"VITAMIN D LEVELS IN PRETERM LABOUR AND ITS IMPACT ON OBSTETRIC OUTCOME IN RURAL TERTIARY CARE HOSPITAL"

By

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IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SURGERY

IN

OBSTETRICS AND GYNAECOLOGY

Under the guidance of

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I hereby declare that this dissertation/thesis entitled **"VITAMIN D LEVELS IN PRETERM LABOUR AND ITS IMPACT ON OBSTETRIC OUTCOME IN RURAL TERTIARY CARE HOSPITAL"** is a bonafide and genuine research work carried out by me under the guidance of **DR. PUSHPA P KOTUR ,**Professor, Department of Obstetrics and Gynaecology, Sri Devaraj Urs Medical College, Tamaka, Kolar.

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"To acknowledge is to know gratitude and gratitude is a valuable duty which ought to be paid to valuable people in a lifetime"

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DR.SHILPA.K.P

LIST OF ABBREVIATIONS USED

1. $1, 25(OH)_2D$	1, 25, DiHydroxy Vitamin D
2. 25(OH) D	25 Hydroxy Vitamin D
3. AOP	Apnea of Prematurity
4. BMI	Body Mass Index
5. GDM	Gestational Diabetes Mellitus
6. HIV	Human Immunodeficiency Virus
7. IL	Interleukin
8. NICE	National Institute for Health Care and Excellence
9. NICU	Neonatal Intensive Care Unit
10. PPROM	Premature Prelabour Rupture Of Membranes
11. RCOG	Royal College of Obstetricians and Gynaecologists
12. ROP	Retinopathy Of Prematurity
13. SGA	Small For Gestational Age
14. TLR	Toll 2 Receptor
15. TNF	Tumor Necrosis Factor
16. VDBP	Vitamin D Binding Protein
17. VDR	Vitamin D Receptor

ABSTRACT

"VITAMIN D LEVELS IN PRETERM LABOUR AND ITS IMPACT ON OBSTETRIC OUTCOME IN RURAL TERTIARY CARE HOSPITAL"

Introduction: Preterm birth is a major determinant of neonatal mortality and morbidity and has long-term adverse consequences for health. The incidence of preterm birth in India has been reported to be 14.5%. Preterm delivery has been associated to vitamin D deficiency in a few studies. The purpose of our study is to determine the correlation of vitamin D in preterm labor and neonatal outcome.

Objectives: 1) To estimate vitamin D levels in women in preterm and term labor and their new borns.

2) To determine the association between vitamin D3 levels and preterm labour.

3) To assess the neonatal outcome of low vitamin D levels in preterm and term.

Study design: This is a prospective case control study conducted in the Department of Obstetrics and Gynecology at R.L. Jalappa Hospital and Research centre, Tamaka, Kolar, from March 2014- August 2015

Materials and methods: A total no of 160 samples will be collected and categorized into 4 groups. Group 1: 40 samples of cases (women in preterm labor) Group 2:40 samples of controls (women in term labor).Group 3: new born of cases .Group 4: new born of controls**.** After obtaining an informed consent under aseptic precautions 5ml of venous blood of median cubital vein of group 1 and group 2 subjects are collected in plain tube. The sample will be centrifuged at 3000rpm for separation of serum and stored at -800C till analysis.10ml of cord

blood of group 3 and group 4 subjects after delivery from fetal part of umbilical cord will be collected and left till the supernatant is separated form vitamin D analysis.

Analysis of vitamin D: The assay of vitamin D will be analyzed using Johnson and Johnson instrument chemiluminescence method.

RESULTS: Majority of the cases were in the age group of 21-25 years (75%) and the incidence of preterm labour was more among the Primigravida (57.5%). The mean gestational age in the study group was 33.42±2 years. The mean value of S. vitamin D among the cases was 18.36 ng/ml and among the controls was 34.3 ng/ml.S. vitamin D levels are significantly low in preterm when compared to term labour.Low vitamin D in mothers is correlated with low vitamin D in newborns. Vitamin D levels in cases with PPROM is 16.52 ng/ml and in cases without PPROM is 20.13ng/ml which was statistically suggesting lower vitamin D levels in women with PPROM.

The most common complication among the cases is respiratory distress with 42.5% and second most common complication is hyperbilirubinemia with 32.5%.The mean vitamin D levels in all the cases was below 20ng/ml.

CONCLUSION: There is an increased risk of preterm labour with hypovitaminosis of vitamin D .Preterm newborns have significantly lower vitamin D levels compared to term newborns. Vitamin D levels are inadequate in women with PPROM compared to women without PPROM.

Keywords: preterm labour, vitamin D, Neonatal outcome

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INTRODUCTION

Preterm birth is the most important problem in modern obstetrics. In 2010, more than 1 million infants born preterm died worldwide, making it the second leading cause of death in children under the age of 5 years[1]. Children who are born prematurely have higher rates of cerebral palsy, sensory deficit learning disabilities and respiratory illnesses compared with children born at term. Unfortunately, efforts to prevent, predict, or delay preterm birth have had limited success. Identifying potential targets for preterm birth prevention is a public health priority.

Recently, maternal vitamin D deficiency has been linked to adverse pregnancy outcomes, including preeclampsia and fetal growth restriction and also may be important in preterm birth.[2] Adequate vitamin D status appears to be relevant to health at all ages, and even in prenatal life. It affects physiological pathways in the pathogenesis of preterm birth, including inflammation, immunomodulation, and transcription of genes involved in placental function .[3,4]

Vitamin D deficiency is unexpected in a tropical country such as India, where there is abundant overhead sun for most or all around the year. However , severe osteomalacia, D has been observed in adolescents in India due to low vitamin.[5] This paradox may be partly explained by the many prevalent social and cultural practices in India that preclude adequate exposure of adolescent girls and young women to sunshine. Revealing clothing is frowned in traditional Indian households, both rural and urban. Newly married females are expected to cover themselves even more and are discouraged from outdoor activity. Increasing urbanization that results in poor outdoor activity and greater pollution, coupled with skin pigment, may further compound this problem.[6]

In a population that already has a high prevalence of vitamin D deficiency, the problem is likely to worsen during pregnancy. Some well-known consequences of severe clinical vitamin D deficiency in pregnancy can be life-threatening to the neonate. Prematurity, low birth weight and lower bone density, as well as later sequelae such as increased incidences of lower respiratory tract infection in the first months of life, asthma, diabetes mellitus, autism and dental problems, are examples of neonatal outcomes known to be related to vitamin D deficiency in pregnancy.[7-14]

NEED FOR THE STUDY

Preterm birth is, worldwide, the most challenging problem in obstetrics, but the prevention of prematurity has been difficult and ineffective because of its multifactorial and partly still unknown etiology.[15] However, infections alone may be associated with up to 40% of spontaneous preterm births, especially those taking place at an early gestational age.[16] During the past two decades, the association between maternal genital tract infections and ascending infection in the choriodecidual interface leading to preterm birth has been of special interest.[17]

The incidence of preterm labor is 5-10% of all pregnancies. Incidence of preterm labour is 23.3% and of preterm delivery 10-69% in India. WHO 2010 shows India has the highest number of preterm birth i.e. 3519100.[18]

Children who are born prematurely have higher rates of cerebral palsy, sensory deficit learning disabilities and respiratory illnesses compared with children born at term. Due to multiple unfortunate consequences caused, the elimination of risk factors, prophylaxis and treatment of this disease represents the golden objective of current obstetrics.

Since vitamin D has immunmodulatory and anti-inflammatory effects, such as the regulation of production and function of cytokines and neutrophil degranulation products that is important and relevant to prevent microbial invasion one may expect a protective effect on spontaneous preterm birth risk.[19-21]The various cells of the immune system express VDRs and are modulated by vitamin D.[22]Although vitamin D action dampens the activation of the acquired immune system in response to autoimmunity, this hormone has key actions that enhance the innate immune system. It is involved in cell-mediated immunity by reducing the production of inflammatory cytokines such as IL-1, 6 and TNF that are involved in spontaneous preterm birth.[23]

Human decidual cells are able to synthesize active 1,25 (OH)2D3. Therefore several studies point to the fact that vitamin D is involved in the regulation of acquired and innate immune responses at the fetal - maternal interface across gestation.[24]Vitamin D reduces the risk of spontaneous preterm birth also by helping to maintain myometrium quiescence. Myometrial contractility is dependent on calcium release within the muscle cell and this process is regulated by vitamin D.[25]

Taking into consideration the above mentioned risks with hypovitaminosis D the necessity for diagnosing hypovitaminosis D in pregnant women and its role in preterm labour, visiting RLJ hospital and Research Centre was felt. This will help for better obstetric outcome and also will help in finding out incidence of hypovitaminosis D this may help in increasing awareness amongst the rural population preventing above mentioned maternal and fetal complications

BACKGROUND

Prematurity is the most common cause for mortality among nonanomalous infants born. Surviving premature infants have significant morbidity. Unfortunately, efforts to prevent, predict, or delay preterm birth have had limited success. Evaluating pathophysiological changes associated with preterm birth that are amenable to therapy could therefore impact both neonatal and maternal outcomes. The etiology of spontaneous preterm birth is multifactorial. Contributing factors include uterine over-distention, abnormal fetal endocrine activation, and uterine infection and inflammation. An emerging area of study that has garnered significant attention is the role of vitamin D and its active metabolite, 1,25(OH)2D.There may be a possible role for vitamin D in preventing spontaneous preterm birth through anti-inflammatory and immunomodulatory effects.

Vitamin D is a preprohormone that is made by most living plants and terrestrial animals. In the true sense of the word, vitamin D is not a "vitamin" because the main source of vitamin D is that which we synthesize ourselves—in our skin—with less than 10%coming from dietary sources. Vitamin D comes in two major forms—vitamin D2 or

ergocalciferol and vitamin D3 or cholecalciferol. While certain plants are capable of making both forms of vitamin D, the major form made by plants is vitamin D2 following ultraviolet B exposure of the provitamin D2 ergosterol. In comparison, humans can metabolize both vitamin D2and D3, but can only synthesize de novo vitamin D3.

Sources of Vitamin D

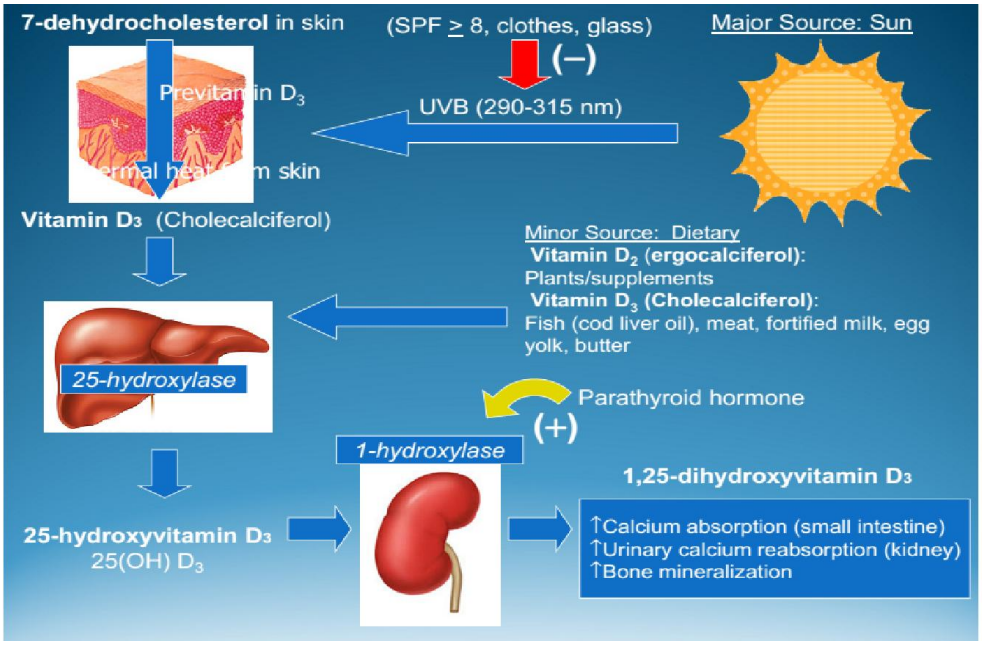

Figure no 1: sources and metabolism of vitamin D

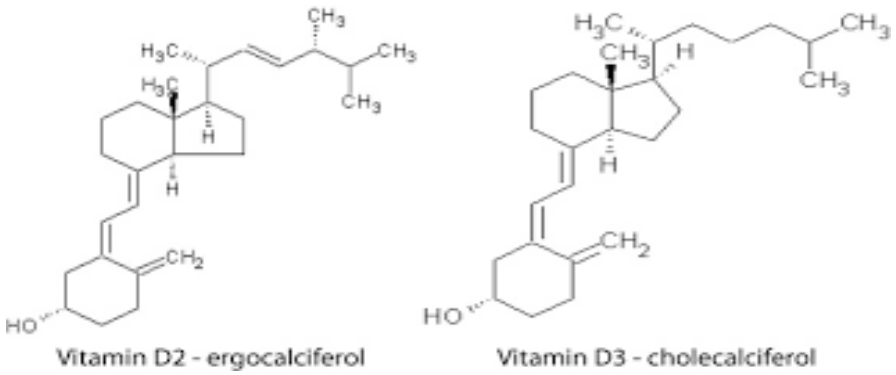

Figure no 2: Structure of vitamin D

As shown in Figure 1, the de novo synthesis of vitamin D3 in humans and other animals begins in the skin with the parent compound 7-dehydrocholesterol or provitamin D3. Following exposure to ultraviolet B radiation in the range of 280–320 nm, 7-dehydrocholesterol becomes previtamin D3. Through a subsequent thermal reaction in the skin, previtamin D3 is isomerized into vitamin D3. It is important to note that unlike other steroid hormones in the body whose main substrate is cholesterol, vitamin D synthesis requires the 7-dehydrocholesterol precursor and sunlight at a specific wavelength and angle. Without this reaction, humans are dependent on dietary intake of vitamin D, which may be in the form of either vitamin D2or D3.

Vitamin D Metabolism

In order to understand the differences between the nonpregnant and pregnant states and their effects on vitamin D metabolism, it is essential to understand the nonpregnant state first. Following its synthesis, vitamin D binds to vitamin D binding protein (VDBP) and finds its ways into the circulation. Dietary and endogenous vitamin D appear to act similarly with half-life between 12 and 24 hours, the length of time depending on how quickly the liver converts vitamin D to 25-hydroxy-vitamin D (also known as calcidiol). Vitamin D is measured in international units (IU) or micrograms with a known conversion of 40 IU equal to 1 microgram**.**

While there appears to be a differential conversion rate of the two forms of vitamin D to 25(OH)D , the conversion of either form is dependent on a functional liver and the activity of 25-hydroxylase. Thus, those with impaired liver function will have diminished conversion of vitamin D to 25(OH) D. Following its synthesis, 25(OH)D then enters the circulation where it is tightly bound to VDBP. Only a small amount of 25(OH) D is unbound or “free”. The half-life of 25(OH) D is 2–3 weeks, making it a much better indicator of the body’s vitamin D status than vitamin D.

Once 25(OH) D is formed in the liver, it enters the circulation. Best known is the processing of 25(OH)D by the kidney where 25(OH)D complexed with VDBP and megalin is taken up by the epithelial cells of the proximal tubules and converted to the active hormonal form of vitamin D—di-hydroxy-vitamin D (1,25(OH)2D or calcitriol)—by the action of the mitochondrial enzyme 1-α-hydroxylase.

1,25(OH)2D's endocrine effects include the following classic triad of action:

(1) Increase intestinal calcium (as Ca2+ions) absorption through the actions of calbindin;

(2) Increase urinary calcium reabsorption; and

(3) Regulation of parathyroid hormone in a negative feedback loop that allows calcium to be absorbed from the gastrointestinal tract, reabsorbed from urine, and metabolized from bone in order to maintain calcium homeostasis within the body.

Adequate vitamin D must be on hand to provide enough substrate to form 25(OH)D, which in turn, is converted to 1,25(OH)2D, whose half-life is 8

hours. In individuals with vitamin D deficiency, only trace amounts of vitamin D will be found in the body because whatever comes into the circulation is quickly converted to 25(OH)D and then to 1,25(OH)2D to maintain calcium homeostasis.

Metabolism of vitamin D during pregnancy

Once ingested or produced by the body, vitamin D3is transported to the liver for hydroxylation to 25(OH)D, the main circulating form of vitamin D and best measure of vitamin D status, and then to the kidney where the active hormonal form of vitamin D,1,25(OH)2D, is produced. Maternal 25(OH)D is thought to freely cross the human placenta as it does in rats. The placenta expresses vitamin D receptors (VDR) and also produces the enzyme CYP27B1 to convert 25(OH)D to its active form.

Immune Modulating Function of vitamin D

For decades, it was thought that only the kidney has the capacity to metabolize 25(OH)D; however, extrarenal metabolism has been demonstrated in every organ system in the body . During pregnancy, the placenta is probably the most prominent site for extra-renal activation of vitamin D . It appears that the extrarenal function of vitamin D has more to do with immune function than with calcium metabolism and homeostasis.

It was first observed by Mellanby et al in his study of rachitic children and dogs noted an increased risk of respiratory infections in those afflicted.[26,27] Additional reports came from those working with tuberculosis patients and the beneficial effect of being in sunlight and outdoors in the treatment of the condition [28]. Weick in 1967 and Rehman in 1994 independently observed that children with rickets appeared ill, with decreased energy and activity, and were more susceptible to respiratory illnesses.[29,30]

Despite these observations, it was concluded that the condition of vitamin D deficiency led to weakness and malnutrition and was not a direct effect of vitamin D on the immune system. The mechanism of action of these

processes and health derangements would not be understood until the advent of molecular biology.

Vitamin D appears to affect immune function in two ways:

(1) Upregulation of the innate immune system; and

(2) Downregulation of the adaptive immune system.

Focusing on the innate immune system first, a major mechanism of action of vitamin D is via an endogenous antimicrobial peptide called cathelicidin (LL-37), which is generated in response to microbial invasion through activation of toll-2 receptors (TLR) on monocytes and macrophages .

Not surprisingly, the vitamin D receptor element (VDRE) is contained in the promoter region of the gene for LL-37. VDRE are found only in the LL-37 gene promoters of primates, suggesting that the ability of vitamin D to promote LL-37 antibacterial action is a relatively recent event in evolution. Both 1,25(OH)2D and 25(OH)D have the ability to induce the expression of cathelicidin in monocyte/macrophage and epidermal lineage in cells that simultaneously have the 25(OH)D hydroxylase.

Significant support for the role of vitamin D in immune processes and function came in 2006 when Liu et al. published their landmark study in

Science[31]. Serum samples taken from African American subjects with low 25(OH)D were inefficient in supporting cathelicidin mRNA induction; however, with the addition of 25(OH)D to those samples with low 25(OH)D levels this pattern was reversed. Thus, in this series of experiments, the addition of 25(OH) D3 restored the ability of sera from individuals with low 25(OH)D concentrations to support TLR2/1L-mediated induction of cathelicidin mRNA.

A related study by Fabri et al showed that IFN-γ-mediated antimicrobial activity of human macrophages, especially important in HIV and tuberculosis patients, is dependent on vitamin D.[32]

Both study findings have implications for the pregnant woman and her developing fetus, but our understanding of such processes following maternal exposure to a pathogen or maternal infection remains scant. There is every reason to suggest that such processes are fully functional in the pregnant woman.

Vitamin D's role as a modulator of the immune system encompasses the adaptive immune system as well. 1,25(OH)2D not only has the ability to affect processes within macrophages and monocytes, but also in T and B lymphocytes as well. The vitamin D receptor (VDR) is found on activated

(but not resting) human T- and B-lymphocytes. Whereas 1,25(OH)2D appears to activate the bacteriocidal process within macrophages and monocytes, it has different effects, that include suppression of T-cell proliferation and modulation of T-cell phenotype—with anti-inflammatory properties .

By binding to the VDR on T cells, 1, 25(OH) 2D acts to:

(1) Inhibit the proliferation of uncommitted TH (helper) cells and

(2) Promote the proliferation of immunosuppressive regulatory T cells, or TregS, with notable accumulation of these cells at sites of inflammation. It appears that 1,25(OH)2D suppresses certain B cell functions such as proliferation and immunoglobulin production and retards the differentiation of B-lymphocyte precursors to mature plasma cells in vitro. These in vitro findings help to explain the significant association between vitamin D deficiency and autoimmune diseases. Additionally, the role of vitamin D in immune function intensifies the need to establish vitamin D sufficiency during pregnancy.

REVIEW OF LITERATURE

Vitamin D was classified as a vitamin in the early 20thcentury and in the second half of the 20thcentury as a prohormone . It is a unique nutrient because it can be synthesized endogenously (skin) and it functions as a hormone. Impaired vitamin D status during gestation is associated with adverse outcomes in pregnancy such as preterm birth and poor neonatal outcome. Maintenance of normal pregnancy requires an effective coordination of anti-inflammatory and antimicrobial responses within the fetoplacental unit. Vitamin D plays a significant role in modulating both these processes thereby helping in maintaining a healthy term pregnancy.

Vitamin D deficiency

As the statistics keep surfacing at the alarming pace, Vitamin D deficiency is recognized as the most un-treated nutritional deficiency currently in the world [33,34]. Vitamin D deficiency is a significant public health problem in both developed and developing countries including India[35]

Vitamin D deficiency is common, especially in women with pigmented skin. In a study conducted in London in antenatal population, vitamin D level of less than 25 nmol/l was found in 47% of Indian Asian women, 64% of Middle Eastern women, 58% of black women and 13% of Caucasian women.[36]In the general adult population, reduced vitamin D concentrations are found in obese subjects. Prepregnancy obesity has been associated with lower levels of vitamin D in both pregnant women and their neonates; 61% of women who were obese (body mass index [BMI] ≥30) prior to pregnancy were found to be vitamin D deficient, compared to 36% of women with a prepregnancy BMI of less than 25.[37]

Study conducted in northern India observed a high prevalence of physiologically significant hypovitaminosis D among pregnant women and their newborns, the magnitude of which warrants public health intervention.[38]

Vitamin D During Pregnancy—Why Is It Important?

From the prior sections, it is clear that vitamin D deficiency during pregnancy is common throughout the world yet what effect does deficiency have on the mother and her developing fetus?

Maternal complications

Pre-eclampsia:

There is conflicting evidence whether hypovitaminosis D in pregnancy is associated with hypertension and pre-eclampsia.

In three studies, women who developed pre-eclampsia were found to have lower levels of vitamin D than women who did not with levels less than 50 nmol/l associated with a five-fold increased risk of severe pre-eclampsia.[39,40,41]

Low levels in the first half of pregnancy were related to the risk of developing pre-eclampsia and the neonates of these mothers had a two-fold increased risk of having vitamin D levels< 37.5 nmol/l.[41]

In a case–control study, women with severe pre-eclampsia before 34 weeks of gestation had reduced levels of vitamin D compared to control women.[42]

However, many studies have shown a weak or no relationship between vitamin D and hypertensive disorders in pregnancy.

A Canadian study showed that women with low circulating maternal vitamin D levels are more likely to have hypertension in pregnancy in the univariate analysis, but not the multivariate analysis.[43]

Two other studies also failed to show any association between vitamin D levels and the development of pre-eclampsia,gestational hypertension or preterm birth.[44,45]

However, two meta-analyses, including a meta-analysis of 31 studies, demonstrated that vitamin D insufficiency was associated with pre-eclampsia and SGA infants.[46,47]

Impaired glucose tolerance in pregnancy

Depending on the diagnostic criteria used, it has been suggested that GDM complicates up to 16% of pregnancies.[48] Although the true incidence can be much greater in some ethnic groups.

There are some data to suggest that the association between 25(OH)D levels and GDM risk is specific to ethnicity. In a majority non-Hispanic white population, 25(OH)D concentrations at 16 weeks of gestation were significantly lower in GDM subjects than in controls, whereas no association was found in Indian mothers where 25(OH)D concentrations were measured at 30 weeks of gestation.[49,50]

Some studies have investigated more than one ethnic group using statistical techniques to correct for the effect of ethnicity, but none have

been designed to describe the association in specific ethnic populations.[49]

Conversely, a well-conducted study has found no association between maternal 25(OH)D and the development of GDM.[51]A meta-analysis of 31 studies demonstrated vitamin D insufficiency was associated with a higher risk of GDM.[46]

Preterm birth

Two studies examined relationships with blood levels of 25(OH)D during pregnancy and preterm birth. In Tanzania, no difference in risk of preterm birth (<37 weeks, RR=0.84 [0.55–1.28]) or early preterm birth (<34 weeks, RR=0.77 [0.50, 1.18]) was observed among HIV-positive women using a cut-off of 80 nmol/L.[52]

Similarly, no difference in the third trimester 25(OH)D levels was found for adolescents in the UK delivering preterm vs. normal gestational length babies.[53]

Observational studies with serum 25(OH)D levels as an exposure did suggest longer gestational duration associated with higher 25(OH)D levels.

In the Netherlands, women with serum levels >50 nmol/L had a slightly longer gestational length of 40.2 weeks vs. 40.0 weeks vs. women in two categories of lower intake (P<0.001).[54]

An Australian study noted a significant 0.7-week shorter gestation [-1.3, -0.1] among women with blood 25(OH)D levels <28 nmol/L compared with those with higher levels.[55]

A hospital-based study from Japan also found lower Mean Difference Mean Difference Control Experimental.[56]

Other complications

Vitamin D deficiency (< 37.5 nmol/l) has been associated with a four-fold increased risk of primary caesarean section (caesarean section performed for the first time),although this has not been demonstrated in all studies.[57]

Vitamin D deficiency is also associated with bacterial vaginosis in pregnant women.[58,59]

Neonatal complications

Neonatal hypocalcaemic seizures

Neonatal vitamin D levels are correlated with those of their mother, with maternal vitamin D deficiency increasing the risk of neonatal vitamin D deficiency.[46]

In an Australian study, hypovitaminosis D was found in 15% of pregnant women and 11% of neonates.[60] Vitamin D deficiency is a major cause of hypocalcaemic seizures in neonates and infants.[61]

Hypocalcaemia is not uncommon in neonates and is a potentially severe problem. [61]Mothers of babies who suffer hypocalcaemic seizures are more likely to be vitamin D deficient (85%) than mothers of babies who do not (50%).[62]

In another study from Egypt, all mothers of babies with hypocalcaemic seizures had severe vitamin D deficiency.[63] Maternal vitamin D deficiency is a common, and potentially preventable, cause of neonatal hypocalcaemia. This is especially common in South Asian women.

Skeletal development and growth

Hypovitaminosis D is associated with impaired growth and bone development in the fetus. Evidence is accruing to show that less profound maternal 25(OH)D insufficiency may lead to suboptimal bone size and density after birth without overt rachitic change.[64] This is likely to lead to an increased risk of osteoporotic fracture in later life.

A retrospective cohort study showed that children who had received supplements with vitamin D in the first year of life had a significant increase in femoral neck bone density at the age of 8 years compared to the group that did not receive supplements.[65]

In a UK mother–offspring cohort, 31% of the mothers had circulating concentrations of 25(OH)D in late pregnancy of 27–50 nmol/ there was a positive association between maternal 25(OH)D concentration in late pregnancy and whole body bone mineral content and density, assessed using dual energy X-ray absorptiometry (DEXA), in the offspring at 9 years of age.[66]

Furthermore, maternal UVB exposure and vitamin D supplementation were associated with the bone mass of the child ($P < 0.05$), while lower levels of umbilical-venous calcium were also associated with lower

Childhood bone mass, suggesting a possible role for placental calcium transport in this process.[66]

Additionally, maternal UVB exposure during pregnancy was positively associated with whole body bone mineral content in the offspring at the age of 9 years in the Avon Longitudinal Study of Parents and Children.[64]

Similar findings have come from another UK cohort, the Southampton Women's Survey, in which neonatal bone area and bone mineral content were reduced in the female offspring of mothers who had 25(OH)D concentrations < 33 nmol/l in late pregnancy.[67]

These findings of altered neonatal bone mass have been confirmed by a Finnish mother–offspring cohort in which babies born to mothers with circulating 25(OH)D status below the median (42.6 nmol/l) had reduced tibial bone mineral content and cross-sectional area, measured by peripheral quantitative computed tomography[68]

In a follow-up study, a deficit in tibial cross-sectional area was still observed at 14 months' follow-up, despite the low vitamin D group catching up with the other group for the bone mineral content.[69]

These findings suggest that the adverse consequences of maternal vitamin D deficiency for the offspring are manifest early in pregnancy.

Fetal lung development and childhood immune disorders

Low maternal vitamin D intake in pregnancy is associated with wheeze and asthma in the offspring.[70]Low cord blood 25(OH)D concentrations have been associated with respiratory syncytial virus bronchiolitis and respiratory infections.[71]

There are plausible physiological mechanisms for an association between prenatal vitamin D status and immune development. The metabolite 1,25(OH)2D has been shown in animal and in vitro models to have an immune-modulatory role and low levels of neonatal vitamin D have been linked to childhood asthma.[70,71]

Maternal vitamin D supplementation is associated with cord blood gene expression of tolerogenic immunoglobulin such as immunoglobulin-like transcripts 3 and 4 (ILT3 and ILT4).Cord blood 25(OH)D is correlated with mononuclear cell release of IFN-γ and hence Th1 cell development.[72]

Screening for vitamin D deficiency in pregnancy

There are no data to support routine screening for vitamin D deficiency in pregnancy in terms of health benefits or cost effectiveness. There is an argument that some groups of women who are pregnant should have a screening test: for example, on the basis of skin colour or coverage, obesity, risk of pre-eclampsia, or gastroenterological conditions limiting fat absorption.[73]

As the test is expensive, offering it to all at-risk women may not be cost effective compared to offering universal supplementation, particularly as treatment is regarded as being very safe. At present, there are no data to support a strategy of measurement followed by treatment in the general female population.

Measurement of vitamin D in a hypocalcaemic or symptomatic woman as part of their management continues to be applicable. This includes women with a low calcium concentration, bone pain, gastrointestinal disease, alcohol abuse, a previous child with rickets and those receiving drugs which reduce vitamin D.

Supplementation and treatment in pregnancy

Daily vitamin D supplementation with oral cholecalciferol or ergocalciferol is safe in pregnancy. The 2012 recommendation from UK Chief Medical Officers and NICE guidance state that all pregnant and breastfeeding women should be informed about the importance of vitamin D and should take 10 micrograms of vitamin D supplements daily.[74]

Particular care should be taken over high-risk women. The recommendations are based on the classical actions of vitamin D, although many of the nonclassical actions of vitamin D may be beneficial. As mentioned above, the review and meta-analysis by Aghajafari et al. found associations between vitamin D insufficiency and risk of gestational diabetes, pre-eclampsia, bacterial vaginosis and SGA infants.[14]

Three categories of vitamin D supplementation are recommended.

1. In general, vitamin D 10 micrograms (400 units) a day is recommended for all pregnant women in accord with the national guidance.[74]

2. High-risk women are advised to take at least 1000 units a day (women with increased skin pigmentation, reduced exposure to sunlight, or those who are socially excluded or obese).[75]

The RCOG has highlighted the importance of addressing suitable advice to these women. Women at high risk of pre-eclampsia are advised to take at least 800 units 61 a day combined with calcium.[76]

The limitation to therapy compliance mostly relates to the calcium which has a side effect of tasting of chalk, rather than the vitamin D element of oral therapy. It is often more appropriate to give vitamin D alone for patient acceptability. However, this is limited by the availability of suitable agents; vitamin D cannot be prescribed at low doses without calcium. 800-unit formulations of cholecalciferol without calcium are available .There may be particular benefits of vitamin D/calcium supplementation in women at risk of pre-eclampsia.[76]

3. Treatment. For the majority of women who are deficient in vitamin D, treatment for 4–6 weeks, either with cholecalciferol 20 000 IU a week or ergocalciferol 10 000 IU twice a week, followed by standard supplementation, is appropriate.[77]

For women who require short-term repletion, 20 000 IU weekly appears to be an effective and safe treatment of vitamin D deficiency. A daily dose is likely to be appropriate to maintain subsequent repletion (1000 IU daily).[78]

In adults, very high doses of vitamin D (300 000–500 000 IU intramuscular [IM] bolus) may be associated with an increased risk of fractures and such high doses are not recommended in pregnancy. A 2011 study demonstrated that supplemental doses of 4000 IU cholecalciferol a day were safe in pregnant women and most effective compared to the lower doses.[78]

Safety of vitamin D

In pregnancy there is enhanced intestinal calcium absorption. Vitamin D toxicity is manifested through hypercalcaemia and hypercalciuria. Therefore, there is a hypothetical concern that when secondary hyperparathyroidism follows vitamin D deficiency, calcium given with vitamin D may be associated with temporary hypercalcaemia. However, this is self-limiting due to the associated hungry bone and has not been demonstrated to represent a clinical problem.[73]

AIMS AND OBJECTIVES

1) To estimate vitamin D levels in women in preterm and term labour and their new borns.

2) To determine the association between vitamin D3 levels and preterm labour.

3) To assess the neonatal outcome of low vitamin D levels in preterm and term.

MATERIALS AND METHODS

STUDY DESIGN

Type of study: Prospective case control study

SOURCE OF DATA

Pregnant women attending R.L.Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Kolar.

DURATION OF THE STUDY

We conducted the present from March 2014- August 2015.

SAMPLE SIZE

Sample size was estimated based on comparison of proportions of previous studies and was derived as sample size of 40 per group.

Formula used $n= [(z\alpha/2 + z\beta)^2 \times (\sigma_1^2 + \sigma_2^2)]/ L^2$

Where: n=sample size.

σ_1=standard deviation of cases.

σ_2=standard deviation of controls.

L=difference in mean

$Z\alpha/2$ at 0.05

$Z\beta$ at 90%

Considering 10% noncompliance 34+4=38.

A total no of 160 samples will be collected and categorized into 4 groups.

Group 1: 40 samples of cases (women in preterm labor)

Group 2:40 samples of controls (women in term labor)

Group 3: new born of cases

Group 4: new born of controls.

INCLUSION CRITERIA

A. CASES

1. Singleton pregnant women who are in preterm labour.

Preterm labor defined as occurrence of regular uterine contractions (4 or more in 20mins or 8 or more in 1 hour) and cervical changes (effacement equal or greater than 80 % and dilatation equal or greater than 1 cm) in women with intact fetal membranes and gestational age less than 37 weeks and greater than 28 weeks.

B.CONTROLS

Singleton pregnant women who are in term labor.

EXCLUSION CRITERIA

1. Pregnant women with medical illness, multiple gestation and polyhydramnios, uterine anomalies.

2. Induction of labor before 37 completed weeks for maternal or fetal indications.

3. Intra uterine fetal demise.

4. Congenital anomalies of the fetus.

5. Women who has received steroid injection for fetal lung maturity.

METHOD OF COLLECTION OF DATA

A participant fulfilling the inclusion criteria of the study were counseled and informed written consent was taken. History regarding age, parity, duration of gestation, menstrual history, obstetric history and any complications in present pregnancy was noted.

General clinical examination was done. Pulse rate, blood pressure & temperature was noted. Symphysio fundal height was measured. Uterine size, presentation was noted. Fetal heart rate was counted. Per- speculum & per -vaginum examination was done to see any rupture of the membranes. Necessary investigations was done.

Under aseptic precautions 5ml of venous blood of median cubital vein of group 1 before administration of steroid for fetal lung maturity and group 2 subjects are collected in plain tube. The sample was centrifuged at 3000rpm for separation of serum and stored at -80^0C till analysis.10ml of cord blood of group 3 and group 4 subjects after delivery from fetal part of umbilical cord was collected and left till the supernatant is separated form vitamin D analysis.

After the delivery, examination of the newborns of cases and controls will be done and followed for 7 days.

Analysis of vitamin D:

The assay of vitamin D was analyzed using Johnson and Johnson instrument chemiluminescence method.Vitamin D levels and its association with vitamin deficiency will be done according to following reference values as per Institute of medicine classification (2010).

TABLE 1: ICM Classification (2010)

REFERENCE RANGES	
Vitamin D deficiency	<12ng/ml
Vitamin D Insufficiency	12-20ng/ml
Vitamin D sufficiency	20-50ng/ml
Vitamin D intoxication	>150ng/ml

Statistical analysis

Data was entered into Microsoft excel data sheet and analysis will be done using EPI INFO 7 VERSION. Descriptive statistics like frequencies, proportions, mean and standard deviation was computed for qualitative and quantitative data. Student t test was used to see the mean difference between two groups for continuous data. Odds ratio was computed to measure the strength of association.

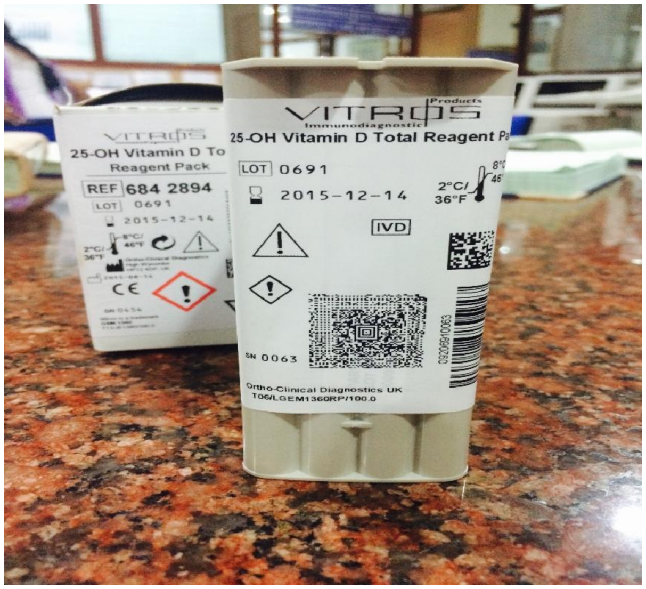

Figure no3: vitros vitamin D chemiluminecence kit

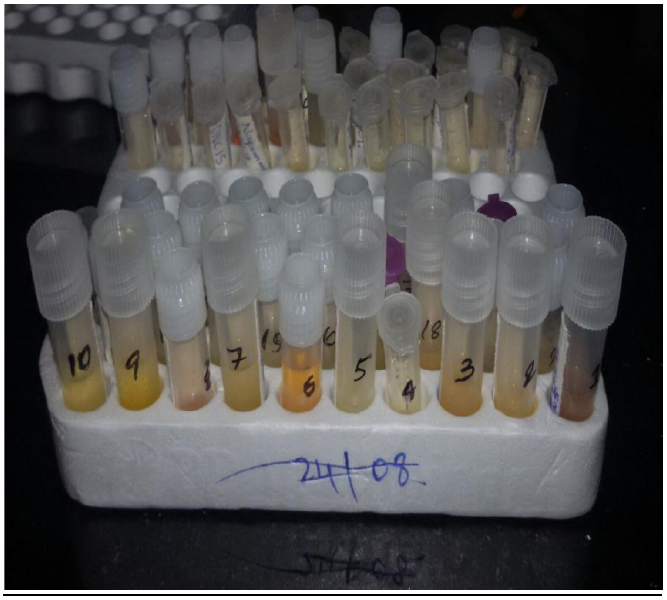

Figure no 4: serum samples of cases and controls

Figure no 5: Vitros chemiluminecence analyzer

OBSERVATIONS AND RESULTS

This prospective study was conducted in the Department of Obstetrics and Gynecology, R.L. Jalapa Hospital (Sri Devraj Urs Medical College), Tamaka, Kolar, Karnataka. A total no of 160 samples were collected and categorized into 4 groups.

Group 1: 40 women who came in preterm labor , blood sample of woman and cord blood of new born was collected and similarly in Group 2: 40 women in term labor, blood sample of the woman and cord blood of her new born was collected.

TABLE 2: Age distribution of the subjects under the study groups

Age in years	Cases		Controls	
	N	%	N	%
< 20	3	7.5	5	12.5
21-25	30	75	31	77.5
26-30	5	12.5	3	7.5
> 30	2	5	1	2.5
Total	40	100	40	100
Mean±SD	23.5±3.5		22.9±3.4	

The above table shows the age distribution of the study groups. The maximum number of cases were seen in the age group of 21-25 years. The mean age among the preterm (cases) group was 23.5±3.5 and the mean age among the term (controls) group was 22.9.±3.4

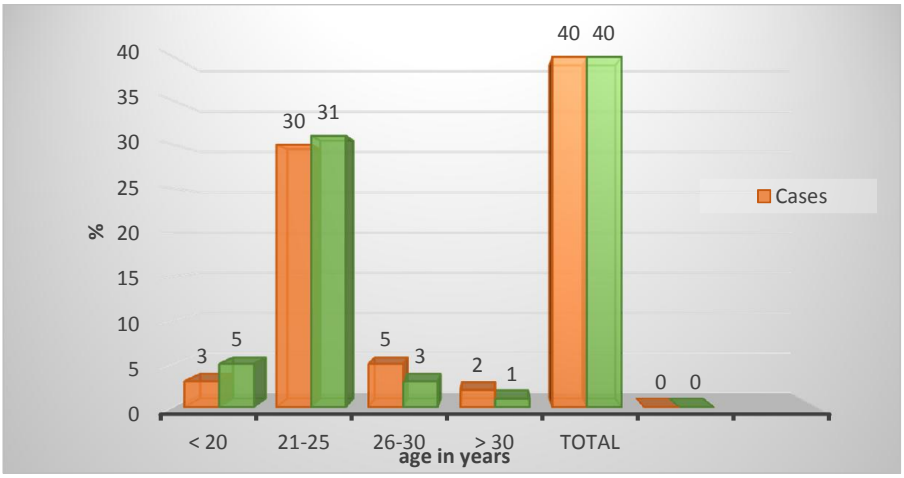

Chart 1: Multiple bar diagram showing the details of age distribution of the subjects under the study groups

TABLE 3: Parity distribution of the subjects under the study groups

Parity	Cases		Controls	
	N	%	N	%
Primigravida	23	57.5	25	62.5
Multigravida - G2	10	25	9	22.5
Multigravida - G3	3	7.5	3	7.5
Multigravida –G4	4	10	3	7.5
Total	40	100	50	100

The above table shows the parity distribution. Among the subjects studied, 60% were primigravida and 40% were multigravida .Majority were primigravida.

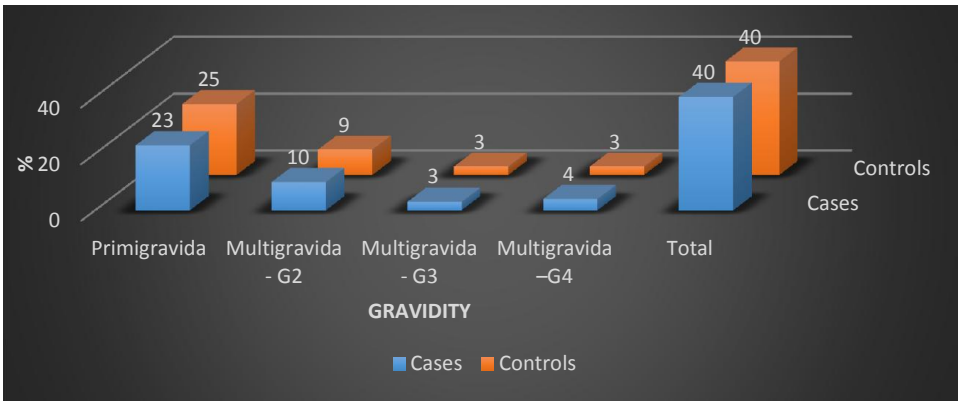

Chart 2: Multiple bar diagram depicting parity distribution among cases & controls

TABLE 4: Gestational age distribution of the subjects under the cases

Gestational Age (weeks)	Cases	
	N	%
28-30+6	3	7.5
31-33+6	20	50
34-36+6	17	42.5
Total	40	100
Mean±SD	33.42±2.98	

The above table shows the gestational age distribution of the subjects under the study groups. Majority of the patients were in the gestational age group of 31.1-34weeks i.e50% .The least number of patients were in the gestational group of 28.1-31 weeks i.e 7.5% .The mean gestational age in the cases was 33.42±2.98 weeks.

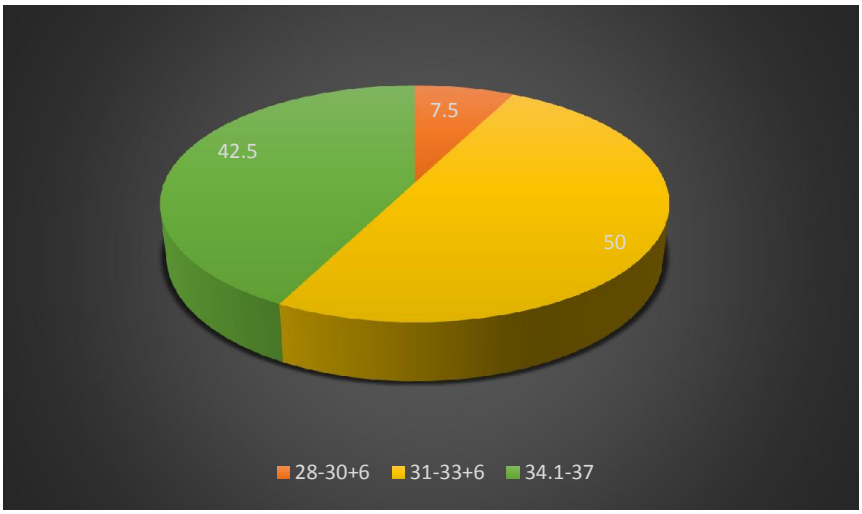

Chart3:Pie chart showing gestational age distribution under the study groups

TABLE 5:Comparison of S.Vitamin D levels between Preterm (cases) group & Term(controls) group

	N	Mean (ng/ml)	Standard Deviation	Median (ng/ml)	P value
Cases	40	18.36	11.6	16.7	<0.001
Controls	40	34.3	13.2	37.7	

The above table shows that the mean value of S. vitamin D among the cases was 18.36 ng/ml and among the controls was 34.3 ng/ml. The median value among the cases was 16.7 ng/ml and among the controls was 37.7 ng/ml. The p value was less than 0.001 hence it was statistically significant

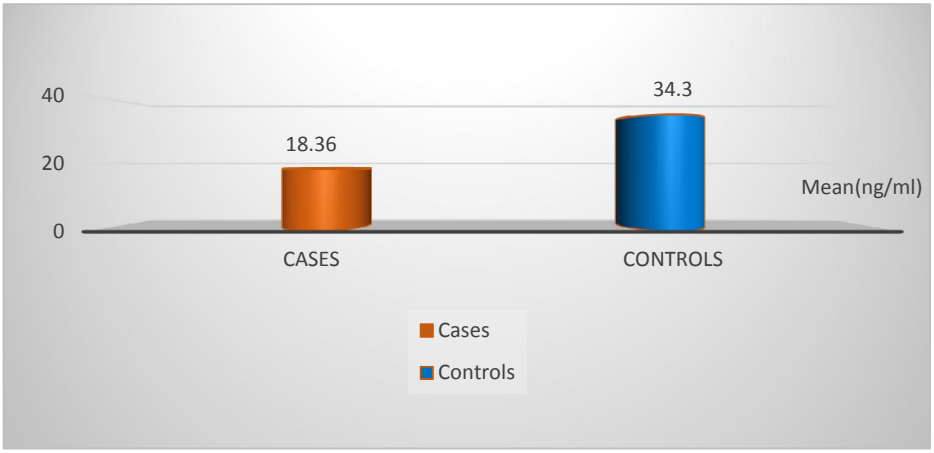

Chart 4: Bar diagram depicting mean vitamin d levels in preterm and term groups.

TABLE 6:Comparison of S.Vitamin D levels between Early preterm and late preterm

Gestational age	Mean(ng/ml)	Std. Deviation	Median(ng/ml)
28-30+6	25.2	3.9	16.4
31-36+6	20.1	12.0	16.7

The above table shows that the mean value of S. vitamin D among the early preterm women was 25.2 ng/ml and among the late preterm women was 20.1 ng/ml. The median value among the early preterm was 16.4 ng/ml and among the late preterm was 16.7 ng/ml

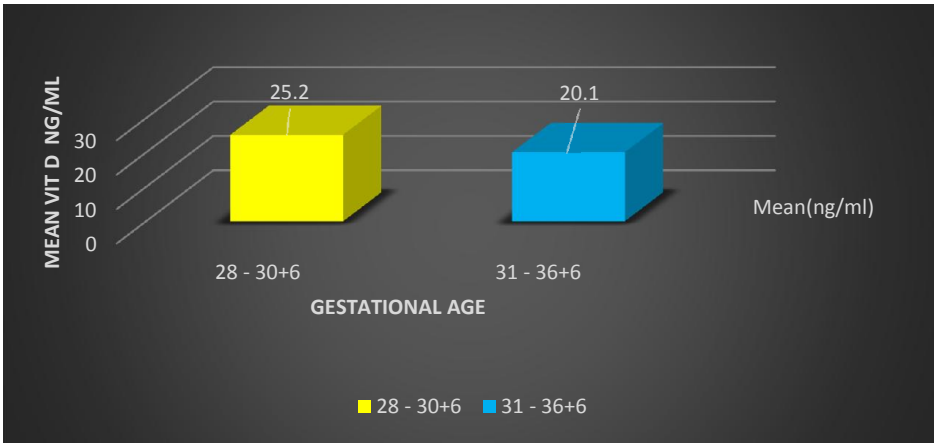

Chart 5: Bar diagram showing mean vitamin d levels in early preterm and late preterm groups.

TABLE:7 Odds ratio and logistic regression value with vitamin d levels

Vitamin d levels ng/ml	Cases	Control	Odds Ratio	95%Confidence Interval		P value
				Lower Bound	Upper Bound	
< 12	1	9				
12- 19.9	4	12	0.33	0.03	3.51	0.361
20- 49.9	33	18	0.06	0.01	0.52	0.001
>50	2	1	0.06	0.00	1.32	0.074

The p value of the group with vitamin d levels between 12-19.9 is < 0.05 and p value of the group with vitamin d levels 20-49.9 is 0.01 hence statistically significant.

TABLE:8 Pearson correlation between maternal vitamin D and neonatal vitamin D

Maternal vitamin D and neonatal vitamin D correlation	Pearson Correlation	significance
	0.837	<0.001

The above table describes the Pearson correlation between maternal vitamin D levels and neonatal vitamin D levels is 0.837 and p value is <0.001 hence statistically significant.

TABLE:9 Comparison of S.Vitamin D levels in cases with PPROM and without PPROM

	N	MEAN (ng/ml)	MEDIAN (ng/ml)	STD DEVIATION	P VALUE
PPROM	21	16.52	16.7	7.82	0.0032
WITHOUT PPROM	19	20.13	16.7	8.0006	

The above tables shows mean vitamin d levels in cases with PPROM is 16.52 ng/ml and median of 16.7 ng/ml and in cases without PPROM is 20.13ng/ml and median of 16.7ng/ml. the p value is <0.05 hence statistically significant.

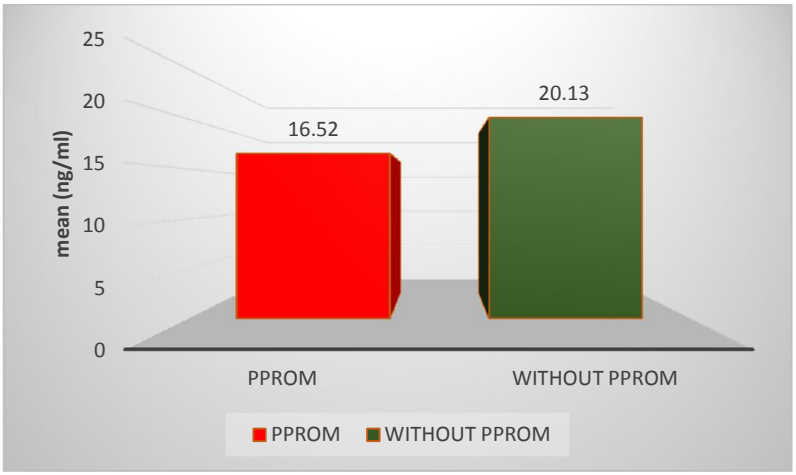

Chart 6: Bar diagram showing mean vitamin d levels in cases with PPROM and without PPROM

TABLE:10 Comparison of S.Vitamin D levels in preterm babies and term babies

	N	Mean(ng/ml)	Std. Deviation	P value
Preterm babies	40	18.6	10.9	<0.001**
Term babies	40	27.0	8.9	

The above table shows that the mean value of S. vitamin D among the preterm babies was 18.6 ng/ml and among term babies was 27.0 ng/ml.The p value was less than 0.001 hence it was statistically significant.

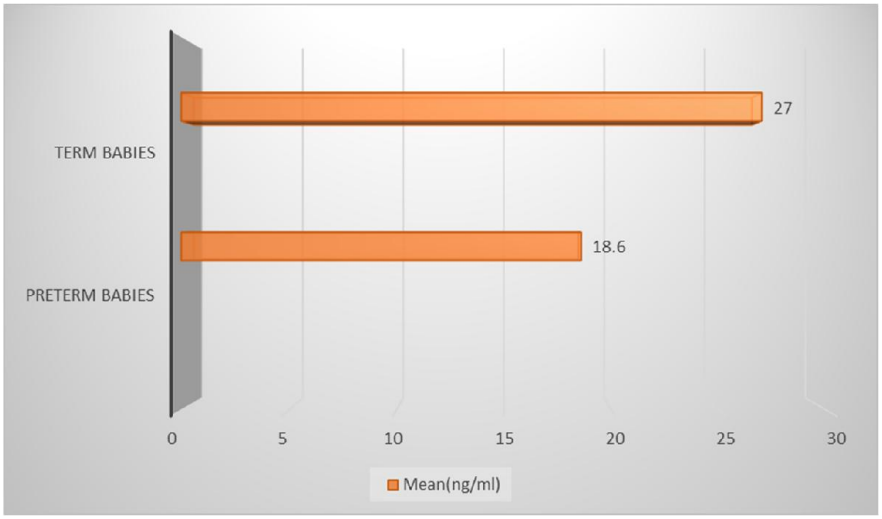

Chart 7: Bar diagram showing mean vitamin d levels in preterm babies and term babies

TABLE:11 Sex of the baby among the groups studied

Sex of baby	Cases		Controls	
	N	%	N	%
Female	28	70	26	65
Male	12	30	14	35
Total	40	100	40	100

The above table shows that in the preterm group, among the babies 70% were female and 30% were male. In the term group, among the babies 65% were female and 35% were male

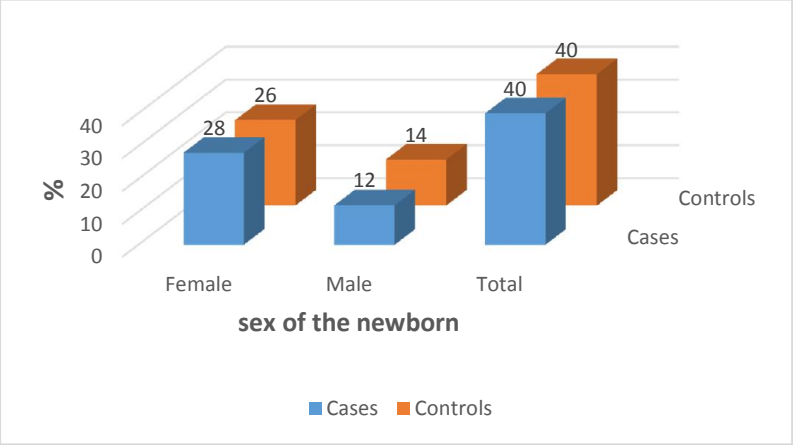

Chart 8: Multiple bar diagram depicting the sex of the baby in the study groups

TABLE:12 Neonatal outcome in cases

Neonatal complications	number	percentage	Mean vitamin D(ng/ml)
Hyperbilirubinemia	13	32.5%	14.23
Sepsis	4	10%	14.25
Birth asphyxia	6	15%	16.1
ROP	1	2.5%	14.7
AOP	5	12.5%	15.6
Respiratory distress	17	42.5%	17.65

The above table depicts that respiratory distress is the most common complication among the cases is respiratory distress with 42.5% and second most common complication is hyperbilirubinemia with 32.5%.

The mean vitamin D levels in all the cases was below 20ng/ml.

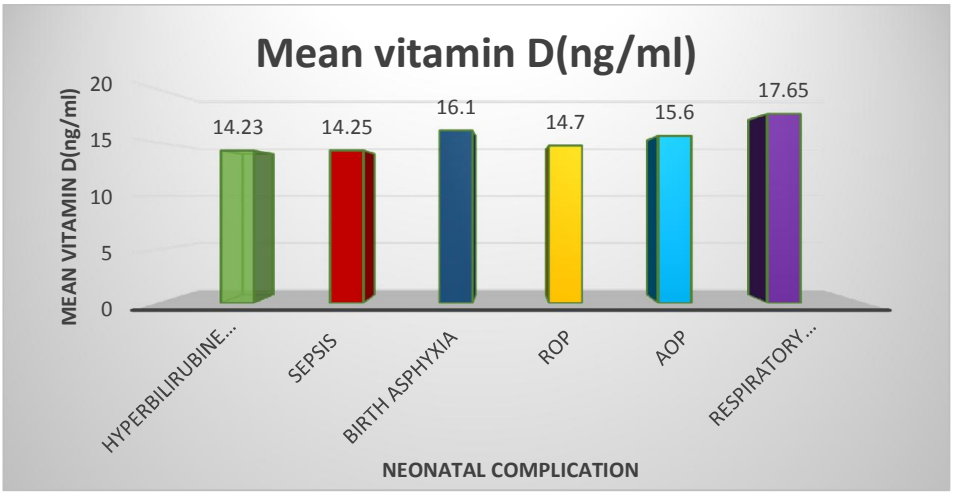

Chart no 9: Bar diagram showing mean vitamin d levels in newborns with neonatal complications

Discussion

Preterm labour is a multi-factorial event, with an interplay of various endogenous pathophysiological features such as stress, genetic factors (predisposition to inflammation, with or without evidence of infections), environmental and occupational factors, that may exist singly or in combination. If incipient preterm labor can be diagnosed, intensive obstetric intervention can be initiated early in patients who are at greater risk, thereby improving maternal and fetal prospects.

Vitamin D is a prohormone which affects established physiological pathways in the pathogenesis of preterm birth, including inflammation, immunomodulation, and transcription of genes involved in placental function.[79] Given the known association between vitamin D deficiency and increased markers of inflammation, some have suggested a role of vitamin D in prevention of preterm birth. Only a few studies have investigated this question.

As the majority female population residing in rural area of Kolar which comprises of women who mostly are housewives and spend most of the time indoors and are negligent towards antenatal care hence risk of hypovitaminosis D is high which was reported in this study.

Table no 13: Comparison of age and gestational age in different studies

Study	Age (yrs.)	Gestational age
Singh J et al.[80]	23.94 ± 3.11	35.10 ± 1.23
Bodnar et al.[81]	24.03±3.99	33.63±2.32
Dziadosz et al[82]	32.5	32.69±1.8
Baker et al[83]	28.5±3.3	30.26±2.4
Tong Zhu et al[84]	26.6±5.6	35.58±2.9
Present study	23.5±3.5	33.42±2.98

Maternal age is one of the important risk factors for preterm labour. In the present study, majority of the cases were in the age group of 21-25years (75%). This was followed by 26-30 years (12.5%) and then <20 years age group (7.5%).

The mean age of present study population was 23.5±3.5 years which is comparable to the study population of Singh J et al. (23.94years), Bodnar et al.(24.03±3.99 years) and Tong Zhu et al.(26.6±5.6 years) .[80,81,84] While it was found that the mean age in our study was different from the study

population of Dziadosz et al. was 32.5 years and by Baker et al. (28.5±3.3 years).[82,83] Among all the studies 3 studies had mean age less than 25 years out of which 2 were Indian studies. This could be because of early marriage practices in India which in turn results in pregnancy at earlier age compared to the western countries.

Bodnar et al also reported in their study that women aged less than 20 years were more likely to be vitamin D deficient and also are at an increased risk of spontaneous preterm birth.[81] In our study the mean vitamin D levels in women less than 19 years was 32 ng/ml which was not comparable to Bodnar et al which could be due our low number of women less than 20 years (7.5%).

Gestational age at delivery is an important factor in view of neonatal outcome. Majority of the cases (50%) were between gestational age of 31.1-34 weeks. The mean gestational age at delivery in this present study was 33.42±2.98 weeks which was comparable with all the other studies that we reviewed. The mean gestational age for Singh J et al. (35.10 ± 1.23), Bodnar et al. (33.63±2.32), Tong Zhu et al. (35.58±2.9), Dziadosz et al.

(32.69±1.8) and by Baker et al. (30.26±2.4) have been mentioned in table no 11 .[80-84]

Table no 14: Comparison of vitamin D levels in different studies

STUDIES	MEAN S.Vitamin D levels in ng/ml		
	Term	Pre term	P value
Singh J et al.[80]	29.85	25.46	<0.05.
Bodnar et al.[81]	32	18.4	<0.003
Dziadosz et al [82]	39	19.3	0.002
Baker et al[83]	35.6	34.6	0.255
TongZhu etal[84]	25.48	18.8	<0.001**
Present study	34.3	18.36	<0.001**

In this present study it was seen that the mean vitamin D levels in preterm labour group was inadequate i.e. less than 20 ng/ml compared to term labour group and the p value (<0.001) was statistically significant. Similar study was done by Singh et al in Wardha in India showed the incidence of preterm labour was seen more in women with mean vitamin D levels of 25.6ng/ml.[80] Although this study had similar environmental conditions as ours the mean vitamin D in preterm was comparatively higher than ours.

Bodnar et al studied vitamin D status among white women with non-white women after adjusting for maternal race, age, socioeconomic position, parity, marital status, prepregnancy BMI, season, smoking during pregnancy, showed that non-white women with vitamin D levels less than 30nmol /L had increased risk of preterm labour which was comparable with our study.[81]

In a retrospective cohort study, Dziadosz et al concluded that Vitamin D levels<20 ng/mL in early pregnancy yielded an increased risk of Preterm birth (between 23 and 37 weeks).[82] In this study they had also supplemented in early gestation and showed preterm delivery despite supplementation.

A study done in northeast China by Tong Zhu et al showed that 63% of women who delivered before 32 weeks of gestation had vitamin D levels less than 20ng/ml.[84] This study also relates to our study as they have studied in rural population with poor antenatal checkup , poor education status and poor dietary vitamin D intake.

While there are other studies that show no association between vitamin D and preterm labour. Baker et al in his nested case control study, studied the association of first trimester vitamin D levels and risk of spontaneous preterm birth and concluded that vitamin D levels was not associated with

Preterm birth.. The incidence of vitamin D deficiency was only 6.9% which was much lower to recently published data.

In Tanzania, no difference was noted in risk of preterm birth (<37 weeks, RR=0.84 [0.55–1.28]) or early preterm birth (<34 weeks, RR=0.77 [0.50, 1.18]) when compared with normal controls for level of Vitamin D among HIV-positive women using a cut-off of 32ng/ml.[52] Since preterm birth with vitamin D deficiency is associated with its immunomodulatory effects and in HIV positive are already immunologically compromised this can add as confounding factor to evaluate the infections and immunology functions.

Similarly, no difference in the third trimester 25(OH) D levels was found for adolescents in the UK delivering preterm vs. normal gestational length babies. [53]

We also studied the vitamin D levels in the newborns of both preterm group and term group, the mean vitamin D level in preterm babies was 18.6 ng/ml and in term group it was 27.0 ng/ml which showed significant difference of vitamin D level in preterm and term newborns which was similar result as concluded by Burris et al. They studied the vitamin D levels in cord blood of preterm and term infants.[85]

The mean vitamin D levels in early preterm (28-31 weeks) was 25.2ng/ml and late preterm (31.1-37 weeks) was 20.1ng/ml. These results were comparable to the study done by Burris et al in Boston where the mean vitamin D levels in preterm babies was <20ng/ml.[85]

In our study there was also significant association between maternal vitamin D levels and neonatal vitamin D levels. A study done by Kumar P et al in south India also showed similar association with mean vitamin D levels in maternal blood of 16.3ng/mL, and mean cord blood level of 12.8 ng/mL.

The mean vitamin D levels in subjects with PPROM and without PPROM in our study were 16.52ng/ml and 20.13ng/ml which shows severe hypovitaminosis in women with PPROM.

The most common neonatal complications in our study were respiratory distress, hyperbirubinemia and sepsis and all the babies with complications had vitamin D levels <20ng/ml.

SUMMARY

The present study entitled "***VITAMIN D LEVELS IN PRETERM LABOUR AND ITS IMPACT ON OBSTETRIC OUTCOME IN RURAL TERTIARY CARE HOSPITAL***" was conducted at R.L. Jalappa Hospital and Research Centre attached to Sri Devaraj Urs Medical College, Kolar from March 2014 to August 2015. The sample size of the study was 80 of which 40 were preterm labour patients (cases) and the other 40 were term labour patients (controls).

Based on the results of the study it can be summarized that:

- Majority of the cases were in the age group of 21-25 years (75%)
- The incidence of preterm labour was more among the Primigravida (57.5%).
- The mean gestational age in the study group was 33.42±2 weeks.
- The mean value of S. vitamin D among the cases was 18.36 ng/ml and among the controls was 34.3 ng/ml which was statistically significant suggesting S. vitamin D levels are significantly low in preterm labour when compared to term labour.
- Mothers with low vitamin D deliver newborn with deficient vitamin D.
- Vitamin d levels in cases with PPROM is 16.52 ng/ml and median of 16.7 ng/ml and in cases without PPROM is 20.13ng/ml and median of

16.7ng/ml, which was statistically suggesting lower vitamin D levels in women with PPROM.

- The most common complication among the cases is respiratory distress with 42.5% and second most common complication is hyperbilirubinemia with 32.5%.The mean vitamin D levels in all the cases was below 20ng/ml.
- The findings of this study may suggest that S. vitamin D levels plays a role in the pathogenesis of preterm labor .It can therefore be evaluated in pregnant women who are high risk for preterm labour and supplementation of vitamin D could be helpful in the early management and prevention of preterm labour.

CONCLUSION

In the present study it was concluded that vitamin D levels in women with preterm labour are significantly lower compared to women in term labour.

There is an increased risk of preterm labour with hypovitaminosis of vitamin D.

Preterm newborns have significantly lower vitamin D levels compared to term newborns.

Vitamin D levels are inadequate in women with PPROM compared to women without PPROM

STRENGTHS:

- In this study we have excluded all the known causes of preterm birth, thereby reducing many confounding factors.
- We have also compared the neonatal outcome in both term and preterm neonates which helps in knowing the need for vitamin D supplementation for affected neonates.

LIMITATIONS:

- Since this was a dissertation due to time constraint seasonal variations in vitamin D and long term complications of hypovitaminosis could not evaluated.

FUTURE

Despite growing interest in the relationships between vitamin D status during pregnancy and perinatal and infant health outcomes, the epidemiological evidence base remains weak for all of the outcomes. Evidence of a potential role of vitamin D on a number of perinatal and maternal health outcomes are needed to evaluate the potential for vitamin D supplementation to prevent adverse outcomes.

There is a need for spreading awareness amongst the society about vitamin D deficiency and its effect on pregnancy. In developing nation like ours were majority of population resides in rural area there is a need for creating awareness regarding importance of regular ante natal checkups and to have a safe and a healthy pregnancy.

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PROFORMA

NAME: **AGE:** **IP NO:**
DOA: **Time of admission:** **DOD:**

OCCUPATION:
ADDRESS:

H/O presenting complaints:

Obstetric history: Married life: Consanguinous/Non consanguinous:
Gravid: Para: Abortions: Living: Dead:
Previous pregnancy details:

Present pregnancy details:

Menstrual history: Age of menarche:
Previous menstrual cycles:
LMP: EDD: POG:
Acc. to wks scan:

Past history:

Family history:

Personal history: Diet: Appetite:
Sleep: Bowel/Bladder habits:

Addiction:

General physical examination

Pallor :
Icterus:
Edema:
Clubbing/ Cyanosis/ Lymphadenopathy
Breast:
Thyroid:
Spine:

Vital signs: Temperature BP:
Pulse rate:
Respiratory rate:

Systemic examination

RS: **CVS:**
CNS:

Per abdomen:
Uterus size:
Relaxed / Irritable / Acting
Presentation: cephalic/ Breech/
FHS:

Per speculum:

Per vagina: Effacement
Dilatation
Station
Membranes
Pelvis

DIAGNOSIS:

TREATMENT:

DETAILS OF DELIVERY:

Mode of delivery: Vaginal delivery/ Caesarean section

VAGINAL-
spontaneous /induced : TD -
IDI –

CAESAREAN-
Indication:

DETAILS OF NEONATE:

Sex : Date: Time:
Birth weight :
APGAR : 1'- 5'-
Admission to NICU:

Perinatal morbidity/ mortality:

INVESTIGATIONS:

Hemoglobin: PCV: RBC:
WBC: Blood group:
Platelet count: BT: CT:
RBS:

Urine analysis:
OBS scan:

S. Vitamin D ::

Maternal -
Neonatal-

SRI DEVARAJ URS MEDICAL COLLEGE & RESEARCH CENTRE, TAMAKA, KOLAR

Patient consent form

Case no

Title: "VITAMIN D3 LEVELS IN PRETERM LABOUR AND ITS IMPACT ON OBSTETRIC OUTCOME IN RURAL TERTIARY CARE HOSPITAL"

Name of the investigator:

Name of the participant: _____

I _____d/o,w/o_____ give my full, free and voluntary consent to participate in the study entitled "VITAMIN D3 LEVELS IN PRETERM LABOUR AND ITS IMPACT ON OBSTETRIC OUTCOME IN RURAL TERTIARY CARE HOSPITAL." I have read (or it has been read to me) and understood this consent form. I have understood that I have the right to refuse consent or withdraw it at any time during the study and this will not affect my treatment in any way. I was free to ask questions and undergo examination and they have been answered to my satisfaction. I have been explained about the intent of the study.

Signature / Thumb impression of the Participant

Name: _____ Date: _____ Time: _____

Researcher to Complete I …… certify that I have explained the nature and procedures of the research project to …… and consider that she/he understands what is involved.

Signed …….. Date ……..

Name and Address of Principal Investigator:

KEY TO MASTER CHART

1. Sl nl -serial number

2. hosp no-hospital number

3.gest age – gestational age

4.obs score- obstetric score

Pprom- Premature prelabour rupture of membranes

MOD- mode of delivery

Bsex- baby sex

Wt- weight of newborn

Nicu-neonatal ICU admission

Mort- Neonatal mortality-

N.C- neonatal complication

m vit d - maternal vitamin D

N vit d- Neonatal vitamin D

Neonatal complication

1 hyperbilirubinemia

2 sepsis

3 birth asphyxia

4 retinopathy of prematurity

5 apnea of prematurity

6 respiratory distress

sl no	age	hosp no	gest age	obs score	pprom	MOD	Bsex	Wt	nicu	mort	N.C	m vit d	N vit d
1	19	98225	33	primi	yes	vag	m	1.9	y	no	1,5	27.5	17.7
2	23	98338	34	primi	no	vag	f	1.9	y	no	3	23.4	17.6
3	20	14112	33+5	primi	yes	vag	f	2.4	n	no	6	22.3	14.8
4	25	1715	32	G2P1L1	yes	vag	f	1.4	y	no	2	22.6	11.8
5	23	468	36	primi	no	vag	m	2.3	y	no	6	9.6	8
6	26	1014123	35+5	primi	yes	vag	f	2.4	n	no	6	14.3	13.4
7	28	233	36	G4P3L3	no	vag	f	2.3	y	no	6	8	10
8	22	1012653	34+3	primi	no	vag	f	2.3	y	no	2,6	9.52	10.7
9	26	1012618	35	G2P1L1	no	vag	m	2.3	y	no	1	11.5	10.7
10	24	25880	35	G3P2L1D1	yes	vag	f	2.2	y	no	5	27.1	18.6
11	25	59727	33+2	primi	no	vag	m	1.7	y	no	2,5	40	19.1
12	25	54359	34+1	primi	yes	vag	m	2	y	no	6	28.5	32.7
13	23	5698	33	primi	yes	vag	m	1.6	y	no	6	20	27.8
14	20	52262	35	G2A1	no	vag	f	2	y	no	1	8	14.5
15	23	39369	29+4	G4A3	no	vag	f	1.1	y	no	1,2	15.7	12.8
16	19	44221	31+5	primi	no	vag	f	1.4	y	no	6	14.2	19
17	20	42452	32+4	primi	no	vag	m	1.4	y	no	5,6	8	12.4
18	20	47658	35+3	primi	no	vag	f	2.1	y	no	6	14.2	18.2
19	22	24160	36	primi	no	vag	f	2.4	y	no	nil	23.1	20.5
20	25	4081	31+5	G4PILIA2	yes	vag	m	1.8	y	no	1	22.3	15.7
21	30	4228	32	G4P3L3	yes	vag	m	2.1	y	no	nil	20.4	12.7
22	23	16838	34+4	G2P1L1	yes	vag	f	2.3	y	no	nil	22.5	23
23	23	4970	35+1	primi	yes	vag	f	2.3	y	no	nil	29.6	30.2
24	20	4996	36	primi	yes	vag	f	1.9	y	no	1	33.2	31.4
25	22	6220	34+4	primi	yes	vag	m	1.7	y	no	1	24.4	15.1
26	19	21433	33	primi	no	vag	m	1.8	y	no	6	16.4	16.6
27	27	5469	31	G3PILIA1	yes	vag	m	2.2	y	no	5,6	24.8	19.5
28	24	168342	32+4	primi	no	vag	f	1.9	y	no	1	14.8	8
29	24	4231	32	G2p1l1	no	vag	f	2.1	y	no	1	19.2	17.9
30	24	64150	34	G2P1L1	yes	vag	f	2.2	y	no	6	8.5	18.9
31	22	6424	34+5	G3A2	no	vag	f	1.7	y	no	6	17	25.9
32	25	90615	33	G2P1L1	yes	vag	f	1.7	y	no	6	13.7	13.9
33	20	88237	35	primi	yes	vag	f	1.9	y	no	5,6	13.9	8
34	22	83308	32+5	primi	yes	vag	f	2	y	no	1	14.1	14
35	36	76920	29+5	G2A1	no	vag	f	1.2	y	no	2,5	8.61	13.9
36	32	68547	34	G2P1LI	yes	vag	f	2.1	y	no	3	8	14.6
37	22	65771	32	G2P1L1	yes	vag	f	1.7	y	no	2,6	9.21	17.2
38	20	89875	32	primi	no	vag	f	1.4	y	no	1	25.3	8
39	24	89147	34	primi	yes	vag	f	1.9	y	no	1	21.2	12.4
40	24	86303	35	primi	yes	vag	f	2.4	y	no	1	14.8	8
41	20	90637	39+3	primi	no	vag	f	3.2	n	no	nil	28	18
42	28	90633	38+3	pimi	yes	vag	f	2.9	n	no	nil	13.5	9.24
43	19	24346	38+6	primi	yes	vag	f	3	n	no	nil	28	19.6
44	25	988281	37+5	primi	yes	vag	f	2.8	n	no	nil	36	28.3
45	24	18791	38+2	primi	yes	vag	f	2.9	n	no	nil	21.4	19.7
46	36	88017	39+4	primi	yes	vag	f	2.7	n	no	nil	28	28.25
47	23	28557	37+5	primi	yes	vag	f	3.2	n	no	nil	24.8	22.7
48	25	21868	38+6	primi	no	vag	f	3.1	n	no	nil	67.2	67.9
49	18	1020271	39+1	primi	yes	vag	f	3.4	n	no	nil	46.3	40.6

50	22	57485	38+3	primi	no	vag	f	3.2	n	no	nil	21.4	26.1
51	22	3911	37+5	primi	no	vag	m	2.9	n	no	nil	21.1	26
52	20	931298	39+4	primi	yes	vag	m	2.8	n	no	nil	49.7	49.7
53	22	99723	39+2	g2p1l1	no	vag	m	3.1	n	no	nil	24.3	25.2
54	19	15932	38+5	primi	yes	vag	f	2.8	n	no	nil	49.8	33.3
55	22	101805	39+6	primi	yes	vag	f	3.1	n	no	nil	44.3	42
56	24	990026	38+4	primi	yes	vag	f	3.2	n	no	nil	15.1	14.6
57	22	20966	37+5	primi	no	vag	m	3	n	no	nil	42.9	38
58	21	9913	37+3	G2A1	yes	vag	f	2.8	n	no	nil	46.3	22.4
59	23	101797	39+4	g2p1l1	yes	vag	f	3.1	n	no	nil	47.7	30.6
60	24	100344	37+4	primi	no	vag	f	2.4	n	no	nil	42.3	31.6
61	25	23096	39+3	primi	yes	vag	f	2.8	n	no	nil	60.7	42.3
62	25	32259	38+3	g2p1l1	no	vag	f	3.1	n	no	nil	64	41.6
63	23	101391	38+6	primi	no	vag	f	2.9	n	no	nil	19.7	19.2
64	20	96536	37+5	primi	no	vag	f	2.7	n	no	nil	43.8	29.6
65	23	101832	38+2	primi	no	vag	f	2.7	n	no	nil	28.4	22.8
66	19	98825	39+4	g3p2l2	yes	vag	f	2.6	n	no	nil	38.8	32.2
67	20	988637	37+5	g2p1l1	no	vag	f	2.4	n	no	nil	16.8	19.5
68	20	28148	38+6	primi	yes	vag	f	2.5	n	no	nil	48.6	29.8
69	22	98909	39+1	primi	no	vag	f	2.6	n	no	nil	45	34.8
70	25	28533	38+3	g3p2l2	no	vag	f	2.8	n	no	nil	38.2	33.4
71	30	990842	37+5	primi	no	vag	f	3.1	n	no	nil	26.5	29
72	23	20289	39+4	primi	yes	vag	f	2.7	n	no	nil	39.7	28.5
73	23	25839	39+2	primi	yes	vag	f	3	n	no	nil	33.2	20.1
74	20	98826	38+5	g2p1l1	no	vag	f	2.8	n	no	nil	46.6	28.01
75	22	96542	39+6	g3p2l2	yes	vag	f	2.9	n	no	nil	29.8	24.7
76	19	20343	39+3	primi	yes	vag	f	2.6	n	no	nil	37.2	28.74
77	27	95080	38+5	primi	no	vag	f	2.6	n	no	nil	45.8	25.1
78	24	993805	37+5	primi	no	vag	f	2.7	n	no	nil	28.1	22.6
79	24	24726	37+2	primi	no	vag	f	2.9	n	no	nil	30.6	28.2
80	24	978542	39+6	primi	no		f	3	n	no	nil	42.7	37.4