidence of congenital malformation, and they are more likely to be delivered moderately preterm (R.R. 1.95) and very preterm (R.R. 3.45), according to a one year study done by Jordan et al., 2007 [198].

About 10.88 % of the population had no identifiable risk factors for occurrence of preterm birth**.**

They were spontaneous preterm births with unruptured membranes. While a few of these cases may suggest an underlying sub-acute infection or villitis, some may have a placental insult which may have been overlooked or undetected during the short study period also due to the limited resources available at the study setting.

Upon pondering on the contributors of the different risk factors of the preterm births, there is still some amount of clarity that is required to ascertain whether the over-diagnosis of certain maternal and fetal conditions have been leading to iatrogenic preterm births.

The three most important causes of iatrogenic preterm deliveries were identified as placenta previa, multiple pregnancies, and hypertensive disorders during pregnancy. Among the women who underwent induction of labour for medical conditions, 72.8% belonged to the Hypertensive group, (Xi Chen et al., 2021) [186]. While, induction of labour in view of Fetal Intra-uterine Growth restriction was the commonest indication for induction of labour in this study – 34.27% in our study setup, the most common maternal medical condition requiring induction of labour was Hypertensive disorders of pregnancy – 19.5% of the total number of cases that underwent induction of labour. Understamdably, the group undergoing preterm induction of labour significantly belong to the moderate to late preterm.

Administration of antenatal corticosteroids is done as a routine practice in our study setup. Almost 60% of the mothers in preterm labour received atleast 1 dose of Betamethasone. 37.9% of the mothers had received the complete dose. The mean gestational age which received Betamethasone in the study was 32 weeks ± 3 days. About 1% of the participants received Dexamethasone – atleast 1 dose. 39% of the mothers did not receive any steroids. These patients had either Intra Uterine Fetal demise, belonged to gestational ages beyond 36 weeks or were admitted in second stage of labour.

Another important drug - Magnesium sulphate was given for neuroprotection or in women with Pre-eclampsia with imminent signs. Around 10.37% of the mothers who delivered preterm received the same in our study. The mean gestational age at which these women received the drug was 30 weeks ± 3 days.

The rate of preterm LSCS was significant – about 65.95% of the total preterm deliveries. Studies done previously in this hospital had similar results [214]. Among the preterm Cesarean Sections, 5.9% of them were done Electively. As expected, the incidence of Cesarean section was maximum among the moderate to late preterm (94.3%). This corelates well with the fact that the obstetric complications including changes in the hematological parameters, placental and uterine artery changes, [215, 216] are more in the third trimester and the chances of survival of a neonate born in third trimester is associated with a better outcome. A study done by Xi Chen et al., in the United States in 2021, [186] Cesarean section birth was the most in the iatrogenic group – twice more than the spontaneous preterm.

Previous 1 or more LSCS (23.37%) was the most common indication for LSCS in our study, followed by Fetal distress contributing upto 9.61%. An Indian study done in 2022 by Jana et al., also concluded that Previous history of cesarean section was an strongly associated with preterm birth [217]. Hypertensive disorders of pregnancy – Severe Pre eclampsia with imminent signs – contributed to 10.9% of the preterm LSCS in our study. Placenta previa and Abruptio placenta contributed to 2.07% and 1.3% of the preterm Cesarean sections.

The birth characteristics in the preterm neonates were studied. About 58.56% of the preterm neonates were male. Prior studies have shown that it is a risk factor that is relevant to mainly spontaneous preterm incidence [218]. Interestingly, the presence of an amorphous twin in a multifetal gestation was noted during the course of the study. As discussed earlier, 92 (13.98%) of the neonates were stillborn out of which 51% were macerated still birth.

Most of the preterm newborns – 78.45% had an APGAR score between 7-10. Out of the 566 neonates, 298 required NICU care, 92 went to KMC and 31.1%(176) babies were mothers' side. As seen earlier, the incidence of moderate to late preterm occupies the largest weightage and hence, the above results are consistent with the same.

The mean birthweight observed was 1.93 ± 0.7 kg. Out of 658 neonates, 199 (30.24%) had birthweight in the range 2.01 kg to 2.5 kg, 22.64% had birthweight in the range 1.51kg to 2 kg and 18.84% had birthweight in the range 1.01 kg to 1.5 kgs.

In our study, out of the 298 (52.67%) neonates which required admission to NICU at birth or at any point during the hospital stay, the commonest indication was Hyperbilirubinemia (32.8%) following which Very Low Birth weight (20.8%) preterm newborns required NICU admission. The mean duration of NICU stay was 8 days. In 9.7% of the preterm neonates, sepsis was identified as a complication either separately or co-existing with other complications.

Neonatal complications were observed in around 215 (37.98%) neonates. These complications co-relate with the need for NICU admission. The commonest was found to be Hyperbilirubinemia (23.15%). Feeding difficulties were reported in 20.8 % of the cases. Some conditions like Oliguria/ Anuria and Intra Avleolar Hemorrhages, Cerebral hemorrhage and Neonatal shock or Heart failure were serious conditions which were uncommon in this study. 18.95% of the babies did not have any complications throughout the course of the study.

The effect of steroids on the outcome of the newborn was also noted. Around 30.87% of the neonates whose mothers had received atleast one dose of

betamethasone, required NICU admission, 26.9% of the neonates had mortality. Out of the cases that received Dexamethasone, there was a contribution of 1% of the total NICU admissions and 3.8% contribution to the neonatal mortality. These data donot lead us to any conclusion as the long term effects of the steroids have not been studied and also, the neonatal outcome associated with the incomplete dose administration of the drugs were not discussed. The efficacy of both the steroids is unremarkable as the total number of mothers that received Dexamethasone is negligible in comparison to those who have received Betamethasone.

Still births contributed to a total of 14% among the total preterm births. Neonatal mortality was recorded upto 52 (9%) neonates among the 566 live births in our study. Perinatal mortality was a staggering 22% of the total live births over the study period. The mean gestational age at which the mortality occurred was 28 weeks + 6 days. 11 days was the mean time of death. In concordance to a recent Indian study done in 2022 by Jana et al., if the baby was born prematurely, the risk of death within the first 28 days of life increased by a factor of 2.5. [217]

46 neonates were born extremely preterm. A total of 26 were live born. 36.96% of the still borns were Fresh Still Birth. 100% of the neonates were admitted in the Neonatal Intensive Care Unit and all of them had atleast one complication. The commonest was Acute Respiratory Distress Syndrome and the mean birth weight was 0.712 ± 0.09 kg. Only 46.15% of the neonates survived until neonatal period. There is lack of clarity of the cause of death between birth asphyxia or Acute Respiratory Distress.

Among 93 very preterm births, 79 (26.58%) were live births. 10 were macerated still births out of the 14 still births in the study category. 68.3% of the babies required admission in Neonatal Intensive Care Unit and 54.49% of them had some form of complication – the most common being Sepsis. The survival rate was 73.41%.

The group contributing maximum to the total preterm births are the moderate to late preterm. Among 519 neonates born moderate to late preterm, 461(88.8%) were live births. Around 47% of the neonates required the facilities of Intensive Care Unit, nearly 30% of them had complication of some category, the commonest was Hyperbilirubinemia. A humungous 95.66% of the moderate to late preterm neonates survived. This category also contributed maximum to the still birth – 58 still births during the study period, which is analogous to the colossal number of newborns born at this gestational age.

CONCLUSION

The incidence of total preterm births is 17.67%. Moderate to late preterm and iatrogenic preterm births contributed maximum to the overall preterm birth rates. The commonest mode of delivery was Emergency LSCS. Approximately a quarter of preterm births have contributed to perinatal mortality.

Thus, early detection of medical risk factors in the mothers and pre-conceptional control of diseases like Hypothyroidism, Hypertension, Type 2 Diabetes Mellitus is recommended for prevention of preterm births and to achieve better maternal and neonatal outcomes.

Further research should focus on reducing the iatrogenic preterm and for better and early control and diagnosis of obstetric risk factors in the mother.

SUMMARY

Preterm births are a rising issue in the current world and is associated with iatrogenicity. Several maternal and neonatal factors have been linked with preterm birth. Our study was done to probe into the various factors responsible for the preterm deliveries and the subsequent outcomes of the preterm births.

The incidence was found to be 17.67% in the study period. Majority – 79.93% of the preterm births belonged to the moderate to late preterm category. Around 56% of the preterm births were iatrogenic preterm births in our study and FGR contributed to 34.27% of iatrogenic preterm births. 39.6% of the participants had maternal medical risk factor.

Only upto 11% of the mothers had no associated risk factors. The most common maternal medical risk factor was Hypothyroidism.

While significant obstetric risk factors included PPROM (26.02%), Pre-eclampsia (10.2%), FGR contributed to 22.10% fetal risk factors. 15.64% of the neonates were still born. 61% of the patients in the study received atleast a single dose of steroid – 37.9% of them received 2 doses of Betamethasone. MgSO4 for neuroprotection was administered for 10.37% of the mothers.

The most common mode of delivery was by LSCS (65.99%), 94% of them were emergency LSCS. Previous one or more LSCS was the most common indication for LSCS. The mean birth weight was 1.9 kg. 298 (52.65%) babies were admitted to NICU for complications or observation.

The most common complication was Hyperbilirubinemia. 84% of the neonates were stable at the time of discharge and around 9% of the neonates expired as a result of complications and the mean time of death was 11 days.

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ANNEXURE - I

INFORMED CONSENT (ICF) FOR PARTICIPATION IN RESEARCH STUDY

Mr. /Mrs. /Miss.---------- we are requesting you to enroll you in the study titled "**A ONE YEAR CROSS SECTIONAL STUDY OF PRETERM BIRTH IN A TERTIARY CARE CENTRE IN SOUTH INDIA**" conducted by **Dr. _____** Post Graduate in M.D. Obstetrics and Gynaecology under the guidance of **Dr. _____ M.D.,** Associate Professor, Department of Obstetrics and Gynaecology, J.N. Medical College, Belagavi under KAHER, Belagavi.

Respected Sir/Madam, we request you to participate in our study as you are eligible for it. During the study you will be asked some questions regarding your medical history and you are supposed to answer to the best of your knowledge.

Your participation in this research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J.N.Medical College. If you decide to participate you are free to withdraw at any time.

Purpose of the study: This study's objective is to know the prevalence and the risk factors which will give us an advantage to improve the survival rate, minimise the duration of hospitalisation, morbidity and mortality of both the mother and the new born.

Procedure Involved: After obtaining the approval from ethical committee and a written informed consent, a total of 998 patients, after fulfilling the inclusion criteria will be included in the study. Recruits for the study will be questioned and examined for Period of Gestation, Parity, BMI and other details like Mode of Delivery, Duration

of Labour, Complications during or prior to delivery, Baby weight, APGAR, need for NICU admission and neonatal outcomes.

The steps used for data collection as follows:

— Investigator needs to find out the prospective candidates and explain the objectives and steps of study and take an informed consent.

— Data will be interpreted by using descriptive and inferential statistics.

Type of study:

Voluntary Participation/Withdrawal:

Risks: There are no potential risks involved in this study.

Benefits: Your participation in this research will help us understand the prevalence, risk factors and the outcomes of the preterm birth, which will help us improve the current practices and reduce the morbidity and mortality of both the mother and the child.

Privacy and Confidentiality: The only people to know that you are as research subject are you and members of the research team. No information provided by you during the research will be disclosed to other without your written permission except:

1. In emergency to protect your rights and welfare.
2. If required by law.

Financial Incentives for participation: No financial incentives are being offered to enrolled patients. It is purely being done with the idea of research and all the cost of the study will be borne by the investigator.

Authorization to Publish Results: When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with your identity remaining confidential.

Compensation: In the event of injury related to the study, treatment will be made available through KLES Hospital and MRC, Belagavi. There is no compensation or payment for such medical treatment by law. If you get injured you may contact Dr. K ROSHNI at Department of Obstetrics and Gynaecology, J.N. Medical College or by Ph. No: 9840590666.

Questions: If you have any queries about your rights as a study subject, you may call **Dr. HARSHA HEGDE,** Chairperson, JNMC, IEC & Scientist D, ICMR, National Institute of Traditional Medicine and Chairman, J.N. Medical College Institutional Ethical Committee for Human Subjects Research, Phone number- 9448113403, J.N. Medical College, Belagavi.

INFORMED CONSENT FOR PARTICIPATION IN RESEARCH TRIAL

"A ONE YEAR CROSS SECTIONAL STUDY OF PRETERM BIRTH IN A TERTIARY CARE CENTRE IN SOUTH INDIA"

Ms./Mrs. _____ voluntarily agree for the participation of as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Is the participant eligible? Yes ☐ No ☐

Subject Name : _____

Signature or the Left Thumb Print of Subject/Guardian: _____

Date:

Witness Name: _____ Signature: _____

Investigators Name: _____ Signature: _____

Date:

Place : _____.

ANNEXURE - II

PROFORMA

BIO DATA:

SCREENING NUMBER
DATE OF SCREENING
OP/IP NUMBER
ENROLLMENT NUMBER
REFERRAL FROM OUTSIDE

FIRST NAME MIDDLE NAME LAST NAME

HUSBAND'S NAME

PATIENT PH NO.	
HUSBAND PH NO.	

AGE (Yrs) ADDRESS STREET
TALUK
DISTRICT

EDUCATION
OCCUPATION
S.E.C.

HUSBAND PATIENT

REGISTERED (>2 VISITS)	UNREGISTERED
(NO. OF VISITS)	

OBSTETRIC SCORE
DETAILS OF THE PREVIOUS DELIVERIES

MENSTRUAL HISTORY

LMP	
EDD	
POG	

GESTATIONAL AGE BY

LMP	
USG / CRL/ C.EDD	

PAST HISTORY	YES	NO
1. HYPERTENSION	☐	☐
2.DIABETES MELLITUS (OVERT)	☐	☐
3.THYROID DISORDERS HYPOTHYROID	☐	☐
HYPERTHYROID	☐	☐
4.SEVERE ANEMIA/BLOOD TRANSFUSIONS	☐	☐
5.H/O VAGINITIS	☐	☐
6.ACUTE FEVER	☐	☐
7.ACUTE PYELONEPHRITIS	☐	☐
8.DIARRHEA	☐	☐
9.DIAGNOSED UTERINE ANOMALIES	☐	☐
10.ABDOMINAL SURGERIES	☐	☐
11.HEART DISEASE	☐	☐
12.ASTHMA	☐	☐
13.PERIODONTAL DISEASE	☐	☐
14.PREVIOUS HOSPITALISATION	☐	☐
15.H/O ADMISSION FOR PRETERM	☐	☐
16.H/O AIDS	☐	☐

17.H/O HEPATITIS / JAUNDICE ☐ ☐
18.H/O AFLP

19.H/O PSYCHOLOGICAL ILLNESS ☐ ☐

MATERNAL DISEASES	**YES**	**NO**
1 PIH (PE/ E/ SEVERE PE/HELLP)	☐	☐
2 MULTIPLE PREGNANCIES	☐	☐
3 ANTE PARTUM HEMORRHAGE	☐	☐
4 GDM	☐	☐
5 POLYHYDRAMNIOS	☐	☐
6 PPROM	☐	☐
7 CERVICAL INCOMPETENCE	☐	☐
8 APLA POSITIVE	☐	☐
9 DIC	☐	☐
10 STILL BIRTH / IUD	☐	☐

DRUG HISTORY

H/O ADMINISTRATION OF STEROIDS COMPLETED COURSE

BETAMETHASONE	1.1 YES	☐	1.2NO	☐
DEXAMETHASONE	2.1 YES	☐	2.2NO	☐
H/O ADMINISTRATION OF ANTIBIOTICS	YES	☐	NO	☐
MgSO4	YES	☐	NO	☐

OTHERS

ADDICTION HISTORY PATIENT 3
HUSBAND 1
NO -0

FAMILY HISTORY

GENERAL EXAMINATION

HEIGHT (cms) WEIGHT (kg) BMI

PALLOR 1 YES ICTERUS 1 YES

THYROID	
CVS	
RS	
P/A	
P/V (AT ADMISSION)	

POST ADMISSION DIAGNOSIS

ROUTINE INVESTIGATIONS

Hb	
URINE ROUTINE AND MICROSCOPY	
URINE CULTURE	
TSH	
DIPSI / HbA1C	
USG FINDINGS (ANOMALY SCAN)	
HIV	
HBsAG	
VDRL	
TORCH	
OTHERS	

USG FINDINGS DURING ADMISSION

PLACENTA	
AFI	

EFW	
ANY OTHER ABNORMALITIES	

NATURE OF PRETERM DELIVERY SPONTANEOUS ☐ INDUCED ☐

MODE OF DELIVERY	**INDICATION**
EMERGENCY LSCS	
ELECTIVE LSCS	
VAGINAL DELIVERY	
VENTOUSE DELIVERY	

DURATION OF LABOUR

COMPLICATIONS DURING LABOUR

BABY DETAILS

NAME OF THE BABY (BABY OF) IP NUMBER

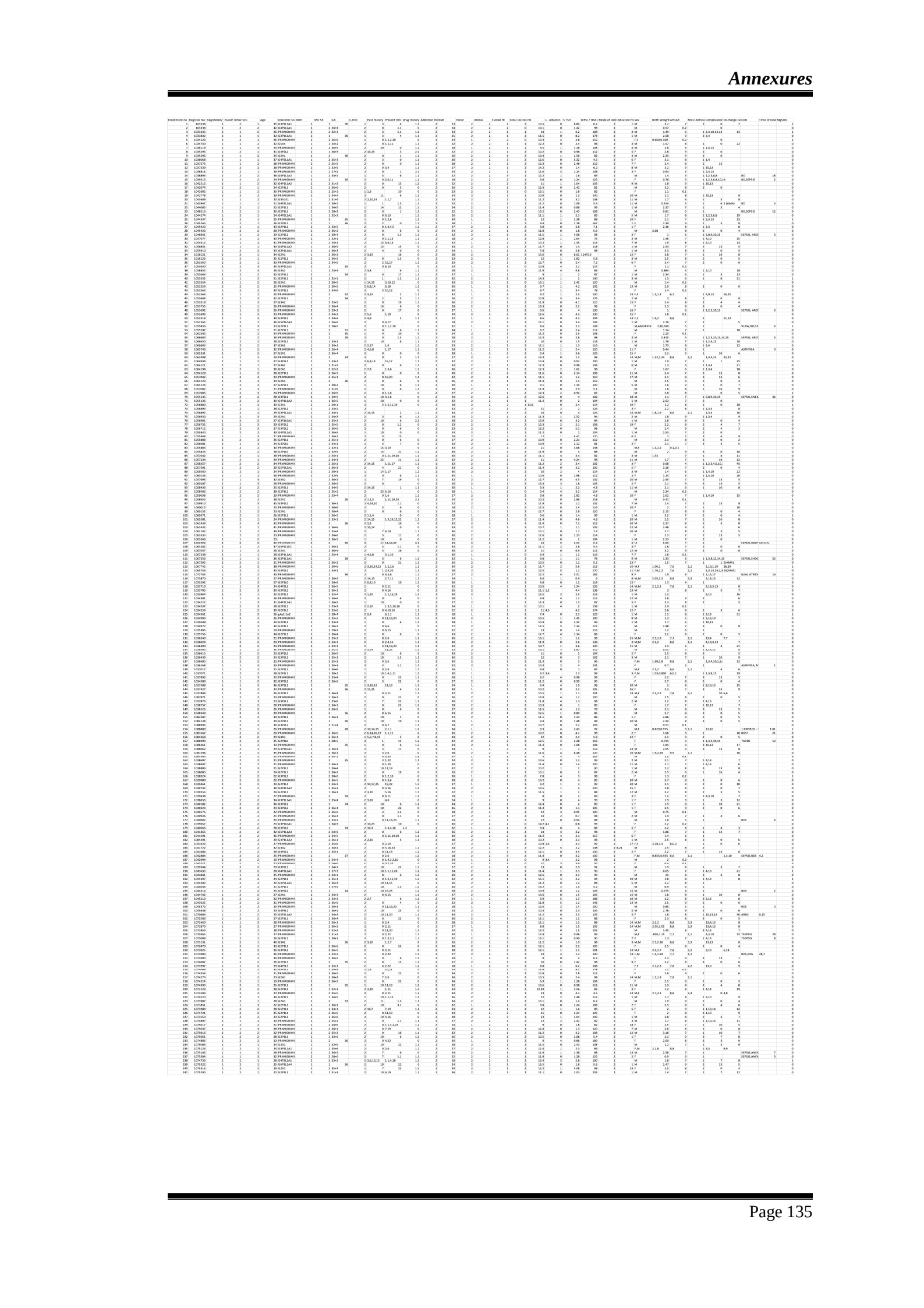
SEX APGAR (AT 5 MINS) BIRTH WEIGHT (KG)

POST DELIVERY STATUS

	NICU ADMSSION	**KMC ADMSSION**	**WARD ADMSSION**
INDICATION			
DIAGNOSIS POST ADMISSION			
DISCHARGE ON DAY			
CONDITION DURING DISCHARGE			

NEONATAL COMPLICATIONS	**YES**	**NO**
ASPHYXIA	☐	☐
HYPOTHERMIA	☐	☐
HYPOGLYCEMIA	☐	☐
HYPERBILIRUBINEMIA/ PATHOLOGICAL JAUND	☐	☐
CEREBRAL HEMORRHAGE	☐	☐
NEONATAL SHOCK	☐	☐
HEART FAILURE	☐	☐
SEPSIS	☐	☐
ANEMIA	☐	☐
ARDS	☐	☐
INTRA ALVEOLAR HEMORRHAGE	☐	☐
OLIGURIA / ANURIA	☐	☐
FEEDING DIFFICULTIES	☐	☐
METABOLIC ACIDOSIS	☐	☐
MORTALITY (DETAILS IF ANY)	☐	☐

ANNEXURE – III - MASTER CHART



																																		0
																																		0
353	1077748	1	1	1	24	PRIMIGRAVI	2	2	31+2	2	0	0	1.1	2	23	1	1	1	2	11	1	2.5	107	2	2	M	1.4	8	1	4	7			0
354	1077867	1	2	2	20	PRIMIGRAVI	2	2	33+4	2	3	6	1.2	1	32	1	2	1	2	10.5	1	0.9	5	2	9	F	1.8	6	1	4	4		52	0
355	1078343	1	2	1	34	PRIMIGRAVI	2	2	35+3	2	0	2,6	1.1	2	29	2	2	3	2	13	0	1.2	5.2	2	9	AMBIGUOUS	1.2,1.9	5,7	1,1	2,3,4,8; 4	12,7			0
356	1078351	2	1	2	23	G2P1L0	1	2	35+5	2	14	22	1.1	2	26	2	2	1	2	12.7	2	5.6	113	1		F	2	8	3	0	4			0
357	1077825	1	1	1	24	PRIMIGRAVI	2	2	33	2	3	1.1,11	1.1	2	28	2	2	1	1	12.5	3	7	101	2	3	F	1.1	5	1	2,3,4				1
358	1078840	1	1	1	30	G4P1L1A2	2	1	35	2	10	6,	1.1	2	27	2	2	1	2	12.2	1	3.51	88	2	1	M	2.5	7	2	4,13				0
359	1078539	1	1	1	30	PRIMIGRAVI	2	2	36+2	2	3	24	1.1	2	24	2	2	1	2	12	1	8	121	2	8	M	2.3	8	3	13	5			0
360	1078435	1	1	1	23	PRIMIGRAVI	2	2	30+2	2	5	6	1.2	2	28	1	2	2	2	10.2	0	1.2	118	1		M	1.44	6	1	8,10,13	15			0
361	1078634	1	2	1	24	PRIMIGRAVI	2	2	34	1	0	6	1.1	2	29	2	2	2	2	11	4	1.34	124	2	14	M,M	2.1,2.1	7,8	1,1	3,13;3,13	8			0
362	1078632	1	2	2	20	PRIMIGRAVI	2	2	34	2	15	22	0	2	26	2	2	2	2	12	0	1.2	122	1		F	1.8	8	2	3	7			0
363	1073689	1	1	1	27	G4P2L1A1	2	1	36+4	2	5	4,5,6	1.1	2	28	2	2	1	2	12.5	0	2.5	116	2	1	F	2.5	9	2		4			0
364	1078635	1	1	1	32	G2P1L1	2	2	36+6	2	10	22	0	1	30	1	2	1	2	13	1	1.2	112	2	1	M	3.2	9	2		3			0
365	1078756	2	2	2	28	G3P2L1	2	2	36+5	1	0	1.1,25	1.2	2	27	2	2	1	2	10.3	2	1.5	87	2	6	M	1.8	8	1	2,3,12,13	10			0
366	1178509	1	1	1	28	PRIMIGRAVI	2	2	29	2	3	11,22	1.1	2	24	1	2	1	0	14.9	4	2	120	2	1	F	1.5	7	1	4,10,14	17			0
367	1178746	1	1	1	30	G3P1L1A1	2	2	35	2	3	1.1	1.2	2	22	2	2	1	1	13.2	4,5	4.2	112	2	12	M	1.46	7	1	16	11			0
368	1178849	1	1	1	28	G3P1L1A1	2	2	34	2	15	6	2.1	2	23	1	2	1	2	11.9	0	2.3	123	1		M	2.5	7	2	0	3			0
369	1179424	1	1	1	39	G6P1L1A4	1	1	36+3	2	10,21	6,7	0	2	24	2	2	1	2	11	1	1.45	100	2	8	F	2.6	8	2	13	4			0
370	1079121	1	1	1	34	PRIMIGRAVI	2	2	26+4	1	3	6	1.1	2	28	1	2	1	3	9	0	2.34	116	1		F	0.659	0.1						0
371	1079619	1	1	1	30	PRIMIGRAVI	2	2	30+4	1	15	19	0	2	27	2	2	1	1	11.2	5	1.34	112	1		M	1.2	0.2						0
372	1079838	1	1	1	22	PRIMIGRAVI	2	2	36+2	2	15	6,15	1.1	2	32	2	2	1	2	11.2	0	1.4	116	1		M	2.7	8	1	0	3			0
373	1080159	1	1	1	34	G3P2L2	1	2	36+4	2	23,10	6	0	2	33	2	2	1	2	12.5	4	1.34	88	2	5	F	2.8	8	2	0	5			0
374	1079948	1	1	1	21	PRIMIGRAVI	2	2	24	2	3	1.4,20	1.1	2	32	2	2	3	2	13.8	1	1.2	98	1		F	0.5	0.1						0
375	1079999	2	1	2	22	PRIMIGRAVI	2	2	29+6	2	16	1.3,25	1.2	2	30	2	2	3	2	11.9	0	2.6	112	1		F	0.58	2	1	10,12,14,15		ASPHYXIA, M	1	0
376	1080020	1	1	1	23	G2A1	2	2	34+2	1	15	2,7,11	1.2	1	34	2	2	2	1	13.2	1	3.6	120	2	8	M,M	1.7,1.46	8,6	1,1	13,2,3,4	7,8			0
377	1079326	1	1	1	23	PRIMIGRAVI	2	2	36+1	2	3	1.3	1.2	2	32	2	2	1	1	10.1	4	6.87	112	1		F	2.5	2	8	0	3			0
378	1080410	1	1	1	23	G2P1L1	2	2	36+6	2	4	6	0	2	33	2	2	1	2	11	0	2	104	2	2	F	2.5	8	3		5			0
379	1080518	1	1	1	24	PRIMIGRAVI	1	1	36+6	2	10	1.3,10	1.1	2	36	2	2	1	2	12	0	3	102	2	1	M	2.4	0.2						0
380	1080301	1	1	1	22	PRIMIGRAVI	2	2	36+4	2	3	4,6	1.2	2	30	2	2	1	2	11.3	0	3	96	2	2	F	2.1	8	2	13	4			0
381	1080517	1	1	1	23	PRIMIGRAVI	2	2	36+3	2	0	22	1.1	2	32	2	2	1	2	10.3	2	4	101	1		M	2.6	8	2	0	4			0
382	1080405	1	1	1	24	G2P1L1	1	2	36+6	1	0	3	1.2	2	26	1	2	3	1	9.8	0	1	85	2	7	M	4.8	8	2	3,13	8			0
383	1080734	2	1	2	28	PRIMIGRAVI	2	2	32	1	1	3.2,10	0	2	30	1	1	3	1	9.2	3	2.3	99	1		M	1.2	0.1						0
384	1080720	1	2	1	26	G2P1L1	2	2	35+6	2	15	10	0	2	28	2	2	1	2	10	4	2.2	119	1		F	1.7	0.2						0
385	1080127	1	1	1	35	PRIMIGRAVI	2	2	32+1	2	3	1.1,24	1.1	2	30	1	2	1	1	10	1	2	87	2	3	F	1.62	6	1	8	13			1
386	1080773	1	1	1	30	PRIMIGRAVI	2	1	36+3	2	14,15	2,15	0	2	32	2	2	2	2	14.3	1	2	140	2	14	F,F	2.4,2.7	8,8	2,2	3,13	5,5			0
387	1081314	1	1	1	24	G2P1L1	2	2	35+3	1	8	22	1.1	2	33	2	2	2	0	13.1	1	2.45	120	1		F	2.6	8	2	3	5			0
388	1080420	1	2	2	26	G4P3L3A1	2	2	36	2	3	22	0	2	36	1	2	1	2	11	1	5.4	102	1		F	2.5	8	2	0	6			0
389	1081446	1	1	1	25	PRIMIGRAVI	2	1	35+2	2	17	26	1.2	2	30	1	2	2	0	9.7	1	3.4	78	2	2	F	1.9	8	2	3,4	8			0
390	1081448	1	1	1	30	G2P1L1	1	2	36+5	2	1.1	3,15	0	2	32	1	2	3	2	9.2	1	2.5	100	2	1	M	2.5	8	2	13	5			0
391	1081261	1	1	1	20	PRIMIGRAVI	1	2	36+2	1	0	10	0	2	26	2	2	3	1	10.8	5	3.4	176	2	1	M	2.6	8	2	0	5			0
392	1081435	1	1	1	21	PRIMIGRAVI	2	2	32+5	2	14	1.1,20	1.2	2	30	2	2	1	2	11.9	0	4.1	110	2	15	F	2.4	8	2	4	4			0
393	1081121	1	1	1	29	G3P1L1A1	2	2	35+3	2	3	1.3,16	1.1	2	28	2	2	1	1	13.3	0	2.2	98	2	3	F	1.2	6	1					0
394	1088847	1	1	1	26	G6P1L0A3	2	1	36+5	2	15	7,22	1.2	2	27	1	2	1	2	11	0	3.1	130	1		M	2.7	7	2	13	4			0
395	1081758	1	1	1	23	G2A1	2	2	35+5	2	3	22	1.1	2	24	2	2	2	2	12.6	4	5	130	2	6	M	2.46	6	2	0	5			0
396	1081794	2	2	1	27	G3A2	1	2	36+3	2	18	1.4	1.1	2	30	1	2	3	2	8.6	0	4.3	104	2	16	M	3.1	0.2						0
397	1082057	1	1	1	24	G3P2L2	1	1	36	2	10	6	0	2	18	2	2	1	2	12.1	0	3.4	106	2	5	F	2.2	8	3	0	5			0
398	1082360	2	1	1	20	PRIMIGRAVI	2	2	36+5	2	3	6	0	2	32	1	2	3	1	10.6	0	2.3	108	1		F	3	7	2	13	5			0
399	1081783	2	2	1	38	PRIMIGRAVI	2	2	36+6	2	3	25	0	2	34	1	2	1	2	12.6	1	2.4	112	2	22	F	2.2	8	2	3	6			0
400	1082394	1	1	1	23	PRIMIGRAVI	2	2	36	1	0	2,7	0	2	24	2	2	1	2	11.2	1	2.5	108	2	14	F,M	1.1,2.4	7,8	1,3					0
401	1082393	1	1	1	26	PRIMIGRAVI	2	2	28+3	2	0	1.2	1.1	2	28	2	2	1	2	12.3	3	2.8	98	2	19	M	1.08	4	1	1,2,3,10,13,14,15				0
402	1082626	2	1	1	28	G2P1L1	2	1	29+3	2	0	10	0	2	23	2	2	1	2	10	0	1.5	118	2	1	F	1.1	0.2						0
403	1082768	1	1	1	30	PRIMIGRAVI	1	2	33+6	2	0	1.2	1.1	2	23	2	1	1	2	12.1	1	1.3	116	2	19	M	1.5	6	1					0
404	1082535	1	2	1	37	PRIMIGRAVI	2	2	35+1	2	15	20,24	1.2	2	24	2	2	1	1	11.2	1	2.4	120	2	2	F	1.2	1				ASPHYXIA	0	0
405	1082875	1	1	2	34	G3A2	1	1	36+1	2	0	6	0	2	24	1	2	1	2	9	0	2	122	2	6	F	2.6	9	2	0	5			0
406	1082805	1	1	1	26	G2P1L1	2	2	31	2	1	11,19	1.1	2	22	2	2	1	2	10	0	1.42	98	2	9	F	2.2	8	3	0	6			0
407	1083256	1	2	1	22	G2P1L0	2	2	36	1	0	22	0	2	18	1	2	3	1	8.8	1	6.2	108	2	1	M	2.6	8	2	13	5			0
408	1083501	2	1	2	26	G3P2L1	2	2	31+6	2	14,15	2.1,6	1.1	2	24	2	2	2	0	12.6	0	8.2	117	1		F,F,F	1.5,1.4,1.3	6,7,6	1,1,1					0
409	1083239	1	1	1	21	G2P1L1	2	1	35+6	2	10	6	1.1	2	34	2	2	1	2	10.8	0	2.8	112	2	1	F	1.76	8	1	2,3,4	9			0
410	1083256	1	2	2	22	G2P1L0	2	1	36	2	10	6	0	2	36	2	2	3	2	10.5	0	2.4	98	2	1	M	2.5	8	2	0	5			0
411	1082095	1	1	1	21	G2P1L1	2	2	34+3	2	0	2,25	0	2	34	2	2	1	2	9.9	1	1.28	108	2	14	M,M	1.8,1.3	7,8	1,1					0
412	1082587	1	1	1	34	G2P1L1	1	2	36+1	1	10	1.3	1.2	2	32	2	2	1	1	10.6	0	0.98	112	2	1	F	2.86	9	2	4	5			0
413	1083554	1	1	1	27	G3A2	2	2	34+4	1	17,18	1.3,19,9	1.1	2	30	1	2	1	0	6.9	1	1.2	116	2	7	M	2.8	0.1						0
414	1083748	1	1	1	26	PRIMIGRAVI	1	2	36+6	2	10	1.1	0	1	32	1	2	1	2	11	1	1.1	78	1		M	2.4	8	2	0				0
415	1083103	1	1	1	20	PRIMIGRAVI	2	2	33	2	14	22	1.1	2	26	2	2	1	2	10.5	0	1.2	5.2	1		M	1.9	7	2	4,16	6			0
416	1083913	1	1	1	38	PRIMIGRAVI	2	1	36+6	2	0	19	0	2	30	2	2	3	2	11.7	2	5.6	113	2	22	M	2.4	8	2	16	5			0
417	1083908	1	1	1	30	PRIMIGRAVI	2	1	36+3	2	0	2,6	0	2	28	2	2	1	1	12.5	5	1.2	170	2	14	F,F	2.4,2.4	8,8	3,3	13,4;4	5,6			0
418	1083934	2	1	1	33	PRIMIGRAVI	2	2	36	2	0	6	0	2	27	2	2	1	2	12.2	4	3.51	118	2	9	M	2.2	8	2	4	6			0
419	1083967	1	2	1	27	PRIMIGRAVI	2	2	35+1	2	0	1.1	1.1	2	24	1	2	3	1	11	1	0.9	6	2	2	M	1.7	8	2	4	4			1
420	1083738	1	1	1	27	PRIMIGRAVI	2	2	36+6	2	0	22	1.1	2	30	1	2	2	2	9.8	0	1.2	118	1		M	2.4	9	2	0	3			0
421	1083480	1	1	1	26	G2P1L1	2	2	33+2	1	14,15,23	2,22	1.2	2	32	2	2	3	1	10.6	4	1.34	126	2	14	M,M	1.8,1.9	7,8	1,1	3,13;3,13	8			0
422	1084108	1	2	1	30	G2P1L1	1	2	30	2	10	10,20,1.1	0	2	26	2	2	1	2	11.1	1,5	4.4	138	1		M	0.9	0.2						0
423	1084031	1	1	2	24	PRIMIGRAVI	1	2	28	2	10	2,22	1.1	2	30	2	2	1	2	12.5	3	2.5	116	1		M,M	0.8,0.9	6,5	1,1					0
424	1083993	1	2	1	30	G3P2L2	2	2	22	2	0	6	0	1	28	1	2	1	2	9.8	4	1.2	112	1		M	0.4	0.1						0
425	1084138	2	1	1	29	G2P1L1	1	2	36	1	10	19	0	2	27	2	2	1	2	12.3	0	1.5	87	2	5	F	2.7	8	2	0	5			0
426	1084633	1	1	2	26	PRIMIGRAVI	2	2	36+2	2	3	1.3,11,13	1.2	2	24	1	2	1	0	10.1	4	2	123	2	22	M	1.4	7	1	1,4,8	16			0
427	1084313	2	1	1	30	PRIMIGRAVI	1	2	34	2	9	25	1.2	2	22	2	2	1	1	11	4,5	4.2	122	2	2	M	1.3	8	1	3,4,14	11			0
428	1085005	1	1	1	24	PRIMIGRAVI	2	2	36+1	2	0	10,11	0	2	18	1	2	1	2	10	0	2.3	123	1		M	1	0.2						0
429	1085107	2	1	2	25	PRIMIGRAVI	2	2	34+6	2	0	22,15	0	2	24	2	2	1	2	10.5	1	1.45	100	1		F	2	8	3	2,13	6			0
430	1084792	1	2	1	33	G3P2L2	1	2	36+5	1	10	2,1.3,4	0	2	28	1	2	1	2	10.4	0	2.34	99	2	5	M,F	2.4,2.5	8,7	2;1	0;1,8	5,18			0
431	1084368	1	1	2	29	G4A3	2	1	36+3	2	6,7,5	16	0	2	27	2	2	1	2	12.5	5	1.34	112	2	8	M	3.1	9	2	0	5			0
432	1085208	1	2	1	22	G2P1L1	2	2	35+6	2	0	22	1.1	2	32	2	2	1	2	13	0	1.4	116	1		F	2.7	9	2	13,16	4			0
433	1085303	1	1	2	26	PRIMIGRAVI	2	2	34+6	2	0	22	0	2	33	2	2	1	2	12.7	4	1.34	88	2	17	M	1.7	8	1	1,10,4	9			0
434	1085745	1	1	1	19	PRIMIGRAVI	2	2	36	2	0	22	1.1	2	36	2	2	3	2	13.1	1	1.2	98	1		M	2	8	2	3,4	7			0
435	1088817	2	2	1	21	PRIMIGRAVI	2	2	36	2	0	6	0	2	30	2	2	3	2	11.9	0	2.6	138	2	2	M	2.2	8	2	4,13	7			0
436	1085628	1	1	1	23	G2P1L1	2	2	34+2	1	3	4,25,15	1.2	1	32	2	2	2	1	10.7	1	3.6	156	2	22	M	1.1	6	1					0
437	1086055	2	1	2	27	PRIMIGRAVI	2	2	35+3	2	3	2	1.1	2	32	2	2	1	1	10.1	4	6.87	112	1		M,M	1.4,2.3	6,8	1,2	1,14,15;0	12,5			0
438	1086062	1	2	1	34	G3P1L0A1	2	2	36	2	3	25	0	2	33	2	2	1	2	11	0	2	104	2	8	M	2.05	8	3		7			0
439	1086255	1	1	2	34	G3P1L1A1	2	1	27+4	2	0	1.1,11,19	1.1	2	36	2	2	1	2	12	0	3	102	1		F	0.64	0.1						1
440	1086521	1	1	1	25	G2A1	2	2	34+6	2	3	22	1.1	2	30	2	2	1	2	11.3	0	3	96	1		M	2.3	8	3	4	6			0
441	1086532	2	2	1	22	G2P1L1	2	2	34+3	2	0	6	1.1	2	32	2	2	1	2	10.3	2	4	101	1		F	1.9	7	1	10	11			0
442	1086461	1	1	2	21	PRIMIGRAVI	2	2	35	1	0	22	1.2	2	26	1	2	3	1	9.8	0	1	85	1		F	1.84	7	1	4,10	12			0
443	1086569	1	1	1	26	G2P1L1	2	1	28+6	1	0	13	1.2	2	30	1	1	3	1	11	3,4	2.3	99	1		M	0.23	0.2						0
444	1086830	2	2	1	36	G2P1L1	1	2	36+5	2	10	11,19	0	2	28	2	2	1	2	11.9	4	4.8	86	2	1	F	2.1	7	1	10,8	12			0
445	1083659	1	2	2	25	PRIMIGRAVI	2	1	34+5	2	0	1.2,19	1.2	2	27	1	2	1	1	9	1	2	87	2	19	M	1.7	6	1	3,10	13			0
446	1087039	1	1	1	27	G3P2L2	2	2	32+5	2	8	6	1.1	2	32	2	2	2	2	14.3	1	2	140	1		M	1.7	6	1	8	21			0
447	1086828	1	2	1	26	PRIMIGRAVI	2	2	35	1	0	19	1.1	2	33	2	2	2	0	13.1	1	2.45	120	1		M	2	8	3	4,13	7			0
448	1086831	2	1	1	22	PRIMIGRAVI	2	2	29	2	6,14	6,18	1.1	2	36	1	2	1	2	9.7	1	4.2	102	2	13	M	2.9	8	2	0	6			0
449	1087387	1	1	1	30	G2P1L1	2	2	26+3	2	3	6	0	2	30	1	2	2	0	9.7	1	3.4	78	1		F+ZZ459:AA4	1.1	0.1		17		POTTERS STAGE 1,2 - AR		0
450	1087561	2	1	2	23	PRIMIGRAVI	2	2	34+4	2	6,8	1.1	1.2	2	32	1	2	3	2	9.2	1	2.5	100	1		F	1.4	6	1	4,9,13	11			0
451	1087621	1	2	1	24	PRIMIGRAVI	2	1	32	2	0	22	1.1	2	26	2	2	3	1	10.8	5	3.4	176	1		M	1.2	6	1					0
452	1087738	2	1	2	28	PRIMIGRAVI	2	2	35+2	2	3	22	1.1	2	30	2	2	1	2	11.9	0	4.1	110	2	13	F	2.4	8	1	1	8			0
453	1087576	1	2	1	20	PRIMIGRAVI	2	2	32	2	5	1.1,11	0	2	28	2	2	1	1	13.3	0	2.2	98	2	2	M	1.4	7	1	1,4,8	9			1
454	1088494	1	1	1	26	PRIMIGRAVI	2	2	35+3	2	0	22	1.1	2	27	1	2	1	2	9.6	0	4	130	1		F	2.4	8	2	4	6			0
455	1088374	1	1	1	24	G2P1L1	1	2	35+3	2	10	2,7,6	1.1	2	24	2	2	2	2	12.6	4	4.2	130	2	14	F	2.4,2.5	8,8	2,2	4;4	7,8			0
456	1088251	1	1	1	30	PRIMIGRAVI	2	2	35+4	2	0	6	1.1	2	22	1	2	3	2	8.6	0	4.3	104	1		F	3.2	8	2	3,4	8			0
457	1088437	1	1	1	21	PRIMIGRAVI	2	2	36+4	2	0	6	0	2	18	2	2	1	2	12.1	0	3.4	106	2	9	M	2.3	7	2	4	5			0
458	1088444	1	1	1	30	PRIMIGRAVI	2	2	36+6	2	7	19	0	2	32	1	2	3	1	8.6	0	2.3	108	2	9	F	3	8	2	0				0
459	1088436	1	1	1	29	G3A2	2	1	33+6	2	0	1.3,11,13	1.2	2	34	1	2	1	2	9.2	0	2.4	112	2	9	M	1.2	5	1	2,4,16	18			0
460	1088489	2	1	2	24	G3A2	2	2	36	1	0	1.1,11	0	2	24	2	2	1	2	11.2	0	2.5	108	2	3	F	2.9	9	2	0	5			1
461	1087903	1	1	1	29	PRIMIGRAVI	2	2	35+5	2	4,3,6	11	1.1	2	28	2	2	1	2	6.4	0	2.8	98	1		M	1.69	7	1	1,4,8				0
462	1088851	1	1	1	25	G4P2L1A1	1	1	36+4	2	10,28	6	1.2	2	23	2	2	1	2	10	0	1.5	118	2	1	M	1.76	7	1	1,2,4,13	10			0
																																		0
463	1088418	2	2	2	27	PRIMIGRAVI	1	2	34	2	3	11,15	1.2	2	23	2	1	1	2	12.1	1	1.3	116	1		M	1.33	8	1	3,4	12			0
464	1054354	1	2	1	21	PRIMIGRAVI	2	2	36+5	2	0	22	0	2	34	2	2	1	2	10.8	0	2.8	112	1		F	2.6	9	2	0	6			0
465	1054237	2	1	2	23	G2A1	2	2	36+3	2	7	2,6	0	2	36	2	2	3	2	10.5	0	2.4	98	2	14	M,M	1.3,1.8	7,8	1,1					0
466	1054224	1	2	1	19	PRIMIGRAVI	2	2	36+5	2	0	22	0	2	34	2	2	1	2	9.9	1	1.28	108	1		F	2.5	9	2	0	5			0
467	1054393	2	2	1	25	G2P1L1	2	1	35	1	10	11,19	1.2	2	32	2	2	1	1	10.6	0	0.98	112	2	11	M	1.9	8	3	4	8			0
468	1053129	2	2	2	28	G2P1L1	2	1	32+3	2	3,10	1,11	1.2	2	33	2	2	1	2	12.39	1	1.56	82	2	3	F	1.2	8	1	4,14	19			0
469	1053503	2	2	2	22	PRIMIGRAVI	2	2	35+5	2	0	2,11	1.2	2	34	2	2	1	2	13	0	4.3	4.5	2	14	M,F	2.7,2.1	8,8	2,3	0	4,8			0
470	1054520	2	2	1	30	G2P1L1	2	1	34+5	1	10	1.1,15	1.1	2	36	2	2	1	2	12	2	2.48	112	2	3	M	1.7	8	1	3,10	9			0
471	1053987	2	2	1	28	G2A1	2	2	33	2	11	1.3	1.1	2	34	2	2	1	2	13.1	0	1.4	6.2	1		M	1.9	9	2	0	4			0
472	1051851	1	1	3	22	G2P1L1	2	1	36+2	2	10	3.1	0	2	32	1	2	1	2	9.8	0	1.24	108	4	7	F	2.5	8	2	4	6			0
473	1053989	2	2	2	28	G5P4L1	1	1	34+1	2	10,7	7,19	1.1	2	33	2	2	1	2	12	1	1.6	89	2	5	F	2	9	1	1,10,14	12			0
474	1054721	1	2	2	25	G2P1L1	2	2	36+6	2	0	11,19	0	2	34	2	2	2	1	11	0	1.24	125	1		F	2	8	3	1,10	9			0
475	1053559	2	2	2	23	G2P1L1	2	1	36+6	2	10	4,16	0	2	28	2	2	3	2	13	1	1.04	149	2	1	M	2.8	8	2	3	7			0
476	1054897	2	1	2	20	PRIMIGRAVI	2	2	35+2	1	0	1.1	1.1	2	27	2	2	1	2	12	2	2.42	82	2	3	M	1.7	8	1	1,10,14	11			1
477	1055017	2	2	2	21	PRIMIGRAVI	2	2	34+6	2	0	1.1,3.2,23	1.2	2	24	1	2	1	1	9	0	1.8	82	2	18	F	2.5	7	1	10	5			0
478	1055037	1	1	3	28	PRIMIGRAVI	2	2	36+1	2	0	7,19	0	2	30	2	2	1	1	12.4	0	1.3	120	2	20	M	2.6	8	2	0	8			0
479	1055016	2	2	2	22	PRIMIGRAVI	2	2	35+2	2	0	16	1.1	1	32	2	2	1	2	11.2	0	3.2	108	2	12	M	3.16	7	1	10	7			0
480	1055051	1	2	2	28	G2P1L1	1	1	33+6	2	10	6	1.2	2	26	2	2	1	2	10.5	0	1.08	5.4	2	1	F	2.1	9	3	7	8			0
481	1054886	1	2	2	23	PRIMIGRAVI	2	2	36	2	0	4,22	0	2	30	1	2	1	2	9	4	0.86	189	1		F	2.09	8	3	3	9			0
482	1055086	1	2	1	24	G2A1	1	1	32+5	1	10	22	1.1	2	28	2	2	1	2	11.5	0	2.43	108	1		M	1.2	7	1	3	9			0
483	1055126	1	2	1	24	G3P1L1A1	2	2	35+6	2	0	2,6	1.2	2	27	2	2	3	1	12.4	1	2.3	89	1		F,M	2,1.8	8,8	1	3,3	9,9			0
484	1055103	1	1	3	28	PRIMIGRAVI	2	2	36+2	2	7	6	0	2	24	2	2	1	1	11.9	1	1.38	88	2	13	M	2.58	7	1			SEPSIS,ANEN	7	0
485	1055304	1	1	3	32	PRIMIGRAVI	2	2	28+6	2	7	1.1	1.1	2	22	2	2	1	1	11.8	0	1.28	125	2	3	F	0.9	6	1			SEPSIS,ANEN	3	0
486	1054733	2	2	1	28	G4P2L2A1	2	2	33+3	2	3,6,10,15	1.1,4,18	1.2	2	18	2	2	1	2	12.4	3	2.8	190	1		M	1.8	7	1	7	8			0
487	1055322	1	2	1	25	G6P1L1A4	1	1	36	2	10	22	0	2	24	2	2	1	2	13.5	0	1.8	5.6	2	1	M	2.47	9	2	13	5			0
488	1055316	1	2	2	29	G2A1	2	2	35+4	1	7	22	1.2	1	34	2	2	1	2	12.2	1	4.08	98	2	23	F	2.5	8	2	0	4			0
489	1055290	1	2	1	22	G2P1L1	2	1	31+3	2	10	6,19	1.2	1	36	2	2	1	2	11.1	0	2.03	203	2	1	M	1.4	7	1	7	12			0
490	1055284	1	2	1	34	PRIMIGRAVI	2	2	36+5	2	0	4,16,24	0	2	34	2	2	1	2	11.6	0	1.45	113	2	8	M	3.5	9	2					0
491	1055879	2	1	2	28	G3P2L2	2	2	36+5	2	5	6	0	2	32	2	2	1	2	10.2	4	1.4	118	1		F	2.2	8	2	0	8			0
492	1055681	1	1	2	32	G3P2L1	1	2	35+6	2	0	1.1	0	2	33	2	2	1	2	11.4	2	2.8	98	2	3	M	2.9	8	2	13	9			0
493	1055300	2	1	2	28	G2P1L1	2	1	31	2	4,10	10	0	2	34	1	2	1	0	5.8	0	4	114/5.6	2	1	M	1.6	0.2						0
494	1055543	1	1	2	24	PRIMIGRAVI	2	2	34+5	2	0	2,6	1.2	2	18	2	2	1	2	11.8	1	1.82	5.8	2	14	M,M	2.4,2.8	8,8	3,3	3,13;4,13	12,14			0
495	1055611	1	2	2	32	G3P1L1A1	2	1	35	2	3,10	1.3,11,25	1.1	2	24	2	2	1	2	13.6	0	4	89	2	1	M	2.5	8	2	0	6			0
496	1055902	2	2	2	28	G2P1L1	2	2	33	2	3	6	1.1	2	34	2	2	1	2	12.5	1	3	99	2	9	M	2.1	8	3	13	9			0
497	1056089	2	2	2	26	G2P1L1	2	2	36+6	2	0	19	0	1	36	2	2	1	2	10.2	0	4	120	1		M	3	8	2	0	4			0
498	1054394	2	2	2	23	G2P1L1	2	2	36+3	2	7	11	0	2	34	2	2	1	2	11.8	4	2	88	1		F	1.8	7	2	0	8			0
499	1055585	2	2	2	26	G2P1L1	2	2	34	2	0	1.3	1.1,2	2	32	2	2	1	2	11.5	0	2	89	2	14	M,M	2,1.9	7,7	1,1	1,2,3,4;6,11,	8	2ND TWIN D	4	0
500	1056694	1	2	1	37	G2P1L1	2	1	36+3	2	10	3.1	0	2	33	2	2	1	2	12	0	4	99	2	7	M	2	8	3	4,10,13	20			0
501	1056605	2	2	1	32	G4P2L2A1	2	1	32+2	2	3,10	22	1.2	1	34	2	2	1	2	11.4	0	5.2	89	2	5	M	1.5	8	1	7	12			0
502	1056552	2	2	1	33	PRIMIGRAVI	2	2	35+3	2	3,6,8	4,5,14	1.2	1	36	1	2	3	2	8	0	1.3	166	2	20	F	2.3	9	3	13	14			0
503	1056733	2	2	2	31	G3P1L1A1	2	1	36+3	2	10	10	0	2	34	2	2	2	0	9.8	0	4	89	2	1	M	2.58	8	3	0	12			0