CORRELATION OF VITAMIN D LEVELS AND GESTATIONAL DIABETES MELLITUS

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Dissertation submitted to

The Tamil Nadu Dr.M.G.R Medical University, Chennai

In partial fulfillment of the requirements for the degree of

Master of Surgery in Obstetrics and Gynecology

Under the guidance of

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The Tamil Nadu Dr. M.G.R Medical University, Chennai

MAY 2018

CERTIFICATE

This is to certify that the dissertation entitled, **"CORRELATION OF VITAMIN D LEVELS AND GESTATIONAL DIABETES MELLITUS**" is the bonafide original research work of **Dr. KALAIARASI .V.** under the guidance of **Dr. T.V. CHITRA, M.D, DGO, DNB.,** Professor, Department of Obstetrics and Gynecology, P.S.G IMSR, Coimbatore in partial fulfillment of the requirement for the degree of Master of Surgery in Obstetrics and Gynecology.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled Signature of the guide **"CORRELATION OF VITAMIN D LEVELS AND GESTATIONAL DIABETES MELLITUS"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. KALAIARASI .V.** under the guidance of **Dr.T.V.CHITRA, M.D, DGO, DNB,** Professor, Department of Obstetrics and Gynecology, P.S.G IMSR, Coimbatore. This dissertation is submitted to The Tamil Nadu Dr. M.G.R Medical University in fulfillment of the University regulations for the award of MS degree in Obstetrics and Gynaecology. This dissertation has not been submitted for award of any other degree or diploma.

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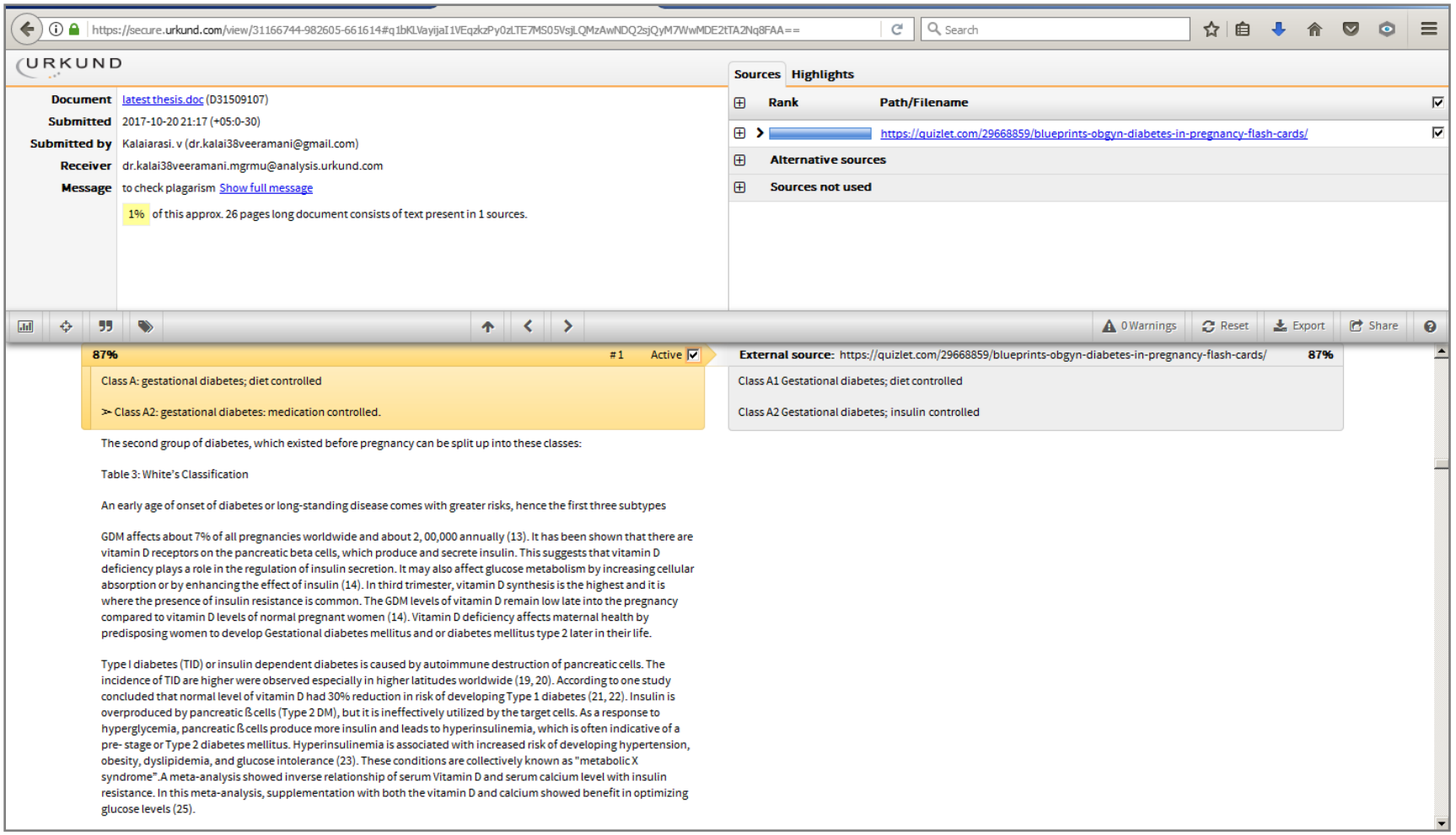
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Class A1 Gestational diabetes; diet controlled
Class A2 Gestational diabetes; insulin controlled
The second group of diabetes, which existed before pregnancy can be split up into these classes:
Table 3: White's Classification
An early age of onset of diabetes or long-standing disease comes with greater risks, hence the first three subtypes
GDM affects about 7% of all pregnancies worldwide and about 2, 00,000 annually (13). It has been shown that there are vitamin D receptors on the pancreatic beta cells, which produce and secrete insulin. This suggests that vitamin D deficiency plays a role in the regulation of insulin secretion. It may also affect glucose metabolism by increasing cellular absorption or by enhancing the effect of insulin (14). In third trimester, vitamin D synthesis is the highest and it is where the presence of insulin resistance is common. The GDM levels of vitamin D remain low late into the pregnancy compared to vitamin D levels of normal pregnant women (14). Vitamin D deficiency affects maternal health by predisposing women to develop Gestational diabetes mellitus and or diabetes mellitus type 2 later in their life.
Type I diabetes (TID) or insulin dependent diabetes is caused by autoimmune destruction of pancreatic cells. The incidence of TID are higher were observed especially in higher latitudes worldwide (19, 20). According to one study concluded that normal level of vitamin D had 30% reduction in risk of developing Type 1 diabetes (21, 22). Insulin is overproduced by pancreatic ß cells (Type 2 DM), but it is ineffectively utilized by the target cells. As a response to hyperglycemia, pancreatic ß cells produce more insulin and leads to hyperinsulinemia, which is often indicative of a pre- stage or Type 2 diabetes mellitus. Hyperinsulinemia is associated with increased risk of developing hypertension, obesity, dyslipidemia, and glucose intolerance (23). These conditions are collectively known as "metabolic X syndrome".A meta-analysis showed inverse relationship of serum Vitamin D and serum calcium level with insulin resistance. In this meta-analysis, supplementation with both the vitamin D and calcium showed benefit in optimizing glucose levels (25).

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CONTENTS

INTRODUCTION

One billion of world population, all ages and ethnic groups are affected by Vitamin D deficiency. Nowadays, Gestational vitamin D deficiency is common. High prevalence of vitamin D was seen in developing (such as Bangladesh, India, Iran, Pakistan, Somalia) as well as developed countries (such as Australia, Finland, Japan, the Netherlands, United Kingdom and USA).

Normal body function is regulated by vitamin D. Vitamin D is a fat soluble vitamin. Vitamin D is naturally present in few foods, produced endogenously when exposed to ultraviolet rays. Vitamin D biologically inert and must undergo hydroxylation in our body for activation .There are two major forms of vitamin D are vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) (1). Vitamin D is a derivative of cholesterol. Naturally Vitamin D is available in food like fish -Tuna, fish liver oil, egg yolks, cheese and mushroom. Fatty flesh fish and fish liver oil is the best source of vitamin D.

Vitamin D is produced in the skin when exposed to ultraviolet light. The ultraviolet light acts on 7-dehydrocholesterol producing pre-vitamin D. Pre-Vitamin D is then converted to vitamin D, which enters the circulation

which travels to the liver. In the liver, vitamin D is 25-hydroxylated to form 25-hydroxyvitamin D [25(OH) D] levels of 25(OH) D are measured to assess the levels of vitamin D in the body and is a precursor to the active metabolite 1, 25-dihydroxyvitaminD [l,25(OH)2D]. Exclusively released from the kidneys, 1, 25-(0H)2 D plays an important role in calcium homeostasis along with parathyroid hormone produced and released from the parathyroid glands. The action of 1, 25(OH) 2 D is to increase the absorption of calcium from the intestine and inhibit the secretion of parathyroid hormone to maintain a normal serum level of calcium level. Vitamin D acts on vitamin D receptors that are found in many different tissues in the body, and plays an important role in glucose regulation, cardiovascular system, bone mineral density and many other biological functions.

Vitamin D plays a role in glucose metabolism by regulating insulin secretion and/or by increasing the sensitivity of tissue to insulin. High blood pressure is found in vitamin D deficiency. Low levels of vitamin D were associated with low vascular endothelial growth factor (VEGF) and increased pro-inflammatory cytokines which can cause damages in the vessel. It increases intestinal absorption of calcium and reduces the secretion of parathyroid hormone. This is to maintain serum calcium levels. Low levels of vitamin D lead to the release of parathyroid hormone, which takes up calcium

out of the bone and decreases bone mineral density which affect the bone strength. Normal range of vitamin D facilitates the absorption of calcium from intestine, increases the calcium channel and calcium binding protein.

Vitamin D is needed to maintain various body functions like immunity, increases calcium absorption from intestine, decreases PTH synthesis ,decreases Left ventricular hypertrophy, improves bone osteoclastic differentiation, improves hematopoiesis and increases insulin secretion from Vitamin D Deficiency can lead to imbalances in the regulation of many systems. Vitamin D deficiency can predispose the individuals to Gestational diabetes mellitus, hypertension, cancer, bone development issues in children and many other conditions. Getting adequate vitamin D is important to help maintain normal serum calcium levels and homeostasis within the body Vitamin D facilitates active absorption of the calcium in the small intestine by increasing the calcium channel and increasing the calcium binding protein expression and it interacts with vitamin D receptor in osteoblasts and promotes the maturation of preosteoclasts.

Vitamin D has a number of extra skeletal functions. Vitamin D binding to the vitamin D receptor (VDR) and regulates the hundreds of genes (either directly or indirectly) including those that control key processes affecting cell

fate. The complexity of vitamin D action is further increased by VD-0gene polymorphism. The reported associations with plethora of phenotypes (including cancer, autoimmune, cardiovascular, metabolic, and renal and many other diseases) have been extensively met analyzed and reviewed. Vitamin D also exerts Reno protective and antiproteinuric effects with several mechanisms involved including inhibition of renin-angiotensin aldosterone system (by decreasing renin expression), suppression of inflammation (by reducing accumulation of inflammatory cells), and restoration of glomerular filtration barrier (by attenuating podocyte damage) According to the committee of the Institute of Medicine.

Table-1: Serum 25-Hydroxyvitamin D [25(OH)D] Concentrations and Health

Serum 25-Hydroxyvitamin D [25(OH)D] Concentrations and Health* [1]		
nmol/	**ng/mL***	**Health status**
<30	<12	Associated with vitamin D deficiency, leading to rickets in infants and children and osteomalacia in adults
30 to <50	12 to <20	Generally considered inadequate for bone and overall health in healthy individuals
≥50	≥20	Generally considered adequate for bone and overall health In healthy individuals
>125	>50	Emerging evidence links potential adverse effects to such high levels, particularly >150 nmol/L (>60 ng/mL)

* Serum concentrations of 25(OH) D are reported in both nano moles per liter (nmol/L) and nanograms per milliliter (ng/mL).

** 1 nmol/L = 0.4 ng/ml

Vitamin D deficiency during pregnancy can have many negative health effects for the mother and developing fetus. The fetus gets vitamin D from the mother. When the mother has vitamin D deficiency, the fetus is also predisposed to vitamin D deficiency in early infancy, which may lead to many health issues

in the future including delayed milestones, Rickets etc. Normal level of maternal l, 25(OH)2 D which increases gradually from the first trimester to the third trimester. The increase in serum level of vitamin D is due to the increase in production of 1, 25 (OH)2 D (l). Fetal calcium levels depend on the maternal vitamin D level and are normally higher than maternal levels throughout the gestation. Calcium is actively transported across the placenta into fetal circulation. Fetal vitamin D levels are usually 20% lower than maternal levels.

Vitamin D crosses the placenta during the last trimester of gestation. This develops the fetal vitamin D stores. If the mother has vitamin D deficiency, then, less vitamin D will be transported across the placenta and the fetus will have a low vitamin D store at birth (6). Low levels of vitamin D at birth may predispose the infant to low calcium levels and rickets over the first few months of life. This indicates that vitamin D deficiency in the mother can have a direct impact on the developing fetus (1).

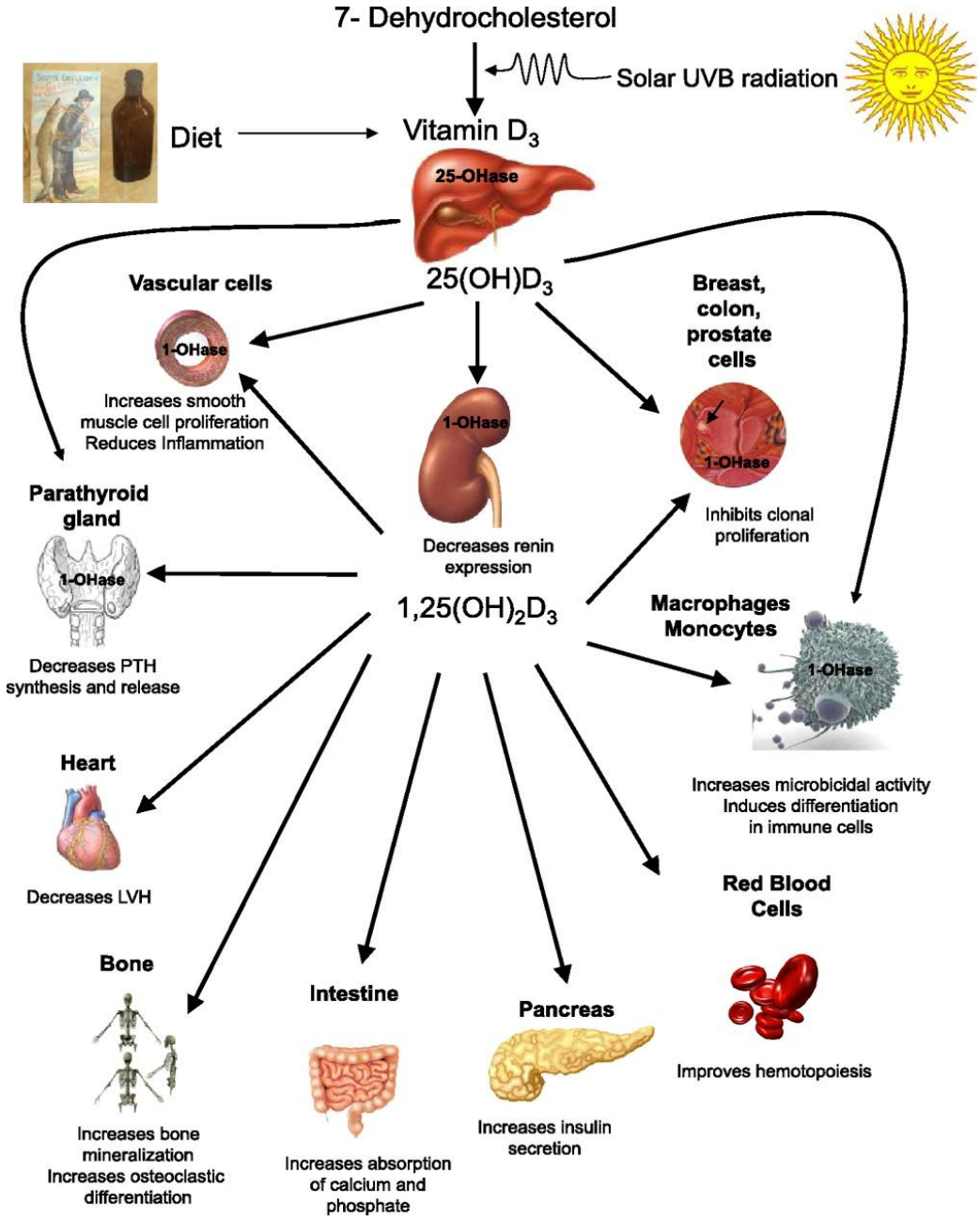
Lower levels of vitamin D in pregnant women has increased due to multiple risk factors such as lack of adequate sun exposure, darker skin pigmentation, sunscreen usage , clothing coverage full body and latitude of residence and ethnicity.

One study has shown that approximately 29 % of Black pregnant women and 5% of white pregnant women living in northeastern United States are vitamin D deficient (2).

Vitamin D deficiency during pregnancy has been linked. Some of the adverse outcomes for the mother are pregnancy induced hypertension, preeclampsia, gestational diabetes, and an increased rate of cesarean section (four fold increases risk –according to RCOG 2014) [1]. Although it is not clear with adequate levels of maternal and neonatal vitamin D, these adverse outcomes can be avoided .

The largest and main source of vitamin D in adults is synthesis from solar radiation; half an hour of sunlight delivers 50 000 is of vitamin D with white-complexioned skin. Dietary intake of vitamin D makes a relatively small contribution to overall vitamin D status as there is little vitamin D that occurs naturally in the food supply which absorbed through intestine and circulate. Melanin absorbs ultraviolet B (UVB) from sunlight and diminishes cholecalciferol production by at least 90%.

Figure-1: Pathophysiology of Vitamin D



Maternal hypocalcaemia leads to Pre-eclampsia and neonatal hypocalcaemia which is the most prevalent complications and associated with

morbidity. A statistical association of glucose intolerance and low level of vitamin D has been done.

EFFECT ON FETUS - Maternal low vitamin D leads to certain fetal complication which include

A) Poor lung development and neonatal immune conditions such as asthma,

B) Small size at birth

C) Skeletal problems in infancy and childhood and neonatal morbidity including Childhood Rickets.

D) In an Australian study,-. Maternal Vitamin D deficiency is a major cause of hypocalcaemia seizures in neonates and infants. Hypocalcaemia is not uncommon in neonates and is a potentially severe problem. Mothers of babies who suffer hypocalcaemia seizures are more likely to be vitamin D deficient (85%) than mothers of babies who do not (50%).In another study from Egypt; all mothers of babies with hypocalcaemic seizures had severe vitamin D deficiency. Supplementation with vitamin D to pregnant women can prevent these complications.

E) Schizophrenia

F) Autism

G) Mental retardation

H) Three times more likely to develop juvenile diabetes before the age of 15

I) Craniotabes is softening of the skull bones that occurs in 1/3 of “normal” newborns. Recent evidence indicates it is yet another sign and sequela of maternal vitamin D deficiency.

EFFECT ON MOTHER :

A) Caesarean section

B) Preeclampsia

C) Gestational diabetes

D) Bacterial vaginitis

Marya et al., (72) conducted randomized case control study involving 200 Asian Indian pregnant women. She randomly grouped. Group 1 100 – they received 6 lakhs IU of vitamin D twice during last trimester. Group 2- includes 100 pregnant women without supplementation. High Serum calcium level and Serum Alkaline phosphatase were low in pregnant women who were treated with vitamin D and they were compared. Cord blood sample were collected between these two groups and compared the values of high Serum calcium level and low alkaline phosphatase level in Group 1. Group 1 infant had greater intrauterine growth, greater birth weight greater head-toe length, and greater head circumference than group 2.

Recent American study (74) published in April 2017 says that 400 IU of vitamin D daily per orally had the greatest benefits in preventing preterm birth and IUGR and infection. Vitamin D is needed to improve in immune function, healthy cell division and healthy bone development in neonates and in mother. Vitamin D supplementation in addition to reducing insulin resistance it also reduces the preeclampsia. Vitamin D hormone is available in sunlight. Due to certain factors the absorption of vitamin D is delayed.

PREVALENCE OF GESTATIONAL DIABETES

The prevalence of Type II Diabetes is increasing globally including India. In 1997 WHO estimates the prevalence of diabetes in adults showed an expected total rise of >120% from 135 million in 1995 to 300 million in 2025. As of today, we have no current national data regarding the occurrence of abnormal glucose tolerance in the pregnant women. Southern Asia is at the top of the diabetes projections list with an expected total rise of 79.4 million people by 2030. Current national diabetes prevalence is 4.3 % Studies conducted in India in the last decade have highlighted that the prevalence of type 2 diabetes high and also that it is increasing rapidly especially in the urban population than rural population. An urban-rural difference in the prevalence rate was found, indicating that the environmental factors related to urbanization had

significant role in increasing the prevalence of diabetes. Boddula at al (75)., reported a prevalence of diabetes of 21.2 % and an Impaired Glucose Tolerance rate of 18.2% in an urban south Indian population of high socio-economic group with significant difference which is explained by obesity.

Diabetes mellitus is diagnosed in Reproductive age group women more frequently. Such reproductive age group women become pregnant with their pregnancy complicated by diabetes mellitus and complication associated with uncontrolled diabetes. With increasing sedentary life style, lack of physical exercise and lack of activities they are increased chance of obesity and development of Type II diabetes mellitus at early age. Family history also contributes to development of Diabetes Mellitus at earlier. The trend toward late marriage and late conception, the epidemic of obesity and diabetes, decrease in physical activity, adoption of modern lifestyles, diet high in saturated fat and smoking may all contribute to an increase in the prevalence of DM.

GDM is associated with severe perinatal complications, offspring of GDM mother are at risk of developing DM in life. Besides obesity, another major independent risk factor for GDM is vitamin D deficiency is now being postulated along with multiple other effects on the mother and the fetus.

The main purpose of this paper is to find out the new emerging issues of vitamin D deficiency during pregnancy. Estimation of Vitamin D level in normal pregnant women and Gestational diabetes mellitus. Its deficiency has effect on both the mother and the developing fetus. This project includes a review of the literature regarding vitamin D during pregnancy in India and foreign countries. The need for universal screening for pregnant women who are at risk of vitamin D deficient and provide them with the necessary supplementation is still not recommended.

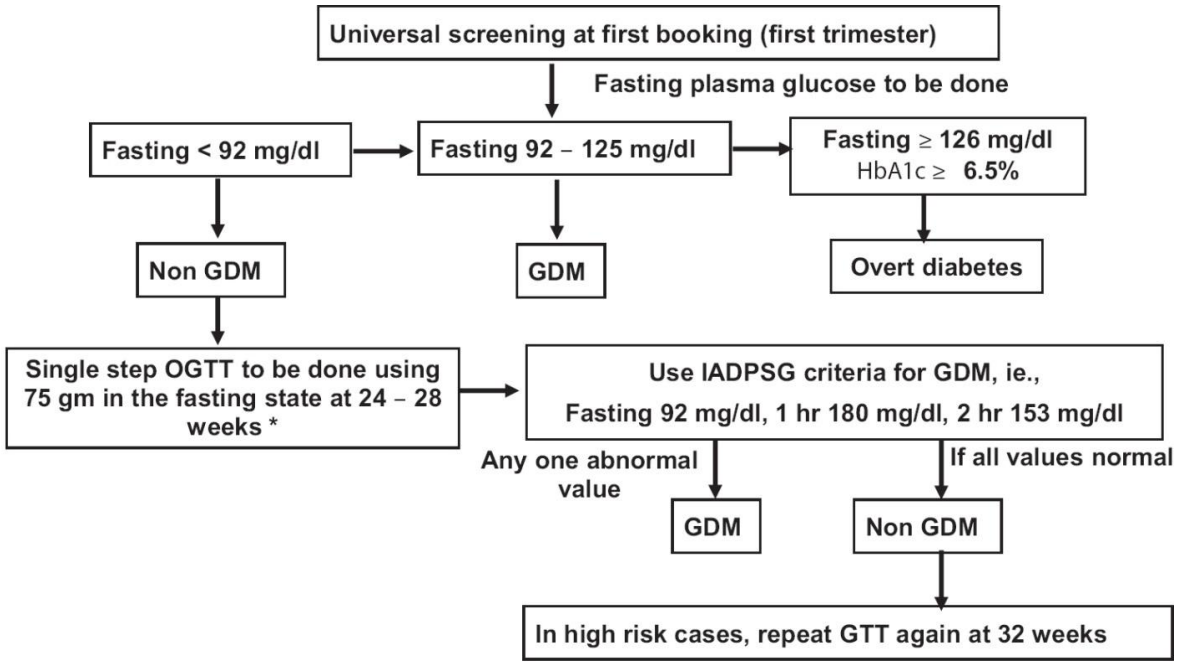
Vitamin D and GDM:

Gestation diabetes mellitus (GDM) is one of the adverse effects of vitamin D deficiency. Gestational Diabetes Mellitus complicates up to 14% of pregnancies depending on ethnicity, diagnostic methods employed and criteria used. About 8% of Asian mothers have a pregnancy complicated by gestational diabetes. In most of the cases the carbohydrate intolerance reverts after pregnancy, itself back but heralds the onset of type 2 diabetes later in life. Women diagnosed to be diabetic early on in pregnancy are probably cases of pre-gestational diabetes who have become overt due to the stress of pregnancy. A woman with random plasma glucose > 200mg/dl with features of polydipsia, polyphagia and polyuria with unexplained weight loss or with plasma fasting glucose > 126 mg/dl is probably a pregestational diabetes, which was latent

during the pre-gestational period and has become overt later in their life. Nevertheless, assessment 6 weeks after delivery is necessary and regular follow up is needed in their life.

In our hospital, we routinely screen for GDM between 24-28 weeks of gestation by ingesting a 75 gram glucose load irrespective of meal and plasma blood is drawn and measured and they are classified according to diet controlled or medication controlled. In some hospital, it is followed up by a 100gram, 3-hour glucose tolerance test (GTT). A fasting glucose level is measured followed by an hourly glucose measure in the 3-hour GTT for a total of 4 glucose readings. If two or more of the four measurements are high in the 3-hour GTT, then the patient is diagnosed with GDM (5).

Figure 2:Universal screening for all antenatal patient



* When a single step fasting OGTT is not possible, do a 2 step procedure, ie., 50 gm glucose challenge test (GCT) in the non fasting state followed by 3 hr OGTT in the fasting state using 100 gm Carpenter and Coustan criteria in those who screened positive in the GCT.

Table 2: 100g OGTT diagnostic criteria for gestational diabetes mellitus

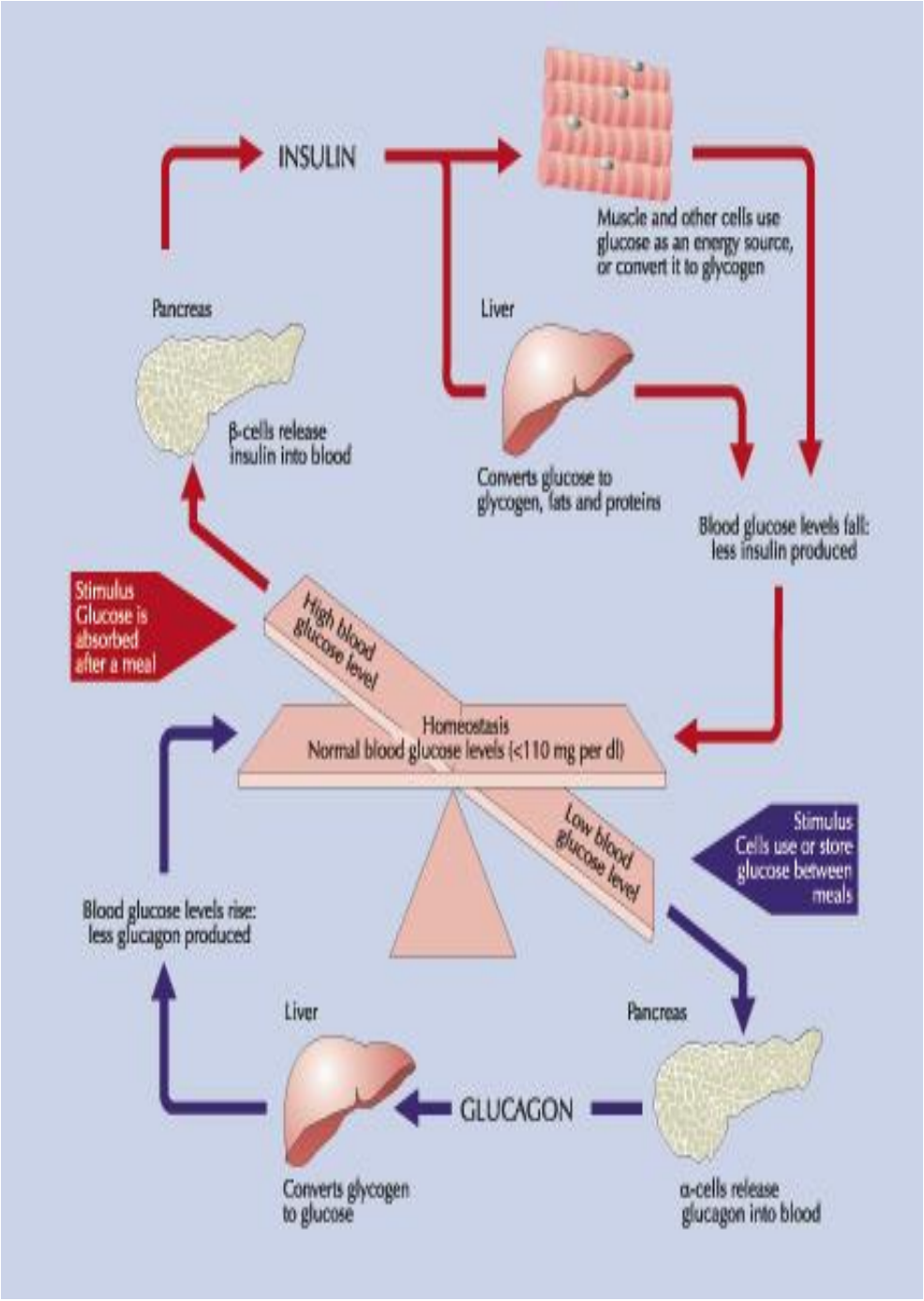
Status	Carpenter-Coustanplasma or serum glucose level	National Diabetes Group plasma level
	Mg/dl	Mg/dl
Fasting	95	105
One hour	180	190
Two hour	155	165
Three hour	140	145

RISK FACTORS FOR GDM

1. l. Previous history of gestational diabetes or glucose intolerance
2. A family history of diabetes
3. Previous macrosomia (> 4,000 g)
4. Previous unexplained stillbirth
5. Previous neonatal hypoglycemia, hypocalcemia, or Hyperbilirubinemia
6. Advanced maternal age
7. Obesity
8. Repeated glycosuria in pregnancy

Figure:3 showing the risk factor for Vitamin D deficiency

Figure 4: Pathophysiology of glucose Metablolism:



IMPAIRED GLUCOSE TOLERANCE (IGT) and IMPAIRED FASTING GLUCOSE (IFG):

a) Fasting plasma glucose >= 100mg/dl but <126 mg/dl

b) 2-hour value in OGTT >= 140mg/dl but <200mg/dl

The White classification, named after Priscilla White who pioneered research on the effect of diabetes on perinatal outcome, is widely used to assess maternal and fetal risk. It distinguishes between gestational diabetes (type A) and diabetes that existed before pregnancy (pre-gestational diabetes). These two groups are further subdivided according to their associated risks and management.

According to American Diabetes Association 2014

Criteria for diagnosing Overt diabetes

- ✓ HBA1C > 6.5 %
- ✓ Fasting blood glucose $\geq$ 126 mg/dl (no caloric intake for last 8 hours)
- ✓ 2 hour plasma glucose $\geq$ 200 mg/dl during 75 gm of OGTT (WHO CRITERIA)
- ✓ Random plasma glucose $\geq$ 200 mg/dl with symptoms of hyperglycemia.

There are 2 classes of gestational diabetes:

- Class A: gestational diabetes; diet controlled
- Class A2: gestational diabetes: medication controlled. The second group of diabetes, which existed before pregnancy can be split up into these classes:

Table 3: White's Classification

White's classification during pregnancy	
Gestational diabetes	Discovered during pregnancy, glycemia may or may not be maintained by diet alone; insulin may be required
Class A	Discovered before preg, controlled with diet alone, any duration or age of onset
Class B	Onset age 20 yr or older, duration less than 10yrs
Class C	Onset age 10-19yrs, duration 10-19yrs
Class D	Onset age under 10yrs, duration >20yrs, background retinopathy
Class R	Proliferative retinopathy, or vitreous hemorrhage
Class F	Nephropathy with proteinuria over 500mg/day
Class RF	Criteria for both classes R and F coexist
Class H	Arteriosclerotic heart disease clinically evident
Class T	Prior renal transplantation

An early age of onset of diabetes or long-standing disease comes with greater risks, hence the first three subtypes

GDM affects about 7% of all pregnancies worldwide and about 2, 00,000 annually [13]. It has been shown that there are vitamin D receptors on the pancreatic beta cells, which produce and secrete insulin. This suggests that vitamin D deficiency plays a role in the regulation of insulin secretion. It may also affect glucose metabolism by increasing cellular absorption or by enhancing the effect of insulin (14). In third trimester, vitamin D synthesis is the highest and it is where the presence of insulin resistance is common. The GDM levels of vitamin D remain low late into the pregnancy compared to vitamin D levels of normal pregnant women (14). Vitamin D deficiency affects maternal health by predisposing women to develop Gestational diabetes mellitus and or diabetes mellitus type 2 later in their life.

Type I diabetes (TID) or insulin dependent diabetes is caused by autoimmune destruction of pancreatic cells. The incidence of TID are higher were observed especially in higher latitudes worldwide (19, 20). According to one study concluded that normal level of vitamin D had 30% reduction in risk of developing Type 1 diabetes (21, 22). Insulin is overproduced by pancreatic ß cells (Type 2 DM), but it is ineffectively utilized by the target cells. As a response to hyperglycemia, pancreatic ß cells produce more insulin and leads to

hyperinsulinemia, which is often indicative of a pre- stage or Type 2 diabetes mellitus. Hyperinsulinemia is associated with increased risk of developing hypertension, obesity, dyslipidemia, and glucose intolerance (23). These conditions are collectively known as "metabolic X syndrome".A meta-analysis showed inverse relationship of serum Vitamin D and serum calcium level with insulin resistance. In this meta-analysis, supplementation with both the vitamin D and calcium showed benefit in optimizing glucose levels (25).

The Third National Health and Nutrition Examination Survey (NHANES Ill) did not demonstrate an association between 25(OH) D levels and diabetes or insulin resistance in African Americans, in contrast to Caucasians and Mexican Americans. In another study of European Caucasian subjects, insulin secretion and action were not associated with levels of 25(OH) D. It is vital that such studies are controlled for obesity, a risk factor itself for vitamin D deficiency.

Scientific impact paper no.43 from RCOG says that depending on the diagnostic criteria they were used, it has been suggested that GDM complicates up to 16% of pregnancies (55, 56) although the true incidence can be much greater in some ethnic groups. There are some data to suggest that the association between vitamin D levels and GDM risk is specific to ethnicity. In a majority non-Hispanic white population, vitamin D level at 16 weeks of

gestation were significantly lower in GDM subjects than in controls, whereas no association was found in Indian mothers where vitamin D (54,58) concentrations were measured at 30 weeks of gestation. 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. Conversely, a well conducted study has found no association between maternal 25(OH) D and the development of GDM in ethnic group. A meta-analysis of 31 studies demonstrated vitamin D insufficiency was associated with a higher risk of GDM (59).

Other adverse effects of Vitamin D deficiency in the mother:

Pregnancy induced hypertension (PIH), or gestational hypertension, is defined as a systolic blood pressure equal to or above 140 or a diastolic blood pressure equal to or above 90 that is recorded on two different occasions with 6 hours apart develops after 20 weeks' gestation and return to normal value within 6 weeks post-delivery , without proteinuria. According to one theory PIH may be caused by an altered metabolism of calcium and parathyroid hormone due to vitamin D deficiency (4,74) Maternal Vitamin D levels increase greatly in the third trimester than in early trimester. If pregnant mother is vitamin D deficient, there are alterations in calcium absorption and

homeostasis. This alteration in calcium absorption, homeostasis mechanisms leads to development of hypertension in pregnancy or gestational hypertension.

Another theory suggests that an increased release of cytokines into the maternal blood stream causes vessel injury and develop Gestational hypertension (16). There are many complications associated with PIH such as placental ischemia, the development of preeclampsia and later the development of eclampsia (16) and study suggested that may be associated with vitamin D deficiency. These adverse effects can greatly increase the morbidity and mortality of both the mother and fetus. Placental ischemia causes decreased oxygen and nutrients to be delivered to the fetus which can lead to increased morbidity and mortality of the fetus.

Preeclampsia (PE) is a serious and life-threatening condition consisting of hypertension, proteinuria (protein in the urine) and other clinical findings (16). It is a pregnancy specific syndrome that affects 37% of first pregnancies (2). Vitamin D deficiency has been implicated in the development of Preeclampsia by its effect on controlling blood pressure (4). Other theories suggest that increased vascular endothelial growth factor (VEGF) during pregnancy leads to PE. VEGF causes vascular damage and dysfunction, which leads to an increase in the blood pressure which predisposes the mother to

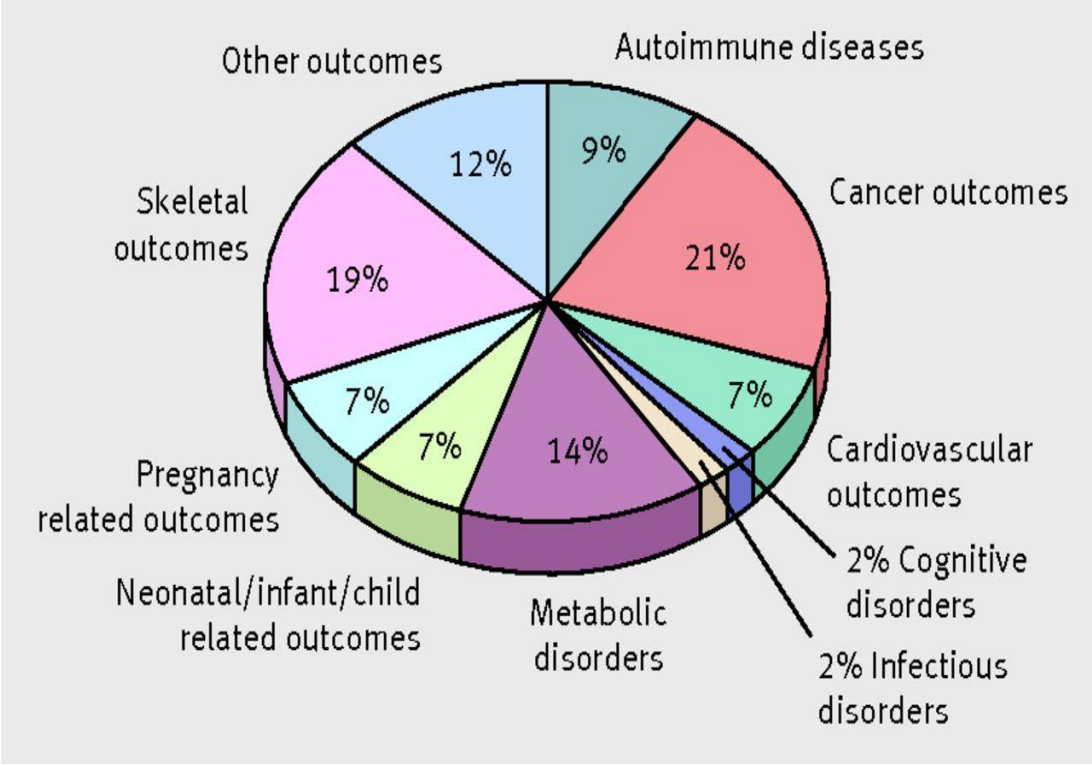
develop PE (16). **Vitamin D insufficiency (vitamin D levels between 37.5 — 80 nmol/L) is an independent risk factor for developing preeclampsia**. PE affects maternal health by increasing her risk for developing eclampsia and other life threatening complications associated with it (16). If eclampsia develops fetus is also at risk (16).

Mothers who are vitamin D deficient are at increased risk of having a caesarian section. As of 2009, the current U.S birth rate by C-section is 30.2% compared to 5% . Several factors can increase the risk of C-section, including muscle weakness associated with vitamin D deficiency, GDM, and PE, which leads to placental ischemia. Women who are vitamin D deficient at the time of delivery are 4 times more likely to deliver by C-section. One theory suggests that skeletal muscle also have vitamin D receptors with muscle weakness as well as suboptimal muscle performance and strength during labor and delivery is associated with vitamin D deficiency. GDM causes the fetus to be larger in size, making it harder to deliver vaginally. If the large fetus is delivered vaginally, there is a higher risk of injury or the fetus can suffer from asphyxia (12). Placental ischemia leads to intrauterine fetal growth restriction and reduced birth weight, which are associated with increased morbidity and mortality to the fetus. In order to save the fetus and reduce the risk of morbidity

and mortality, the fetus is delivered by C-section and is usually delivered prematurely (16).

Vitamin D deficiency is associated with many conditions that greatly affect maternal health. Not only ones' deficiency affects the mother during pregnancy, but it also affects her health in the future. Long term vitamin D deficiency increases the mother's risk of developing diabetes mellitus type 2, osteoporosis and cancer. Vitamin D plays an important role in insulin regulation, bone mineralization and the development of cancer

Figure:5 Vitamin D deficiency and adverse outcome:



Neonatal effects of vitamin D deficiency:

Deficiency not only affects maternal health during pregnancy but it also affects neonatal health. The fetus develops its vitamin D store from the mother in the third trimester. If the mother is deficient, then the fetus will not develop a sufficient vitamin store6. The lack of sufficient vitamin D store predisposes the neonate to increased morbidity and mortality. Some of the issues the neonate faces are bone mineralization issues, which can lead to the development of rickets, and small for gestational age (1). There is a wide range of morbidity that can be seen with vitamin deficiency in the neonate. This includes issues with brain development, heart failure/cardiomyopathy, asthma and type I diabetes.

GDM which is caused by vitamin D deficiency increases the likelihood of morbidity in the fetus by causing the fetus to be large for its gestational age, also known as macrosomia (12). Macrosomia is caused by glucose being transferred across the placenta rather than insulin. Glucose is the primary substrate used for fetal growth. With increased levels of glucose, the fetal growth rate is expected to increase, leading to the overgrowth of the fetus (13). Macrosomia is associated with birth related injuries such as Erb's palsy and asphyxia. Erb's palsy is caused when the fetus is in a breech position and is delivered arm first. Pulling of the arm to deliver the fetus leads to damage to the brachial nerve plexus that is located in the shoulder region (12).

Infant bone mass is influenced by maternal vitamin D levels. The neonate is born with an insufficient store of vitamin D due to maternal deficiency and breast milk is a poor source of vitamin D3 the neonate has no way of getting vitamin D unless they are supplemented with it. Vitamin D plays an important role in bone mineralization through altering maintains calcium homeostasis. This occurs when calcium levels are too low. When vitamin D levels are low, parathyroid hormone is released which stimulates the kidney to convert 25(OH) D to 25(OH) 2 D which increases calcium absorption. Infants who are deficient have increased levels of parathyroid hormone and are hypocalcemia, which affects bone mineral density and can lead to rickets. Infants who are vitamin D deficient are more likely to have lower bone mineral densities as well as bone deformities that can be seen in-utero. Severe vitamin D deficiency during gestation or early infancy is the primary cause of rickets. Rickets is characterized by enlargement of the epiphyses of the long bones, deformities of the legs, growth retardation, bending of the spine, knobby projections from the ribcage and weak and toneless muscles which is also accompanied by seizures in young infants. This leads to long term morbidity due to the bone deformities.

Maternal deficiency has been correlated with low birth weight, length and growth in the first year of the neonate's life. Being born with a low birth weight and length may increase the risk of morbidity and mortality simply because they are small for gestational age. Low levels of vitamin D have been associated with low levels of insulin like growth factor (IGF-I), an important hormone in fetal growth in maternal and umbilical cord blood which may lead to neonates being born small for gestational age 10. Also, placental ischemia caused by PE causes growth retardation causing the baby to be small for gestational age16, Being small for gestational age increases morbidity and mortality for the neonate. If the baby is born at term, they are less likely to have complications associated with their size. If the infant is born prematurely, their organs are not fully developed and are at risk of suffering from morbidity and mortality.

One of the morbidities a neonate can experience from maternal vitamin D deficiency during development is the long-term effect on the brain. It is suggested that vitamin D plays a role in the development of the central nervous system8. The brain is able to synthesize its own active form of vitamin D and expresses its own vitamin D receptors, which are widely expressed in the cortex, cerebellum, mesopontine area, diencephalon, spinal cord, amygdala, and hypothalamus. Vitamin D deficiency during development leads toincreased cellular proliferation in the brain and reduced apoptotic cell death which can

result in long-term or even permanent damage in the brain8. Deficiency during development could be linked to the increased incidence in neurological disorders such as schizophrenia. The incidence of schizophrenia is higher in people living in higher latitudes and in individuals with darker skin. There is a higher incidence of schizophrenia in African Americans and other darker skinned people, since over 40% of African American women of child bearing age are vitamin D deficient. In some populations of females that have high skin pigmentation and low sun exposure, the prevalence of vitamin D deficiency can be as high as 80%, further increasing the risk of the developing fetus developing permanent or long term brain damage (8).

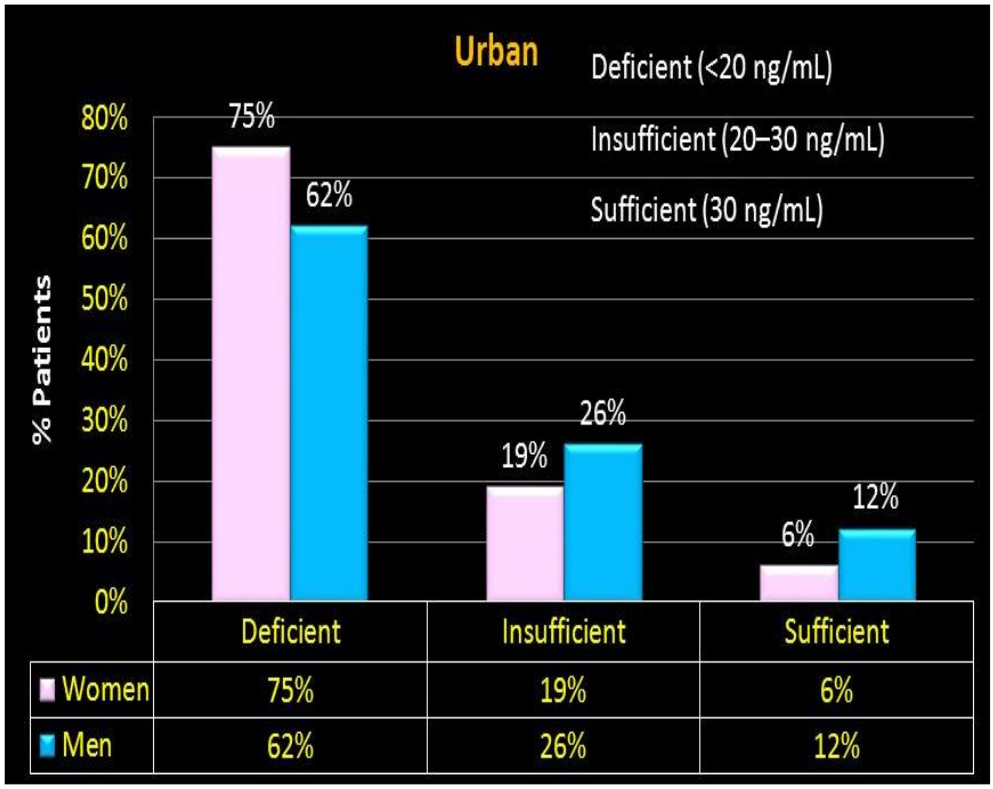
Another serious morbidity a neonate can develop is heart failure due to dilated cardiomyopathy. Dilated cardiomyopathy is a heart condition in which the left ventricle is dilated leading to a decrease in muscle strength and the amount of blood that can be pumped out with each beat. This causes blood to remain in the ventricle after the 9 ventricles contract which leads to an increased and systolic volume. Heart failure occurs due to the low cardiac output which results in hypotension, poor perfusion, breathlessness and even death. Vitamin D plays a key role in calcium balance, which is important for heartcontractility. Vitamin D deficient humans have type IL muscle fiber atrophy as well as increased interfibrillar spaces and fat infiltration, which leads to muscle

weakness. Also, vitamin D deficiency leads to hypocalcemia and an increased level of parathyroid hormone. Parathyroid hormone stimulates the release of calcium from the bones to increase the serum calcium level to correct the hypocalcemia. Hypocalcemia alone is sufficient to cause dilated cardiomyopathy and eventually heart failure (9). This condition can be treated with any drugs and calcium alone, but improvement is slow.

Vitamin D is also linked to the increased incidence of asthma in children of deficient mothers. The lungs epithelial cells express a high baseline lug-hydroxylase, which is an important enzyme that converts inactive 25(OH) to 1, 25 (OH) 2 D, the active form of vitamin D915). The active form of vitamin D acts on the vitamin D receptors (VDR) in the lungs and plays a role in down-regulating airway remodeling, pro-inflammatory modulator release and bronchial smooth muscle proliferation (15). This suggests that lower vitamin D levels could lead to bronchial smooth muscle proliferation, pro-inflammatory modulator release, and airway remodeling. This leads to a hypersensitive airway and remodeling due to the inflammation and activation of metalloproteinase which play an important role in remodeling of the lungs. Vitamin D also interacts with several immune cells such as T-cells, monocytes, macrophages and mast cells (15). Mast cells play an important role in the inflammatory and allergic response associated with asthma. Mast cells are found in higher number

in an asthmatic lung than in a healthy lung. It has been demonstrated that vitamin D increases apoptosis and inhibits maturation of mast cell precursor cells in the bone marrow (15). Adequate Vitamin D leads to aless sensitive airway and decreases remodeling caused by asthma.

Fiigure -6: Vitamin D deficiency in Indian population:



Am J Clin Nutr 2007; 85: 1062-7

Classification of Vitamin D deficiency:

The serum concentration of 25(OH) D is the most reliable marker 0f vitamin D. In the publications, investigators reported their data on 25(OH) D

levels either as nmol (nanomoles per liter) or ng/ml. To simplify information and for the ease of comparison, in this review all the data on 25(OH) D levels were presented in a single concentration unit for serum 25(OH) D levels-ng/ml. Most investigators had used different cutoff levels to define vitamin D as deficiency, insufficiency and normal levels. While some may have done so due to preference, other investigators defined their own cut-off levels as determined by the linear regression between 25(OH) D levels and PTH levels.

Serum Vitamin D estimation:

Plasma 25(OH) D or calcidiol (a summation of and forms) is the most reliable marker of vitamin D status. For estimation of vitamin D various Immunoassays such as radioimmunoassay (RIA), enzyme linked immunosorbent assay (ELISA), chemiluminescence immunoassay and protein binding assays are used in routine testing of 25(OH) D in clinical laboratories. LCTMS (liquid chromatography tandem mass spectrometry) is the widely accepted reference method for 25 (OH) D measurements. However, LCTMS is difficult to perform , very expensive and time consuming and therefore seldom used commercially.

Vitamin D and sun exposure in India:

In India, Vitamin D deficiency is a major health concern not withstanding the brightly shining sun. The "adequacy of exposure to sunlight of an individual's bare skin" required to photosynthesize vitamin D is grossly ill understood. Darker skin have high melanin which acts as a natural sunscreen. Thus, darker skin produces a significantly lesser amount of vitamin D when compared with the individuals with fairer skin Thus, for Indian skin tone, minimum "direct sun exposure" required daily is more than 45 min to bare face, arms and legs to sun's UV rays (wavelength 290—310 nm). Due to changing life style pattern sun exposure is not adequate. Indian social and or religious norms related to public modesty dictate that most parts of an individual's body, irrespective of gender, be covered by clothes. They perforce to live in overcrowded tenements, and closely packed.

Nutritional factors attributing to high prevalence of Vitamin Deficiency in India:

Vitamin D sufficiency by dietary intake is the only solution for Indians. However, this solution itself has many problems.

- Most dietary sources of vitamin D have very low vitamin D content. Animal sources are rich in vitamin D. Most Indians are vegetarians. Commonly, a diet rich in vitamin D are milk and milk products ,

provided milk and milk products has been fortified with vitamin D. But in India it is rarely fortified with vitamin D. The vitamin D content of unfortified milk is very low (2 IU/IOO mL). Due to low socioeconomic status it is unaffordable to buy milk and milk products in India . Another concern in India is the rampant dilution and/or adulteration of milk and milk products.

- Low calcium in Indian diet: Dietary intake of low level of calcium along with low level of Vitamin D is associated with secondary hyperparathyroidism (SHPT). SHPT is further exacerbated by destruction of 25(OH) D and 1, 25(OH) 2D by 24hydroxylase (32). 24 hydroxylasesis the key enzyme of vitamin D catabolism and is regulated by 1, 25(OH) 2D, PTH and FGF 23 (Fibroblast Growth Factor 23) levels. FGF 23 is a phosphate regulator. High level of serum phosphate increases the production of FGF 23 in bone osteocytes via the action of 1, 25(OH) 2D. Subsequently, FGF 23 reduces renal phosphate resorption, indirectly suppresses intestinal phosphate absorption and also suppresses PTH and synthesis. Overproduction of FGF 23 can result in increased morbidity which is associated with vitamin D deficiency. This regulatory mechanism may explain the low 25(OH) D levels in rural subjects on a high phytate and/or low calcium diet, despite plentiful sun exposure.

Most studies reported calcium intake much lower than the RDA (Recommended Daily Allowance) defined by the Indian Council of Medical Research (ICMR). Only two studies reported adequate calcium intake. In both these publications the study subjects were paramilitary soldiers (26, 27).In India calcium intake is lower than that of the western world according to ICMR's - RDA.

- Our body is to maintain calcium balance depending on intake and excretion (34, 35). Even though the Indian diet which is low in calcium content, lower protein content and therefore low endogenous acid production, which may reduce urinary calcium loss. Therefore, the amount of diet rich in calcium is required to maintain calcium balance may be lower than for those in the Occident. The protein-induced alterations in calcium homeostasis (and possibly in bone mass) have been attributed to increases the production of endogenous acid and net acid excretion due to the oxidation of the constituent Sulphur containing amino acids. On the other hand, in India the high salt content diet is likely to increase urinary calcium excretion. A direct relation between the high sodium intake and lower bone mass had been reported (36).

- In India, due to very high intake of caffeine from various sources including coffee. They consume milk which is a part of their tea or coffee. The quantity of milk is very low in these drinks. The level of calcium intake through these beverages is very low. During cooking Vitamin D is stable even up to 200 0C. However, thermal stability of vitamin D during cooking and the duration of cooking is an inverse function. In India, milk is boiled for several minutes and several times before consumption. In India most of the times, beverages including tea and coffee are boiled for several minutes at different temperature to get the right flavor. Repeated boiling of milk may reduce the level of vitamin D . Therefore, these beverages may not contribute significantly to either calcium or vitamin D intake in Indians. Vitamin D is a fairly robust vitamin. The preceding statements about its thermal degradation had been made as precautionary stance to not overstate the thermal robustness of this micronutrient. Additionally, studies had been reported regarding the association of high caffeine intake with increased risk of developing low bone mineral density, osteoporosis, and osteoporotic fractures in middle-aged women. This situation is exacerbated in women with low calcium intake, especially in lean subjects (37) when compared to obese women.

- In India high prevalence of lactose intolerance is a major deterrent pertaining milk consumption, further lowering intake of calcium and vitamin D in these individuals. Ethnic and geographic variations of people with intolerant to lactose were observed, with a higher prevalence in southern (Dravidian descent) and eastern India compared to northern India (Aryan descent).

- Indian diet has high phytate content. Phytate is the principal storage form of phosphorus in many plant tissues, especially in the bran portion of grains and other seeds. Phytate is not digestible to human intestine. Micronutrients such as calcium and iron absorption from intestine is reduced due to phytate . Benefits of sun exposure in rural subjects owing to an agrarian life were seen and there is significantly higher 25(OH) D levels (42) were found . However, due to consumption of diet which is rich in phytate there is insufficient level of these micronutrients in most individuals. Possibly, high phytate content in the diet of soldiers in northern India may have contributed to their vitamin D insufficiency or deficiency, despite adequate exposure to sun light, nutrition and physical exercise (27).

- In India Consumption of diet rich in Phytate especially among the socio-economically lower classes stems from the elementary and immediate need of sufficiency of the calorific need. Cereals and legumes are more affordable and easily available than vegetables, milk and other dairy products. Besides, they are sources of protein for the vegetarians. Many cereals are also sources of calcium, however due to chelation by phytates its bioavailability is limited.
- Notably, nearly all studies pertaining vitamin D status in healthy subjects reported a high level of phytate/ calcium intake ratio. What Indians may require is a higher intake of calcium diet to lower the phytate/calcium intake ratio. Dietary habits in India have been changing significantly. Many people remove a substantial proportion of bran from whole wheat flour before kneading to improve texture and fluffiness of chapattis (unleavened flat bread) and also to increase the taste of the food. Consumption of white bread is also very high. Most people prefer processed, split and polished pulses to whole seeds due to the ease of shorter time required for cooking and the consequent lowered expense of cooking fuel. Consumption of junk foods including burger / instant (or not) noodles/pizza also is on the rise across all socio-economic strata, with exception.

- In the scenario of inadequate calcium intake, vitamin D insufficiency and high phytate content in diet, environmental pollutants such as fluoride add insult to injury. Toxins like fluoride affect bone metabolism severely in the conjunction with inadequate calcium intake and low level of serum vitamin D , especially in children (43,44).

- Cooking practices in India: Indians in general adhere to traditional cooking styles and practices, irrespective of their migration to different part of the world. In tropical climate, perishable food items putrefy quickly. Consumption of uncooked fresh produce, especially vegetables, milk, etc., is generally considered ill-advised. As in the rest of the world, in India too, slow cooking is widely practiced and cooking at varying temperature and stability of vitamin D . Pertaining shallow and deep-frying of food, most cooking fats and oils have smoke points above 180 oc. Shallow and deep frying of foods is very popular in India. When foods are fried, vitamin D in the food comes out into the cooking medium and is thermally degraded (46). Pressure cooking temperatures vary depending on the pressure withstood by the cooker used and may range from 100 oc to 120 oc. Short-time (as short as possible) pressure cooking is definitely advisable to retain at least some of the thermally more stable essential nutrients in cooked food, including vitamin D.

- Publications indicating wide prevalence of vitamin D deficiency in healthy Indians have studied subjects mostly from lower and upper middle classes. Individuals below poverty line were not represented well in these studies. Hence, poor nutrition observed in these studies may also stem from lack of awareness of the features, benefits and necessity of balanced nutrition.

Screening for vitamin D deficiency in pregnancy

There are no data to support routine screening for vitamin D deficiency in pregnancy. There is an argument that some groups of women who are pregnant should have a screening test: for example, on the basis of skin color or coverage, obesity, risk of pre-eclampsia or gastroenterological conditions limiting fat absorption. 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 (60). Measurement of vitamin D in a hypokalemic pregnant women or symptomatic woman 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 (61,62).Particular care should be taken over high-risk women. The recommendations are based on the classical actions of vitamin D, although many of the non classical 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". Of course, this does not necessarily demonstrate that correction during pregnancy will reduce these risks.

Three categories of vitamin D supplementation are recommended (RCOG-2014).

1. **In general**, vitamin D 10 micrograms (400 units) per day is recommended for all pregnant women in accord with the national guidance (61).This should be available through the Healthy Start programme(63)

2. **High-risk women** are advised to take at least 1000 units per day (women with increased skin pigmentation, reduced exposure to sunlight, or those who are socially excluded or obese) (64). Women at high risk of pre-eclampsia are advised to take at least 800 units per day + combined with calcium. Vitamin D may be inappropriate in sarcoidosis (where there may be vitamin D sensitivity) or ineffective in renal disease. Deficient renal I-u hydroxylation necessitates the use of active vitamin D metabolites, such as luhydroxycholecalciferol or 1, 25-dihydroxycholecalciferol. Specialist medical advice should be sought in such cases. 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 (e.g. Fultium-D3, Internis, London; Desunin, Meda, Bishop's Stortford, UK). There may be particular benefits of vitamin D/calcium supplementation in women at risk of Pre-eclampsia (66, 67).

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 (68,69). 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). In adults, very high doses of vitamin D (3, 00,000—5, 00,000 IU intramuscular [1M] 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 (70).

Table4: Supplementation and treatment recommendation (RCOG – 2014)

Supplementation	Daily units	Combined with
Vitamin D	400 (a) 800 (b) 1000 (c)	Not applicable Calcium Not applicable
Treatment Cholecalciferol Ergocalciferol	 2800 2800(d)	 20,000IU once a wk 10,000 IU twice a wk

a. Recommended for all pregnant women
b. Recommended for women with high risk of pre-eclampsia
c. Recommended for women at high risk of vitamin D deficiency
d. To be taken through and after the high-dose supplementation

Vitamin D supplementation and fortification in India:

Supplements commonly available are-D3 (cholecalciferol), and 1 alpha hydroxy vitamin D3 (alfacalcidol). Some formulations have calcium too. Multivitamin formulations are also available and contain about 400 IU of D3. D3 supplement of 60,000 IU is the highest selling one and is available in

powder form in sachets or as oil-based capsules. Recommended dose on the label is once per week. The sachets indicate that half a sachet per week may also be taken. According to some pharmacists, many clinicians recommended one sachet daily for 10 days, followed by one sachet/week for 5—6 weeks to 1 sachet/week forever. The other vitamin D supplements mentioned here are present in lower doses (0.25 pg or 500 IU) and daily intake (1-4 times/day) may be recommended by the clinicians. Calcium supplementation is generally recommended with vitamin D intake. The cost of a single dose of 60,000 IU of vitamin is about INR 30. Vitamin D sufficiency via sun exposure is untenable for most Indians, as discussed earlier. Vitamin D (relatively) rich dietary sources are unaffordable and mostly limited, especially for vegetarians. Most Indians are vegetarians. Vitamin D supplements are unaffordable and not feasible as a population based approach. Fortification of widely consumed staple foods with vitamin D is the only viable solution towards attaining vitamin D deficiency in India (17). Unlike supplementation strategies, fortification of food with vitamin D poses a negligible risk of toxicity.

AIM AND OBJECTIVES

AIM:

The objective of this study is to determine the impact of vitamin D deficiency on maternal complications like Gestational Diabetes Mellitus (GDM).

OBJECTIVES:

Primary Objectives: Assessing the levels of vitamin D in pregnant women.

- To study the vitamin D status of pregnant women with GDM complicating pregnancy after 37 weeks (GROUP –A).
- To study the normal vitamin D levels in pregnant women without any complication after 37 weeks (GROUP- B).

Secondary Objectives: Correlation between vitamin D levels and Gestational diabetes mellitus in pregnant women.

The justification for this study: Low levels of vitamin D status, as measured by 25-hydroxyvitamin D [25(OH) D], are common in pregnant women. There is a positive association between vitamin D status and adverse pregnancy outcomes like Gestational Diabetes Mellitus.

MATERIALS AND METHODS

Source of Data:

The study will be conducted on all low risk antenatal and GDM patients admitted in the PSG IMSR – Labour Ward, Coimbatore.

Study design: Prospective longitudinal observational study.

Study Population:

All low risk antenatal mothers as control group and Gestational diabetes mother as study group admitted in PSG institute of medical sciences and research, Coimbatore – labour ward after 37 weeks of gestation between August 2016 to August 2017.

Study Locale (geographic area): Department of obstetrics and Gynaecology-Labour ward PSG Institute of Medical science and research centre, peelamedu , Coimbatore.

Sample Size: With reference -Vitamin D status and gestational diabetes mellitus according to Jayaraman Muthukrishnan, Goel Dhruv DOI: 10.4103/2230-8210.163175

FORMULA

N =2x(2alpha +2 beta)2 x SD2

(M t – m c)2

SD= 28,

Mt= 24.7

Mc = 45.8

2alpha +2 beta = 7.84

N = 2x7.84 x28 x28

(24.7 -45.8)2

= 12293

445.21

Result = 27 in each group.

So approximately taking 30 in each group.

Sampling Method:

All low risk pregnant mothers visiting labour ward will be selected randomly as control group (Group-B) and Gestational diabetes mother as study group(Group -A). Patients will be randomly allocated to either one of the 2 groups.

Duration of study: 1 year (August 2016- 2017)

Inclusion Criteria:

- All low risk pregnancy
- Vertex and non vertex presentation.
- Age < 35 yrs
- Pregnancy complication (GDM) – on Diet
- Gestational age after 37 weeks

Exclusion Criteria:

- Overt diabetes.
- Abnormal placental presentation
- Other complications (PIH, anemia, preeclampsia, multiple gestation)
- Other medical complications (chronic kidney disease)
- GDM on insulin and OHA

- Gestational age < 37 weeks
- Not willing for study.
- On steroids, Metformin.

Data collection and proforma will be done only by the PI

Methodology

- 30 pregnant women with GDM were selected randomly and classified as GROUP A. 30 low risk pregnant women with normal blood glucose levels were selected randomly and classified as Group B.

- All low risk pregnant women between 24-28 weeks of gestation were screened for GDM by an Oral Glucose tolerance test with 75 gm of glucose in 200 ml of water irrespective of meal.

- 3 ml of venous blood sample were collected after 2 hours.

- 3ml blood will be collected after getting consent form and sent to biochemistry department for Vitamin D level estimation method is ELECROCHEMILUMINESCENCE IMMUNOASSAY (ECLIA).The obtained results will be compared between low risk antenatal patients and Gestational Diabetes Mellitus patients.

REVIEW OF LITERATURE

Robert J et el., Vitamin D deficiency in pregnant women leads to low level of vitamin D in unborn fetus and the complications associated with it.

One study was published in PLOS One by Grass roots health – conducted in South Carolina- 1000 pregnant women - 25-hydroxyvitamin D serum level of greater than or equal to 40 ng/ml had 60% reduction in preterm birth which is significant p=0.0001.

Madhu Jain et el., conducted study in NORTH INDIA- deficiency of Vitamin D as a risk factor for Gestational Diabetes Mellitus- Maternal deficiency of Vitamin D in early pregnancy is highly prevalent and it is an independent risk factor for Gestational diabetes mellitus. Supplementation of Vitamin D to pregnant women would prevent or improve in glycemic control needs further clinical trails.

Heather H Burris et al.,(78) In this study Sixty-eight (5.2%) women met criteria for GDM. Unadjusted analysis revealed that women with vitamin D levels <25 vs. ≥25 nmol/L analyzed and had significantly increased odds ratio for GDM (OR 3.6, 95% CI 1.7, 7.8. Adjustment analysis for race/ethnicity, age, education status, marital status, smoking, parity and season of blood draw made

little difference to this estimate (OR 3.1, 95% CI 1.3, 7.4). Additional adjustment analysis for maternal BMI attenuated the association and the confidence interval included the null value (OR 2.2, 95% CI 0.9, 5.6). Further adjustment for pregnancy weight gain made little difference (OR 2.3, 95% CI 0.9, 5.7). Addition of physical activity and dietary intakes of fish and calcium also made little difference (OR 2.2, 95% CI 0.8, 5.5).

Study conducted in ARMED forces in Pune by **Jayaramam Muthukrishnan et al., (53)** Study concluded that level of Vitamin D is associated with GDM. Low level of Vitamin D was associated with GDM. However replacement of Vitamin D does not reverse the glucose intolerance. There is no justification or standard guidelines at present for routine screening for Vitamin D deficiency in all antenatal pregnant women.

Heather H. Burris et al., (71) conducted another publication, regarding maternal serum level of vitamin D in second trimester in Gestational diabetes mellitus. Low levels of maternal serum Vitamin D is inversely proportional to the risk of GDM. OGTT were done and levels were compared.

Pittsburg Public Health study conducted by **Alison Gernard et al.** used a random sample of 2,146 pregnant women who participated in the Collaborative Perinatal Project, which was conducted in 12 U.S. medical centers from 1959 to

1965. If pregnant mother was deficient before 14 weeks, her baby had twice the risk of developing intrauterine growth restriction in utero.

Hannah Furfaro et al., study was conducted in Netherland and published in June 2017. They have included 4,000 children for this study. At the age of 6, only 68 children had Autism. Researches said statistically significant link between the low levels of vitamin D in pregnant women and children with Autism**.** No one knows the exact mechanism for developing Autism. In this study they recommend low dose of Vitamin D daily till delivery.

Marya et al., (72) conducted randomized case control study involving 200 Asian Indian pregnant women. She randomly grouped. Group 1 100 – they received 6 lakhs IU of vitamin D twice during last trimester. Group 2- includes 100 pregnant women without supplementation. High Serum calcium level and Serum Alkaline phosphatase were low in pregnant women who were treated with vitamin D and they were compared. Cord blood sample were collected between these two groups and compared the values of high Serum calcium level and low alkaline phosphatase level in Group 1. Group 1 infant had greater intrauterine growth, greater birth weight greater head-toe length, and greater head circumference than group 2.

Veronica Boyle et al., (73) - significant number of pregnant women do not meet the recommended levels. Neonates whose mother lad significant low level of vitamin D during her pregnancy had had a thinning of bone at birth and greater risk of developing rickets later in life. Beyond calcium homeostasis the consequences of vitamin D not yet clearly understood. Vitamin D plays a role in other system including inflammation, vascular function and glucose metabolism, renal.

Recent American study published in April 2017 **Carol L.Wagner et al.,** (74) says that 400 IU of vitamin D daily per orally had the greatest benefits in preventing preterm birth and IUGR and infection. Vitamin D is needed to improve in immune function, healthy cell division and healthy bone development in neonates and in mother. Vitamin D supplementation in addition to reducing insulin resistance it also reduces the preeclampsia. Vitamin D hormone is available in sunlight ,in order for the body to manufacture it properly. Due to certain factors the absorption of vitamin D is delayed.

Jain M et al., Maternal Vitamin D Deficiency: done in North India A Risk Factor for Gestational Diabetes Mellitus in North India- case control study was done taking 550 random antenatal women. Two maternal blood samples, one at <20 wks and the other at term along with cord blood were taken. Study

concluded that maternal vitamin D deficiency is highly prevalent in early pregnancy and is an independent risk factor for GDM in North India (52).

Anna PleskaIova et al (76)., confirmed in her article that overall high prevalence of vitamin D deficiency in pregnant women in spite of the GDM presence. The most striking observations of this study are significantly higher prevalence of early postpartum 25(OH)D deficiency in women with GDM history compared to those without. Potentially beneficial effect of vitamin D supplementation and the pathogenic role of vitamin D deficiency in the subsequent development of type 2 diabetes mellitus in women with GDM history has to be further explored considering the role of vitamin D in modulating insulin sensitivity and glucose metabolism.

See Ling Loy et al., (84) published an article **"Association of maternal D status with glucose tolerance and LSCS in an multi ethnic Asian cohort: the growing up in Singapore towards healthy outcome (GUSTO) study**" they have measured vitamin D level and 2 hour Post prandial glucose level were measured between 26-28 weeks of gestation. They defined Vitamin D as inadequacy and adequacy i.e. <75nmol/l (<30ng/ml) and >75nmol/l (>30ng/ml) respectively. Mode of delivery was obtained from hospital records. They have 940 pregnant women from Singapore. They concluded vitamin D inadequacy is

prevalent in pregnant women, particular among the Malay and Indian. This is associated with elevated fasting blood glucose level in Malay women , and increased risk of emergency LSCS among Chinese and Indian women.

Bejat Sasan et al.,(85) "The Effects of Vitamin D Supplement on Prevention of Recurrence of Preeclampsia in Pregnant Women with a History of Preeclampsia." They presented a study which is a randomized controlled clinical trial. Aim of the study is to determine the effect of vitamin D supplement on reducing the probability of recurrent preeclampsia. 72 patients were placed in control group while 70 patients were randomized to the case group. The case group received a 50000 IU pearl vitamin D3 once every two weeks. The control group was administered placebo. Vitamin D or placebo was given until the 36th week of pregnancy. They have concluded that Vitamin D supplementation therapy in pregnancy could help in reducing the incidence of gestational hypertension/preeclampsia.

OBSERVATION AND RESULTS

The mean age of study group is presented in Table 5. It is observed that, the mean age of my case group is 27.53 $\pm$ 3.69 years. The mean age of my control group is 26.67 $\pm$ 3.177 years. Majority of my patients fall between 21-30 years.

Table - 5: Age distribution

Age	Cases	%	Control	%
< 20	0		2	6.6%
21 - 25	9	30%	7	23.3%
26 - 30	16	53.3%	17	56.6%
31 - 35	4	13%	4	13.5%
> 35	1	3.3%	0	

Table - 6: Occupation

Occupation	Case	%	Control	%
House wife	24	80%	26	86.7%
Professional	6	20%	4	13.3%

Table 6 shows that majority of the patients fall under house wife category. Professional category includes staff nurses, IT professionals and Teachers.

Figure- 7: Occupation with study group

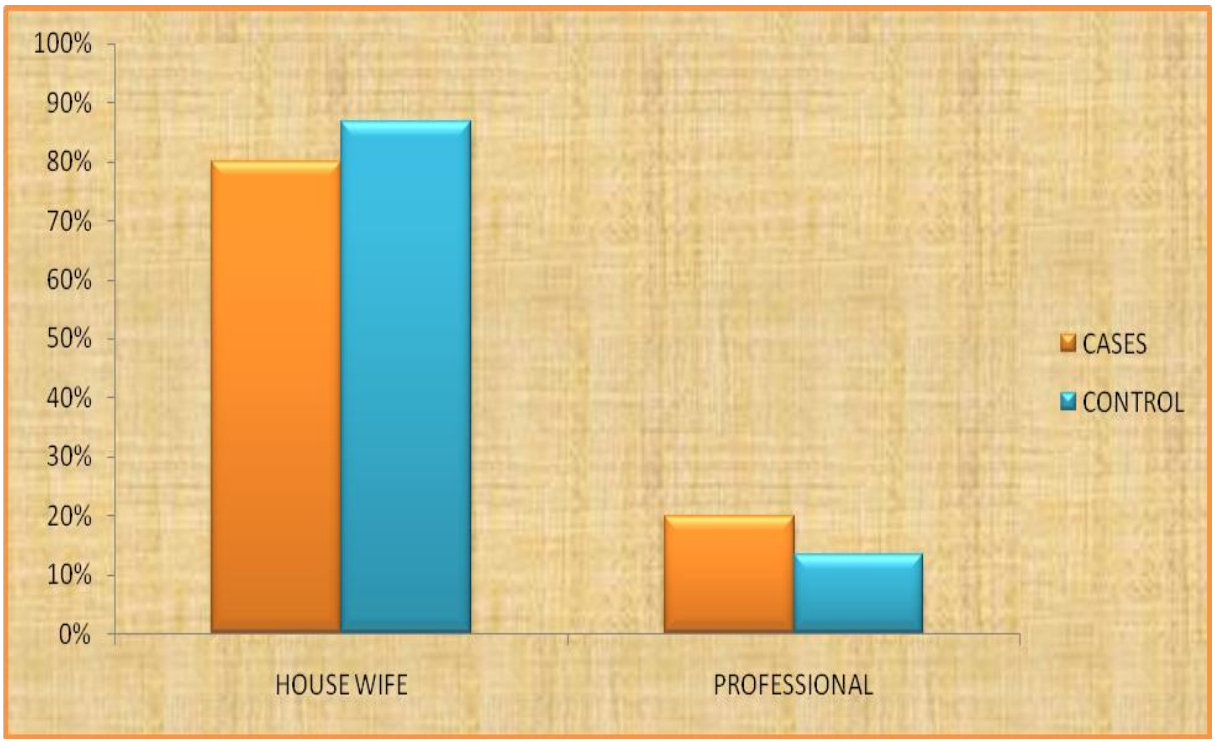


Table -7: Education status

Education	Cases	%	Control	%
School Level	14	46.6%	13	43.3%
Graduates	16	53.4%	17	56.7%

Majority of the patients, almost 58 % were graduates in my groups.

Figure -8: Education status

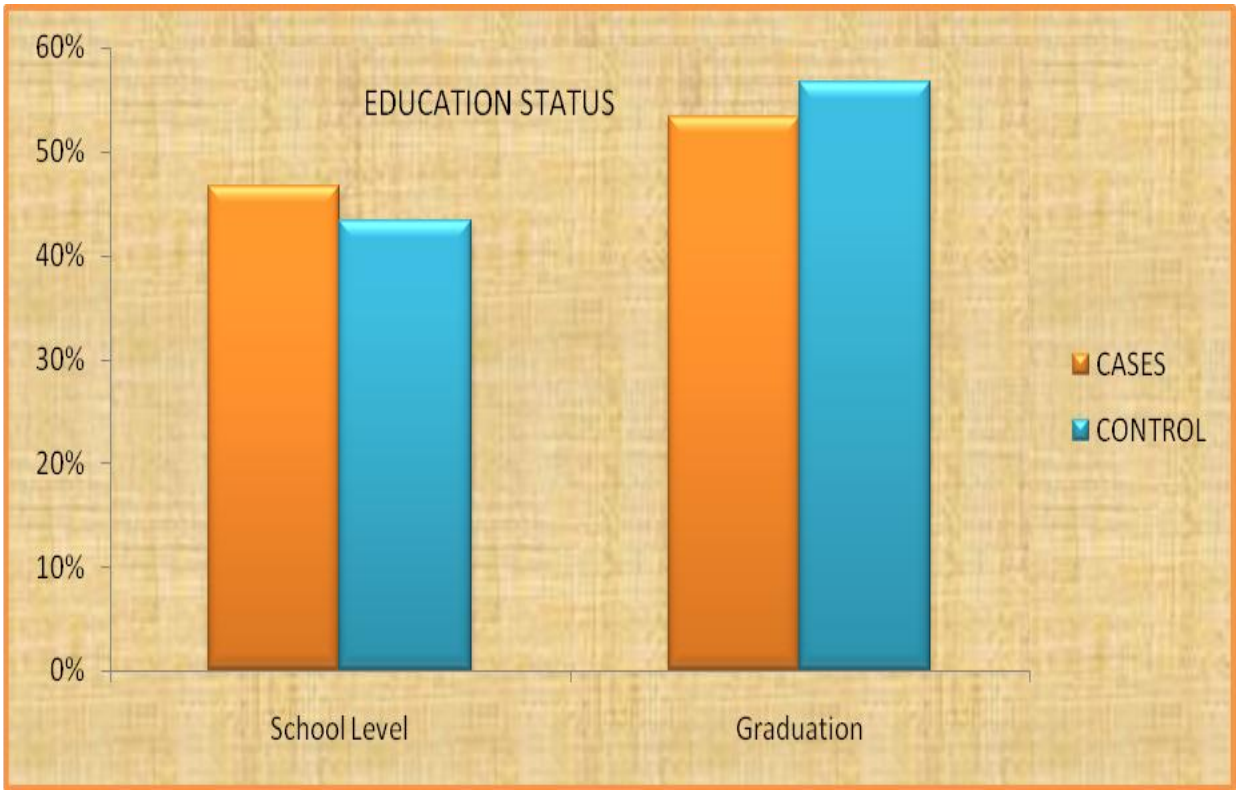


Table-8: Body Mass Index

BMI	Cases	%	Control	%
18.5 - 24.9	14	46.7%	16	53.4%
25.0 - 30.0	12	40%	13	43.3%
> 30.0	4	13.3%	1	3.3%

BMI distribution shows that, in my case group, around 13% of the women had BMI higher than 30 kg/m^2 (obese), while 40% had BMI between 25 and 30 kg/m^2(overweight) and 46 % had BMI below 25 kg/m^2(normal). In my control group, around 3 % of the women had BMI higher than 30 kg/m^2 (obese), while 43% had BMI between 25 and 30 kg/m^2 (overweight) and 53% had BMI below 25 kg/m^2 (normal). It is inferred that the Chi-square test of association is insignificant ($p>0.05$) between these groups.

Table- 9 BMI distribution

		SD	95% CI for Mean		Minimum	Maximum	sig
BMI	Mean		Lower	Upper			
Cases	25.5	4.8	23.7	27.3	18.5	34.3	
Control	24.4	3.9	22.9	25.8	18.5	30.0	>0.05

Mean BMI of my case group is 25.5± 4.8 and for the control group is 24.4 ± 3.9.

Table- 10: Gestational age

GA	Cases	%	Control	%
37 - 38	13	43.3%	7	23.3%
38 - 39	8	26.7%	8	26.7%
39 - 40	9	30%	15	50%

Table- 11: Comparison of gestational age with Vitamin D level

Study			Vitamin D		Total
			< 20	> 20	
CASE	GA	37 - 38	12	2	14
		38 - 39	8	2	10
		39 - 40	4	2	6
CONTROL	GA	37 - 38	1	2	3
		38 - 39	5	2	7
		39 - 40	14	6	20

Gestational age at the time of evaluation was compared between the two groups. Women with gestational age between 37 to 40 weeks were included in my study. From the table 11- it is observed that, 46% and 10 % of women

presented in labour ward between 37 – 38 weeks of gestational age in case and control group respectively. Around 20 % of case group and 66% of control group were presented in labour ward between 39- 40 weeks of gestational age. Patient in case group tend to present in early term than control group but it is not statistically significant.

Table- 12: Duration of sun exposure

Duration	Cases	(%)	Control	(%)
0 - 3 hrs	11	37%	6	20%
4 - 8 hrs	19	63%	23	77%
8 - 12 hrs	0		1	3%
> 12 hrs	0		0	

Table -13: Mean exposure to sunlight

Study Groups	Mean	SD	95% CI for Mean		Minimum	Maximum	sig
			Lower	Upper			
CASES	4.1	1.7	3.4	4.7	1	7	
CONTROLS	4.4	1.6	3.8	5.0	1	9	>0.05

The duration of Sun exposure and mean exposure to sun light is presented in Tables 12 and 13. Majority of women had poor exposure to sun due to changing life style and occupation. Mean exposure to sun in case and control group is 4.1 $\pm$ 1.7 hours and 4.4 $\pm$ 1.6 hours respectively. In Indian population, the exposure of face, arms and legs in sunlight for 2 hours is needed for dark skinned people, but for fair skinned people, only 30 minutes is needed daily.

Table – 14: Chief complaints and safe confinement

Chief Complaints	Cases	%	Control	%
Labour Pain	9	30%	10	33.3%
PROM	11	36.7%	9	30%
Induced labour	10	33.3%	11	36.7%

Table –14 : shows the time of presentation to the labour ward and were categorized. Percentages between these two groups were similar.

Table- 15: OGTT -2 hr

Mg/dl	Cases	(%)	Control	(%)
< 120	0	0	29	96.7%
120 - 140	8	26.7%	1	3.3%
> 140	22	73.3%	0	

Table 15 shows that 73.3% of women in study group had elevated levels of OGTT and 96.7% of women in control group were within the normal range .

Table -16: Mean OGTT - 2 hours

Study Groups	Mean	SD	95% CI for Mean		Minimum	Maximum	sig
			Lower	Upper			
CASES	147.0	9.0	143.7	150.4	130	160	
CONTROLS	98.6	11.6	94.3	103.0	74	128	<0.001

OGTT levels were compared between the case and control group. Mean OGTT of my case group is 147 ± 9. Mean OGTT of the control group is 98.6 ± 11.6. The 'P' value is significant (i.e.) < 0.001. Vitamin D level is inversely proportional to OGTT.

Figure - 9: Correlation of OGTT with Vitamin D (study group)

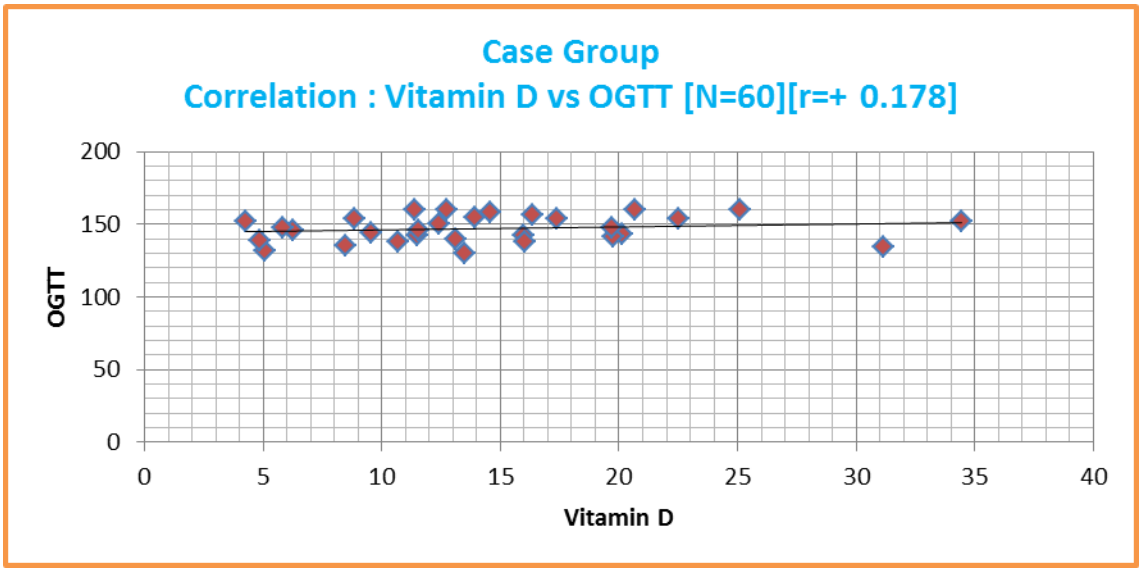
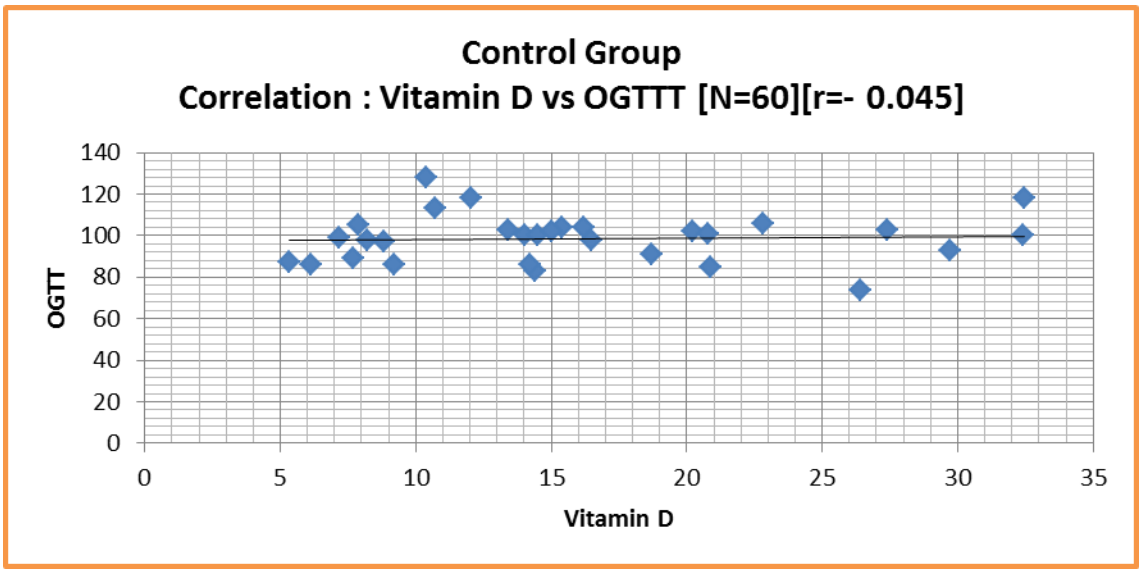


Figure -10: Correlation of OGTT with Vitamin D (control group)



In Figure 9 and 10 - correlation of vitamin D with OGTT level were compared. Women with low levels of vitamin D have elevated OGTT levels. Hence Vitamin D is inversely proportional to OGTT.

Table-17: Comparison of vitamin D status

	Cases	%	Control	%
Deficiency (0-20ng/ml)	24	80%	21	70%
Insufficiency (21-30 ng/ml)	4	13.3%	7	23.3%
Normal (>30 ng/ml)	2	6.7%	2	6.7%

Table- 18: Mean Vitamin D level

Mean Vitamin D with study Groups					
Study Groups	Mean	SD	Std. Error	95% CI for Mean	Maximum
				Lower	
CASE	14.59	7.35451	1.34274	11.8438	34.44
CONTROL	15.9667	7.79572	1.4233	13.0557	32.48

Of the 60 antenatal women included in the study, only 6.7% of women were found to have normal vitamin D levels, all others having either insufficiency 18.3% or deficiency 75 %. In India, there is a very high prevalence of low levels of vitamin D among pregnant women in spite of our country being tropical. This may be attributed to diets low in vitamin D , dark pigmented skin , social and religious norms related to public modesty dictating

that most of the body must be covered (lack of sun exposure). Mean exposure to sun in case group is 4.1 ± 1.7 and control group is 4.4 ± 1.6.

The Vitamin D status is analyzed in table 17 and 18. It is observed that, in case group, around 80% of women had vitamin D deficiency, whereas it is only 70% in control group. In case group around 13.3% of women had vitamin D insufficiency whereas it is 23.3% in control group. In both case and control groups, around 6.7% of women were within the normal range. Mean vitamin D is 14.5 ± 7.3 in case group and 15.96 ± 7.7 in control group. By comparing the Vitamin D deficiency between the 2 groups by Chi-square test, the levels were found to be statistically insignificant.

Figure - 11: Comparison of vitamin D status

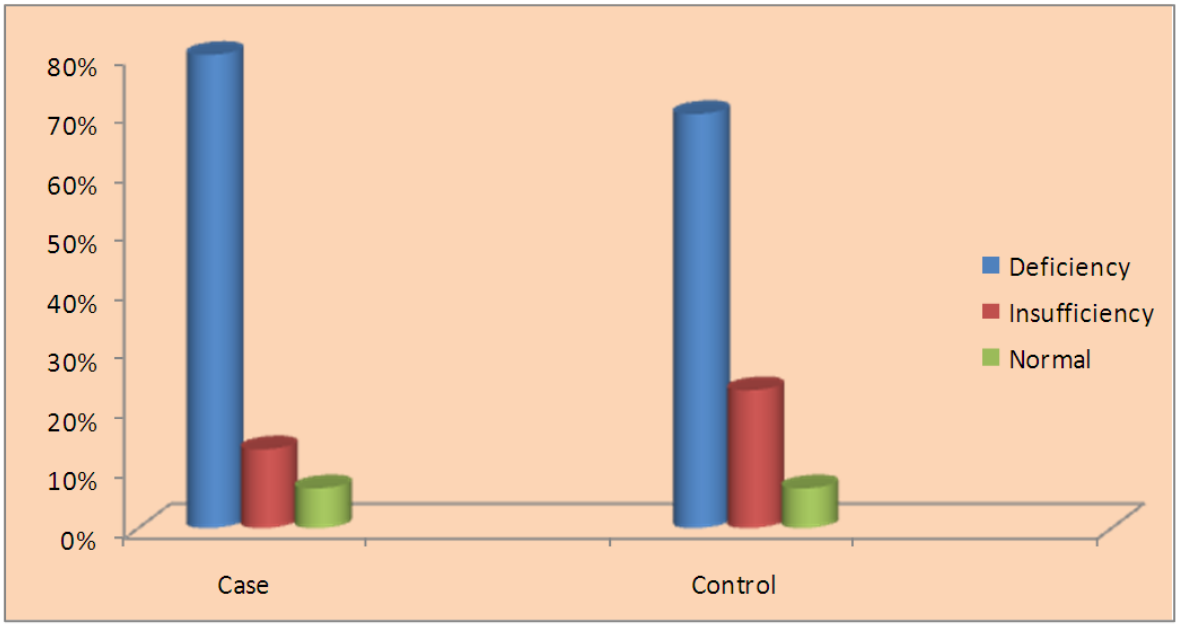


Table -19: Association of Mode of Delivery with Vitamin D levels

	CASE				CONTROL			
Vitamin D	NVD	(%)	LSCS	(%)	NVD	(%)	LSCS	(%)
Deficient	20	66.7%	4	13.3%	17	56.7%	4	13.3%
Insufficient	4	13.3%	0	0%	4	13.3%	2	6.7%
Normal	2	6.7%	0	0%	3	10%	0	0%

Table 19 shows the mode of delivery between two groups. It is observed that, 56.7% of control group had normal vaginal delivery. In case group 66.7% had normal vaginal delivery. In deficiency, 13.3% of case and control group underwent LSCS.

Table-20: Duration of labour

Duration	Cases	(%)	Control	(%)
<12Hrs	5	17%	15	50%
12 - 16 Hrs	8	27%	4	13%
17 - 24 hrs	14	47%	9	30%
>24 hrs	4	13%	2	7%

Table-21: Mean Duration of labour

Study			95% CI for Mean				
Groups	Mean	SD	Lower	Upper	Minimum	Maximum	sig
CASES	17.5	7.0	14.5	20.6	4	29	<0.05
CONTROLS	14.1	6.7	11.4	16.8	3	28	

The relationship between the duration of labour and Vitamin D status is analyzed by Pearson correlation coefficient. The obtained p value of <0.05 is significant. It is inferred that the duration of labour is prolonged with low level of vitamin D. The mean duration of labour among case group is 17.5± 7 hours and among control group is 14.1± 6 hours.

Figure -12: Duration of labour

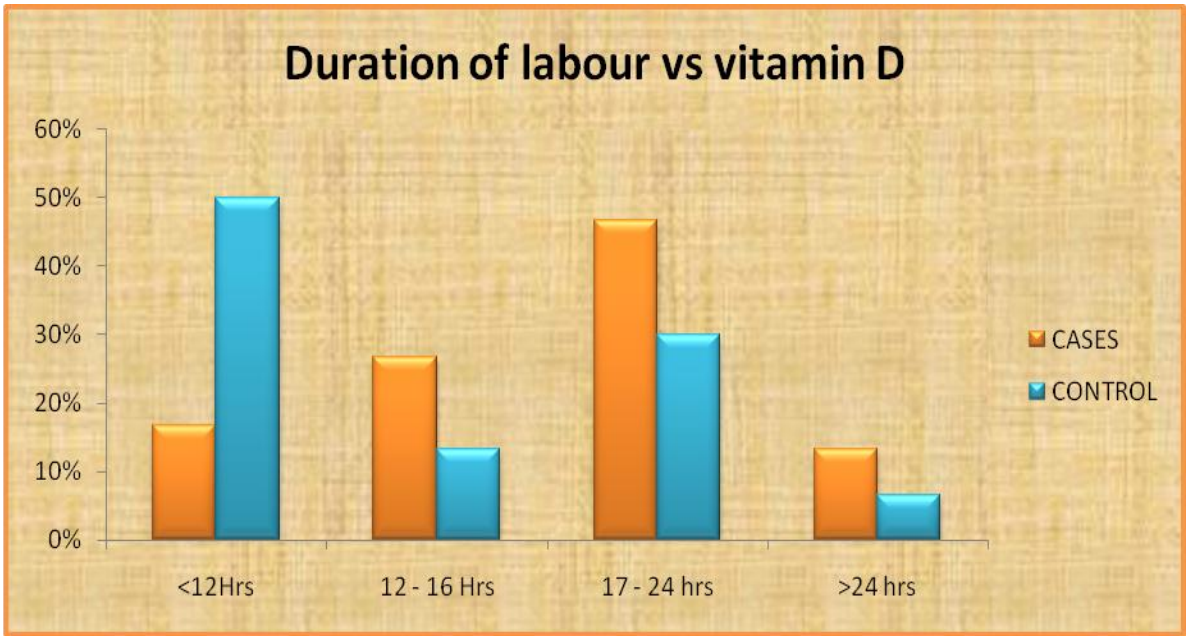


Table -22: Neonatal birth weights

Baby Weight [kgs]	Cases	%	Control	%
<2.5	5	16.6%	1	3.3%
2.51 - 3.0	14	46.6%	19	63%
3.01 - 3.5	11	36.7%	8	26.7%
>3.5	0		2	6.6%
Total	30		30	

The mean birth weight of babies between these two groups is 2.51 – 3 kg. The Pearson correlation shows insignificant relationship ($p>0.05$) for birth weight. Therefore the Vitamin D levels of antenatal women does not significantly influence the birth weight.

Table- 23: Mean neonatal birth weight between groups

Study Groups	Mean	SD	95% CI for Mean		Minimum	Maximum	sig
			Lower	Upper			
CASES	2.8	0.3	2.7	3.0	2.2	3.5	>0.05
CONTROLS	2.9	0.3	2.8	3.0	2.3	3.6	

It is observed from table 23: that, the mean birth weight of babies for case group is 2.8 $\pm$ 0.3 kg whereas the mean birth weight of babies in control group is 2.9 $\pm$ 0.3 kg. The Pearson correlation shows insignificant relationship ($p>0.05$) for birth weight.

Figure- 14: correlation of vitamin D vs birth weight (case group)

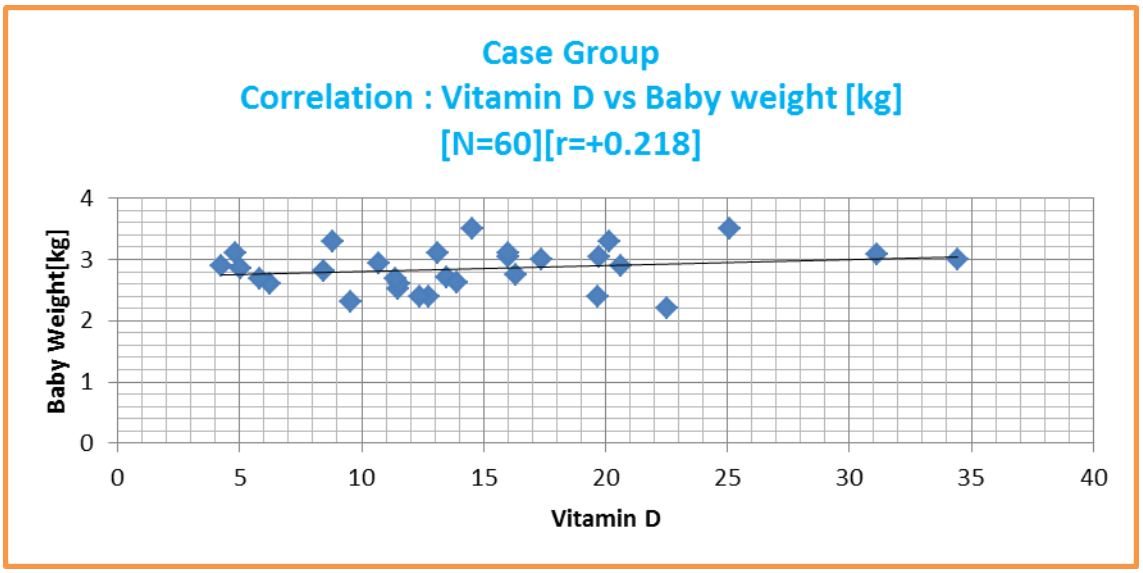


Figure- 15: correlation of vitamin D vs birth weight (control group)

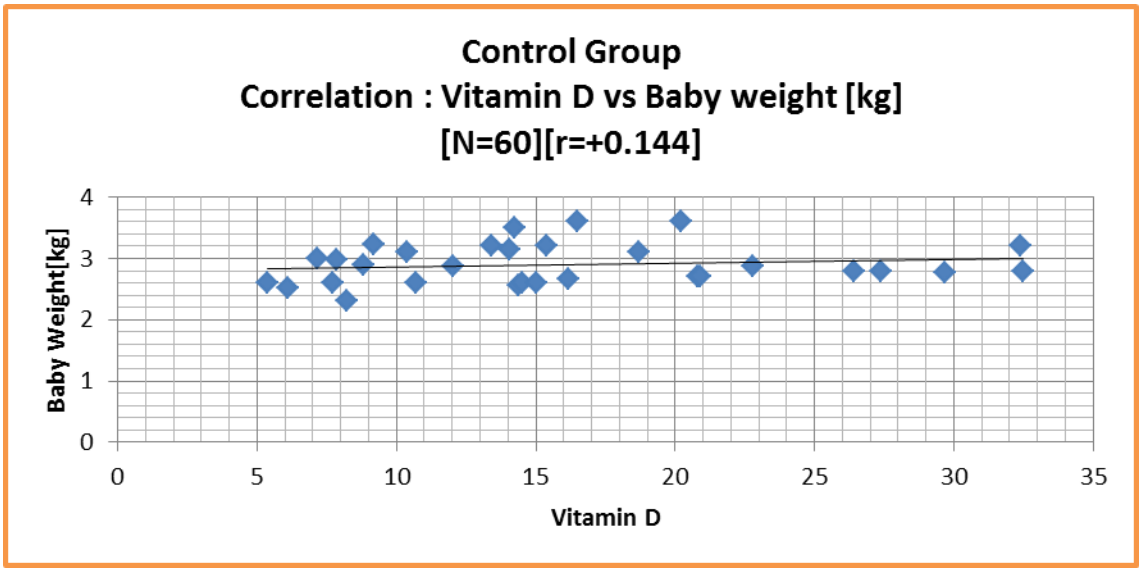


Table- 24: Comparison of case and control

CLINICAL VARIABLES	CASES	CONTROL
Age		
Mean+/-SD	27.5+/-3.7	26.7+/-3.2
Occupation		
House Wife	32%	35%
Professional	8%	5%
Education		
School Level	47%	43%
Graduation	53%	57%
BMI		
Mean+/-SD	25.5+/-4.8	24.4+/-3.9
Chief Complaints		
Abdominal Pain	30%	33%
PROM	37%	30%
Induced	33%	37%
GA		
37 - 38	43%	23%
38 - 39	27%	27%
39 - 40	30%	50%
Exposure of sun light		
Mean+/-SD	4.1+/-1.7	4.4+/-1.6
GCT		
Mean+/-SD	147+/-9	98.6+/-11.6
Vitamin D		
Mean+/-SD	14.59+/-7.35	15.97+/-7.80
Duration of labour		
Mean+/-SD	17.52+/-7	14.1+/-6.7
Birth Weight		
Mean+/-SD	2.8+/-0.3	2.9+/-0.3

STATISTICAL ANALYSIS:

- The data is reported as the mean +/- SD or the median, depending on their distribution.
- The differences in quantitative variables between groups were assessed by means of the unpaired T test. Comparison between groups was made by the Non parametric Mann - Whitney test.
- The Chi-square test was used assess differences in categorical variables between groups.
- Correlation was used to assess the variables.
- A p value of <0.05 using a two-tailed test is considered significant for all statistical tests. All data was analyzed with a statistical software package. (SPSS, version 16.0 for windows)

DATA ANALYSIS

The present work aims to find out whether VITAMIN 'D' is an independent risk factor for GDM. A total of 60 antenatal women were enrolled in my study. They were randomly allocated into two groups. The antenatal women in group A are those with Gestational Diabetes Mellitus and the antenatal women in group B are those without GDM. The association of Vitamin D status with reference to age, occupation, education status, Body Mass Index, mode of delivery, chief complaints, exposure to sun light, mean GCT between these two groups, Mode of delivery, duration of labour and birth weight. The data are reported as the mean +/-SD or the median, depending on their distribution. The difference in quantitative variable between the groups was assessed by means of the unpaired test. Comparison was made between these two groups by the non-parametric MANN- Whitney 'U' test. The chi square test was used to assess the difference in categorical variables between these two groups. P values of < 0.05 using a two tailed test is considered significant for all statistical tests. All data was analyzed with a statistical software package of social sciences (SPSS- Version 16.0 for windows)

DISCUSSION

The Study was conducted in the Department of Obstetrics and Gynaecology- PSG IMS &R. It was conducted on pregnant women with Gestational Diabetes Mellitus on diabetic diet as my study group and on term low risk antenatal patients as my control. A sample size of 60 was taken-30 cases in control group and 30 cases in study group. Additional blood samples (2 ml) were collected in antenatal patients who were admitted in labour ward between 37 weeks and 40 weeks gestation, along with other blood samples.

The study was analyzed for age, parity, BMI and gestational age (37 to 40 weeks). They were divided into three groups according to the serum vitamin D levels: group 1 (0–20)ng/ml (deficiency), group 2 (21–30)ng/ml (insufficiency), and group 3 (more than 30 ng/ml) normal

The mean age of my case group is 27.53 $\pm$ 3.69 years and control group is 26.67 $\pm$ 3.177 years.

Majority of patients fell under house wife category.

Majority of patients, almost 58 % were graduates.

BMI distribution shows that, in case group, around 13 % of the women had BMI higher than 30 kg/m^2 (obese), while 40% had BMI between 25 and 30 kg/m^2 (overweight) and 46 % had BMI below 25 kg/m^2 (normal). In control

group, around 3 % of the women had BMI higher than 30 kg/m^2 (obese), while 43% had BMI between 25 and 30 kg/m^2 (overweight) and 53% had BMI below 25 kg/m^2 (normal) in control group. Mean BMI of the case group is 25.5$\pm$ 4.8 and for the control group is 24.4 $\pm$ 3.9. It is inferred that Chi-square test of association is statistically insignificant ($p>0.05$) between these groups.

Gestational age at the time of evaluation was compared between the two groups. Women with gestational age between 37 to 40 weeks were included in my study. From the table 11- it is observed that, 46% and 10 % of women presented in labour ward between 37 – 38 weeks of gestational age in case and control groups respectively. Around 20 % of case group and 66% of control group were presented in labour ward between 39- 40 weeks of gestational age. Patient in case group tend to present in early term than control group but it is not statistically significant.

The association of Sun exposure and Vitamin D status is presented in Table 13 -both groups were compared. Majority of women had poor exposure to sun due to changing lifestyle and occupation. Mean exposure to sun in case and control group is 4.1 $\pm$ 1.7 and 4.4 $\pm$ 1.6 respectively. For Indian population, exposure of face, arms and legs for 2 hours is needed for dark skinned people, but for fair skinned people, only 30 minutes is needed daily.

Vitamin D level and OGTT levels were compared between the case and control group. Mean OGTT of my case group is 147 $\pm$ 9. Mean OGTT of the control group is 98.6 $\pm$ 11.6. The 'P' value is significant (i.e.) < 0.001. Hence, Vitamin D level is inversely proportional to OGTT.

Of the 60 antenatal women included in the study, only 6.7% of women were found to have normal vitamin D levels, all others having either insufficiency 18.3% or deficiency 75 %. In India there is a very high prevalence of low level of vitamin D among pregnant women in spite of our country being tropical. This may be attributed to diet low in vitamin D , dark pigmented skin , social and religious norms related to public modesty dictating that most of the body must be covered (lack of sun exposure). Mean exposure to sun in case group is 4.1 $\pm$ 1.7 and control group is 4.4 $\pm$ 1.6.

The Vitamin D status is analyzed in table 17 and 18: It is observed that, in case group around 80% of women had vitamin D deficiency, whereas it is only 70% in control group. In case group around 13.3% of women had vitamin D insufficiency whereas it is 23.3% in control group. In case and control group around 6.7% of women were within the normal range. Mean vitamin D is 14.5 $\pm$ 7.3 in case group and 15.96 $\pm$ 7.7 in control group. By comparing the Vitamin D

deficiency between the 2 groups by Chi-square test, the levels were found to be statistically insignificant.

The study conducted in Armed Forces in Pune by **Jayaramam Muthukrishnan et al.,** (53) in India concluded that low levels of Vitamin D is associated with GDM. However replacement of Vitamin D does not reverse the glucose intolerance. There are no justifications or standard guidelines at present for routine screening of Vitamin D levels in all antenatal pregnant women.

A study "Deficiency of Vitamin D among Females of Northern India" published by **RekhaJalandra et al**., on pregnant mothers in India, revealed that 74% of the mothers had vitamin D deficiency (25OHD < 30ng/ml) . Low intake of vitamin D by mother in pregnancy is associated with wheeze and asthma in the offspring. Vitamin D deficiency has also been noted in pregnant women in tropical countries, but all studies were in Muslim populations, in whom the practice of purdah might have played an important role. Vitamin D deficient pregnant female may suffer from hypertension, low glucose tolerance whereas low birth weight and other complications may be found in new born. Studies on pregnant mothers from southern and northern states of India have reported high vitamin D deficiency levels with values ranging from 67% to 96%. A study

conducted among pregnant mothers in India, reported that 74% of the mothers had vitamin D deficiency (< 30ng/ml).

Vitamin D levels are compared with mode of delivery. Table 19: showed mode of delivery between two groups. It is observed that, 56.7% of control group had normal vaginal delivery. In case group 66.7% had normal vaginal delivery. In deficiency, 13.3% of case and control group were underwent LSCS.

See Ling Loy et al., published an article "Association of maternal Vitamin D status with glucose tolerance and LSCS in the multi-ethnic Asian cohort - Growing up in Singapore towards a healthy outcome" (GUSTO) study the vitamin D levels and 2 hour Post prandial glucose levels were measured between 26- 28 weeks of gestation. They classified Vitamin D levels as inadequacy and adequacy i.e. <75nmol/l (<30ng/ml) and >75nmol/l (>30ng/ml) respectively. Mode of delivery was obtained from hospital records. They had 940 pregnant women from Singapore. They concluded vitamin D inadequacy is prevalent in pregnant women, particular among the Malay and Indian. This is associated with elevated fasting blood glucose level in Malay women, and increased risk of emergency LSCS among Chinese and Indian women.

The relationship between duration of labour and Vitamin D status is analyzed by Pearson correlation coefficient. The obtained p of <0.05 is significant. It is inferred that duration of labour is prolonged with low level of vitamin D. The mean duration of labour among case group is 17.5± 7 hours and among control group is 14.1± 6 hours.

The mean birth weight of babies between these two groups is 2.51 – 3 kg. The Pearson correlation shows insignificant relationship (p>0.05) for birth weight. Therefore a Vitamin D level of antenatal women is not significantly influencing the birth weight.

SUMMARY

- Vitamin D levels were compared between GDM patients and normal patients.
- Women with GDM associated with Vitamin D deficiency tend to present at an earlier gestational age for delivery with complaints of abdominal pain/PROM than normal patients.
- In both groups vitamin D level is deficient due to changing lifestyle.
- Women with low vitamin D levels had prolonged duration of labour when compared to low risk women which is statistically significant.
- There is insignificant association observed between Body Mass Index and Vitamin D status.
- The association of antenatal maternal vitamin D status with birth weight of neonate yields insignificant relationship.
- The comparison of vitamin D levels between GDM and low risk antenatal patients showed statistically insignificant results.

CONCLUSION

Based on the study conducted in the department of Obstetrics and Gynaecology, PSG IMSR, there are many women who are deficient in Vitamin D and many others who are insufficient. Prevalence of Vitamin D deficiency is alarmingly high in pregnant women in India and has become a re-emerging public health issue. Due to lack of Vitamin D level screening, many women go undetected and are suffering from adverse outcomes including in new born. So there is a need to identify them early in pregnancy and supplementing pregnant women with vitamin D and to decrease the likelihood of them developing complications. There are some limitations that should be noted. The sample size taken was small and hence a large randomized controlled trial is necessary to determine the vitamin D levels in pregnancy and to draw guidelines regarding screening and supplementation.

I would like to conclude this study saying that in a country like India where the prevalence of vitamin D deficiency among pregnant women is high, adequate sun exposure, dietary intake and supplementation is necessary. Only viable option is fortification of food products and supplementation of vitamin D to population at risk. Policies and recommendations should be drawn up by the Government of India to combat the pandemic that’s rising silently.

This study shows that overall the vitamin D levels were low in both groups. In the study group, mothers went into labour at an earlier gestational age and had prolonged labour. However in the control group the gestational age was advanced and labour was shortened. Vitamin D levels were slightly higher in control group. However this was not statistically insignificant.

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PSG Institute of Medical Sciences & Research
Institutional Human Ethics Committee

Recognized by The Strategic Initiative for Developing Capacity in Ethical Review (SIDCER)
POST BOX NO. 1674, PEELAMEDU, COIMBATORE 641 004, TAMIL NADU, INDIA
Phone : 91 422 - 2598822, 2570170, Fax : 91 422 - 2594400, Email : ihec@psgimsr.ac.in

December 9, 2016

To
Dr V Kalaiarasi
Postgraduate
Department of Obstetrics & Gynaecology
Guide: Dr T V Chitra
PSG IMS & R
Coimbatore

The Institutional Human Ethics Committee, PSG IMS & R, Coimbatore - 4, has reviewed your proposal on 9th December 2016 in its expedited review meeting held at IHEC Secretariat, PSG IMS&R, between 10.00 am and 11.00 am, and discussed your request to renew the approval for the study entitled:

"Correlation of Vitamin D levels and gestational diabetes mellitus"

The following documents were received for review:

1. Request for renewal dated 03.12.2016
2. Status Report

After due consideration, the Committee has decided to renew the approval for the above study.

The members who attended the meeting held on at which your proposal was discussed, are listed below:

Sl. No.	Name of the Member of IHEC	Qualification	Area of Expertise	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
1	Mr R Nandakumar (Chairperson, IHEC)	BA., BL	Legal Expert	Male	No	Yes
2	Dr. S. Bhuvaneshwari (Member-Secretary, IHEC)	MD	Clinical Pharmacology	Female	Yes	Yes
3	Dr S Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
4	Dr Sudha Ramalingam	MD	Epidemiologist, Ethicist Alt. member-Secretary	Female	Yes	Yes
5	Dr D Vijaya	M Sc., Ph D	Basic Medical Sciences (Biochemistry)	Female	Yes	Yes

The approval is valid for one year (28.12.2016 to 27.12.2017).

This Ethics Committee is organized and operates according to Good Clinical Practice and Schedule Y requirements.

Non-adherence to the Standard Operating Procedures (SOP) of the Institutional Human Ethics Committee (IHEC) and national and international ethical guidelines shall result in withdrawal of approval (suspension or termination of the study). SOP will be revised from time to time and revisions are applicable prospectively to ongoing studies approved prior to such revisions.

Kindly note this approval is subject to ratification in the forthcoming full board review meeting of the IHEC.

Yours truly,

SECRETARY
PSG IMS&R
COIMBATORE-641004.
INSTITUTIONAL HUMAN ETHICS COMMITTEE

Dr S Bhuvaneshwari
Member – Secretary
Institutional Human Ethics Committee

PSG Institute of Medical Science and Research, Coimbatore
Institutional Human Ethics Committee
INFORMED CONSENT FORMAT FOR RESEARCH PROJECTS

(strike off items that are not applicable)

I **DR. KALAIARASI .V,** am carrying out a study on the topic**: 'Correlation of Vitamin-D levels and gestational diabetes mellitus'** as part of my research project being carried out under the aegis of the Department of: OBSTETRICS AND GYNAECOLOGY, PSG IMSR

My research guide is**:** **DR.T.V.CHITRA, MD, DGO, DNB.,,** Department of Obstetrics and Gynaecology, PSG IMS&R, Coimbato**re**

The justification for this study is:

Low levels of vitamin D status, as measured by 25-hydroxyvitamin D [25(OH)D], are common in pregnant women. There is a positive association between vitamin D status and adverse pregnancy outcome like Gestational diabetes mellitus.

The objectives of this study are:

Primary : Assessing the levels of vitamin D in pregnant women.
Secondary : Correlation between vitamin D levels and Gestational diabetes mellitus in pregnant women.

Sample size: 30 study group and 30 control group.

Study volunteers / participants are :Uncomplicated antenatal patients and GDM admitted in ward.

Location: PSG IMSR obstetrics and gynecology WARD.

We request you to kindly cooperate with us in this study. We propose collect background information and other relevant details related to this study. We will be carrying out:

Initial interview : 10 minutes.

Data collected will be stored for a period of five years. We will not use the data as part of another study.

Blood sample collection: Specify quantity of blood being drawn: additional 3 ml. (along with other investigation)

No. of times it will be collected: Once

Whether blood sample collection is part of routine procedure or for research (study) purpose:
1. Routine procedure 2. Research purpose ✓

Specify **purpose**, discomfort likely to be felt and side effects, nil
Whether blood sample collected will be stored after study period: No.

Whether blood sample collected will be sold: No

Whether blood sample collected will be shared with persons from another institution: No

Final interview : 10 mts.

Benefits from this study: There is a strong association between low vitamin D level and GDM. In future pregnancy this vitamin D deficiency can be identified at the earliest and can be reduced by giving medical intervention.

Risks involved by participating in this study: nil

How the **results** will be used: from the study we will be able to find out the cutoff value for Vitamin D in Gestation Diabetes Mellitus patients. In future studies wether the risk of GDM can be reduced by supplementing Vitamin D can be made out.

If you are uncomfortable in answering any of our questions during the course of the interview / biological sample collection, **you have the right to withdraw from the interview / study at anytime.** You have the freedom to withdraw from the study at any point of time. Kindly be assured that your refusal to participate or withdrawal at any stage, if you so decide, will not result in any form of compromise or discrimination in the services offered nor would it attract any penalty. You will continue to have access to the regular services offered to a patient. You will **NOT** be paid any remuneration for the time you spend with us for this interview / study. The information provided by you will be kept in strict confidence. Under no circumstances shall we reveal the identity of the respondent or their families to anyone. The information that we collect shall be used for approved research purposes only. You will be informed about any significant new findings - including adverse events, if any, – whether directly related to you or to other participants of this study, developed during the course of this research which may relate to your willingness to continue participation.

Consent: The above information regarding the study, has been read by me/ read to me, and has been explained to me by the investigator/s. Having understood the same, I hereby give my consent to them to interview me. I am affixing my signature / left thumb impression to indicate my consent and willingness to participate in this study (i.e., willingly abide by the project requirements).

Signature / Left thumb impression of the Study Volunteer / Legal Representative:

Signature of the Interviewer with date: Witness:

Contact number of PI: 9566506312

Contact number of Ethics Committee Office: During Office hours: 0422 2570170 Extn.: 5818
After Office hours: 9865561463

பூ. சா. கோ மருத்துவக் கல்லூரி மற்றும் ஆராய்ச்சி நிறுவனம், கோவை

மனித நெறிமுறைக் குழு

ஒப்புதல் படிவம்

தேதி:

மரு. கலையரசி .வீ ஆகிய நான் பூ. சா. கோ மருத்துவக் கல்லூரியின் / மருத்துவமனையின் மகப்பேறு துறையின் கீழ், **"நீரிழிவு நோய் உள்ள கர்பிணி பெண்களுக்கும் மற்றும் அல்லாத கர்பிணி பெண்களுக்கும் இடையே உள்ள வைட்டமின்-டி அளவினை ஒப்பிடுதல்"** என்ற தலைப்பில் ஆய்வு மேற்கொள்ள உள்ளேன்.

என் ஆய்வு வழிகாட்டி: மரு. டி. வீ. சித்ரா, MD., DGO., DNB.,
தலைமை பேராசிரியை, மகப்பேறு துறை

ஆய்வு மேற்கொள்வதற்கான அடிப்படை:

வைட்டமின் டி குறைபாடு தடுக்கக்கூடிய சுகாதார பிரச்சினை. கர்ப்பிணி பெண்கள் மத்தியில் வைட்டமின்-D, குறைபாடு உலகம் முழுவதும் பல மக்கள் தொகையில் காணப்படுகிறது. இவ்வாறு குறைபாடு காணப்படும் கர்ப்பிணி பெண்கள் மத்தியில் நீரிழிவு நோய் மிக அதிக அளவில் காணப்படுகிறது.

ஆய்வின் நோக்கம்:

1. கர்பிணி பெண்களின் வைட்டமின்-டி அளவை கண்டறிதல்.
2. வைட்டமின்-டியின் குறைபாட்டிற்கும் கர்ப்பகால நீரிழிவு நோய்க்கும் உள்ள தொடர்பினை கண்டறிதல்.

ஆய்வில் பங்கு பெறும் நபர்களின் எண்ணிக்கை: 60

ஆய்வில் பங்கு பெறுவோர் மற்றும் வயது: சிக்கலற்ற கர்ப்பகால பெண்கள் மற்றும் கர்ப்பகால நீரிழிவு நோய் உள்ள பெண்கள்.

ஆய்வு மேற்கொள்ளும் இடம்: மகப்பேறு பிரிவு, பூ. சா. கோ மருத்துவக் மற்றும் கல்லூரி மருத்துவமனை, கோயமுத்தூர்.

இந்த ஆய்வில் எங்களுடன் ஒத்துழைக்குமாறு கேட்டுக்கொள்கிறோம். நாங்கள் சில தகவல்களை இந்த

ஆய்விற்காக சேகரிக்க உள்ளோம்.

முதன்மை நேர்காணல்: **10-15 நிமிடங்கள்**

இந்த ஆய்வில் கிடைக்கும் தகவல்கள் **5 வருடங்கள்** பாதுகாக்கப்படும். இந்த தகவல்கள் வேறு ஆய்விற்குப் பயன்படுத்தப் படும்/பயன்படுத்தப் பட மாட்டாது.

மருத்துவ பரிசோதனைகள்:

இரத்த மாதிரி சேகரிப்பு: கூடுதல் 3 மிலி, ஒருமுறை (மற்ற விசாரணை இணைந்து)

இரத்த மாதிரி எடுப்பது வழக்கமான சிகிச்சைக்காகவோ அல்லது இந்த ஆய்விற்காகவோ: குறிப்பிட்ட ஆய்விற்காக

இதனால் ஏற்படக் கூடிய அசௌகரியங்கள் / பக்க விளைவுகள்: இதனால் எந்த அசௌகரியமோ, பக்க விளைவுகளோ ஏற்படாது.

இரத்த மாதிரிகள் ஆய்விற்குப் பின் பாதுகாத்து வைக்கப்படுமா? ஆம் / இல்லை, அழிக்கப்படும்: **இல்லை**

சேகரிக்கப்பட்ட இரத்தம் விற்கப்படுமா? ஆம் / இல்லை **இல்லை**

சேகரிக்கப்பட்ட இரத்தம் வேறு நிறுவனத்துடன் பகிர்ந்து கொள்ளப்படுமா? ஆம் / இல்லை: **இல்லை**

ஆய்வில் பங்குபெறுவதால் ஏற்படும் பலன்கள்:

பேறுகாலத்தில் வரும் நீரிழிவு நோய்க்கும் குறைவான வைட்டமின் -டி அளவிற்கும் உள்ள தொடர்பினை கண்டறிய உதவுகிறது.

ஆய்வின் முடிவுகள் எந்த முறையில் பயன்படுத்தப்படும்?

ஆய்வின் முடிவுகள், அடுத்தகட்ட ஆராய்ச்சிகளுக்கும், வைட்டமின் D, கொடுப்பதினால் நீரிழிவு நோய் குறையுமா என்பதை அரிய உதவும்.

இந்த ஆய்வின் கேள்விகளுக்கு பதிலளிப்பதோ, இரத்த மாதிரிகள் அல்லது திசு மாதிரிகள் எடுப்பதிலோ உங்களுக்கு ஏதேனும் அசௌகரியங்கள் இருந்தால், எந்த நேரத்தில் வேண்டுமானாலும் ஆய்விலிருந்து விலகிக்கொள்ளும் உரிமை உங்களுக்கு உண்டு. எப்பொழுது வேண்டுமானாலும் ஆய்விலிருந்து விலகும் உரிமை உங்களுக்கு உள்ளது. ஆய்விலிருந்து விலகிக்கொள்வதால் உங்களுக்கு அளிக்கப்படும் சிகிச்சை முறையில் எந்த வித பாதிப்பும் இருக்காது என்று உங்களுக்கு உறுதியளிக்கிறோம். மருத்துவ மனையில் நோயாளிகளுக்கு அளிக்கப்படும் சேவைகளை நீங்கள் தொடர்ந்து பெறலாம். இந்த ஆய்வில் பங்கேற்க

ஒப்புக்கொள்ளுவதால் வேறு எந்த விதமான கூடுதலான பலனும் உங்களுக்குக் கிடைக்காது. நீங்கள் அளிக்கும் தகவல்கள் இரகசியமாக வைக்கப்படும். ஆய்வில் பங்கேற்பவர்கள் பற்றியோ அவர்கள் குடும்பத்தைப் பற்றியோ எந்தத் தகவலும் எக்காரணம் கொண்டும் வெளியிடப்படாது என்று உறுதியளிக்கிறோம். நீங்கள் அளிக்கும் தகவல்கள் / இரத்த மாதிரிகள் / திசு மாதிரிகள் அங்கீகரிக்கப்பட்ட ஆய்விற்கு மட்டுமே பயன்படுத்தப்படும். இந்த ஆய்வு நடைபெறும் காலத்தில் குறிப்பிடத்தகுந்த புதிய கண்டுபிடிப்புகள் அல்லது பக்க விளைவுகள் ஏதும் ஏற்பட்டால் உங்களுக்குத் தெரிவிக்கப்படும். இதனால் ஆய்வில் தொடர்ந்து பங்கு பெறுவது பற்றிய உங்கள் நிலைப்பாட்டை நீங்கள் தெரிவிக்க ஏதுவாகும்.

ஆய்வுக்குட்படுபவரின் ஒப்புதல்: இந்த ஆய்வைப் பற்றிய மேற்கூறிய தகவல்களை நான் படித்து அறிந்து கொண்டேன் / ஆய்வாளர் படிக்கக் கேட்டுத் தெரிந்து கொண்டேன். ஆய்வினைப் பற்றி நன்றாகப் புரிந்து கொண்டு இந்த ஆய்வில் பங்கு பெற ஒப்புக்கொள்கிறேன். இந்த ஆய்வில் பங்கேற்பதற்கான எனது ஒப்புதலை கீழே கையொப்பமிட்டு . கை ரேகை பதித்து நான் தெரிவித்துக் கொள்கிறேன்.

பங்கேற்பாளரின் பெயர், முகவரி:

பங்கேற்பாளரின் கையொப்பம் / கை ரேகை / சட்டப்பூர்வ பிரதிநிதியின் கையொப்பம்:

தேதி :

ஆய்வாளரின் கையொப்பம் :

தேதி :

ஆய்வாளரின் தொலைபேசி எண்: 9566506312

மனித நெறிமுறைக் குழு அலுவலகத்தின் தொலைபேசி எண்:

அலுவலக நேரத்தில்0422 2570170 Extn.: 5808

அலுவலக் நேரத்திற்குப்பின்: 9865943043

PROFORMA

Name :

Age :

S. No :

Op. No :

IP. No. :

Occupation :

Exposure to sunlight : _____ duration / day

Address :

Unit No. :

Parity Index :

Gestational Age :

Socia-Economical status :

Menstrual H/o :

Obstetric H/o : GCT-

Other antenatal complication in present pregnancy (PIH, Anemia, thyroid dysfunction)

Liquor :

Family H/o :

Medical H/o :

Drug H/o : Supplementation (Calcium, Vitamin-D)

Duration and Dosage:

Investigation : Vitamin-D level

Total weight gain : 1^{st} Trimester 2^{nd} Trimester 3^{rd} Trimester

On Examination:

Vitals

BP : Pallor :

Pulse Rate : Icteric :

Temp : Pedal Edema :

Height:_____Cms Weight: _____Kgs BMI :_____

Cardio Vascular System :

Respiratory System :

Per Abdomen :

Presentation :

Fetal Heart Rate :

Mode of Delivery :

Indication :

Baby Details :

Sex :

Weight :

APGAR :

ABBREVATIONS

T1D	-	Type 1 Diabetes Mellitus
T2D	-	Type 2 Diabetes Mellitus
GDM	-	Gestational Diabetes Mellitus
IGT	-	Impaired Glucose tolerance
IFG	-	Impaired fasting tolerance
VDR	-	Vitamin D receptor
PIH	-	Pregnancy Induced Hypertension
IR	-	Insulin Resistance
SGA	-	Small for gestational age
RDA	-	Recommended daily Allowance
ICMR	-	Indian council of medical sciences
WHO	-	World Health Organisation
NHANES	-	National health and nutrition examination survey
IGR	-	Insulin Like growth factor
PTH	-	Parathyroid hormone

MASTER CHART

CASE GROUP

Patient name	Age	IP NO	occupation	education	BMI	chief complaints	gestational age	exposure to sun	GCT	controlled sugars	vitamin D	Duration of labour	NVD	INSTRUMENTAL	LSCS	INDICATION FOR LSCS	BABY WEIGHT
sowmiya	22	I17022716	HW	B COM	20.3	PROM	38W +2D	4	138	DIET	10.7	9		VACCUM			2.93
Sarama	24	I17022947	HW	12TH	20	induced	40W	6	142	DIET	15.99	12	NVD				3.04
Sophia	27	I17023072	HW	10TH	18.5	induced	40W	2	142	DIET	11.52	5		VACCUM			2.52
Indhumathi	22	I17021839	HW	12TH	29.9	abdominal pains	38W +2D	4	144	DIET	9.5	17		forceps			2.3
Hemalatha	28	I17023784	HW	12TH	19.6	induced	40	5	160	DIET	12.7	20	nvd				2.4
Reena	32	I17023806	teacher	B.ed	27.1	induced	39	6	130	DIET	13.5	27	nvd				2.7
Poongodi	36	I17024036	HW	10TH	31.7	PROM	37	2	138	DIET	16.02	21	NVD				3.1
Fathima	26	I17024200	HW	11TH	25.7	abdominal pain	38	4	152	DIET	4.26				LSCS	NPL	2.9
Sharmila banu	28	I17024342	HW	12TH	28.4	induced	40	5	132	DIET	5.05	22	NVD				2.85
Priya	27	I17024705	Staff nurse	B.SC	21.2	prom	38	3	135	DIET	8.46	28	NVD				2.81
Bhuvaneshwari	31	I17024642	IT	IT	23.5	induced	39+4D	5	139	DIET	4.85	29		VACCUM			3.1
Yasodha	29	I17025010	teacher	B.ed	29.3	prom	37	4	146	DIET	11.54	15	NVD				2.6
Gowri	28	I17025788	HW	M.Tech	23.5	induced	40	2	143	DIET	20.16		NVD				3.3
Alagiriammal	30	I17024948	HW	12TH	32.5	induced	38	6	154	DIET	17.4	17	NVD				3
Rajeshwari	28	I17025131	HW	IT	34.3	induced	39	2	141	DIET	19.76				LSCS	CPD	3.05
Swathy	24	I17025767	HW	IT	27.6	prom	38	7	134	DIET	31.15	4		VACCUM			3.08
Amsaveni	35	I17029469	HW	12TH	22.8	abdominal pain	37W+4D	3	154	DIET	22.54	23	NVD				2.2
Revathi	25	I17029537	HW	10TH	29.9	abdominal pain	37W3D	5	146	DIET	6.24		NVD				2.6
Vishnupriya	24	I17029540	HW	B.com	28.6	prom	37W+3D	2	150	DIET	12.39	13	NVD				2.4
Rifana	22	I17032108	HW	8th	26.9	prom	39+2	1	148	DIET	5.8			VACCUM			2.68
Priyadharshini	28	I17031211	HW	M.Tech	21.8	prom	39	2	148	DIET	19.69		NVD				2.4
Parimala	29	I17032301	HW	BBM	19.9	abdominal pain	38+6	5	140	DIET	13.14	17	NVD				3.1
Divya	25	I17032626	HW	BBM	29.8	abdominal pain	38+2	7	155	DIET	13.91	15	NVD				2.63
Rameshwari	26	I17032693	HW	11th	19.1	prom	38	4	156	Diet	16.3	17			LSCS	CPD	2.74
Radhika	28	I17032584	IT	IT	20.6	abdominal pains	39	2	154	Diet	8.83	28	NVD				3.3
Megala	30	I17032585	teacher	B.ed	18.9	abdominal pains	38	3	160	DIET	20.66	13		VACCUM			2.89
Sudharani	32	I17033184	HW	BIO TECH	22.6	induced	40	6	160	DIET	11.4	19		VACCUM			2.68
Priya	30	I17048143	HW	10 th	29.4	prom	39+2	6	158	DIET	14.56				LSCS	NPL	3.5
Parveen fathima	21	I17033275	HW	B.A	29.5	abdominal pains	37+1	5	152	DIET	34.44	22	NVD				3.01
Jothi	29	I17033730	HW	BBM	32.2	Prom	38	4	160	DIET	25.1	10	NVD				3.5

CONTROL GROUP

Patient name	Age	IP NO	occupation	education	BMI	chief complaints	gestational age	exposure to sun	GCT	controlled sugars	vitamin D	Duration of labour	NVD	INSTRUMENTAL	LSCS	INDICATION FOR LSCS	BABY WEIGHT
Mary	26	I17022674	HW	BBM	20.3	prom	38	4	91		18.7	21		VACCUM			3.1
Balavathy	25	I17022267	HW	12th	20	abdominal pain	38+4	5	103		27.4	24	NVD				2.8
Jaishree	27	I17023048	HW	B.E	18.5	induced	40	4	128		10.3	18		VACCUM			3.1
Deepika	26	I17023160	HW	12	22.1	prom	37	4	98		16.5		NVD				3.6
Gokilavani	25	I17023966	HW	B.A	21.5	induced	40	5	113		10.7				LSCS	Fetal distress	2.6
Prema	26	i17024030	HW	B.COM	21.8	induced	40+2	5	74		26.4	3	NVD				2.8
Vasudha	29	I17023707	HW	12TH	27	induced	40+2	6	100		14.05	4		FORCEPS			3.15
Deepa	30	I17024572	HW	BBM	28.2	abdominal pain	38+3	2	87		5.3	13		VACCUM			2.6
Soundharya	31	I17024663	HW	12	28.5	prom	38+4	5	83		14.4				LSCS	Fetal distress	2.56
Shymala	29	I17024662	HW	HW	28.2	induced	40	3	86		9.27				LSCS	NPL	3.24
Malathy	31	I17024936	LAB tech	Lab tech	18.9	induced	40+1	6	103		13.4	12		VACCUM			3.2
Fowzia	25	I17025172	HW	12TH	25.8	abdominal pain	38+3	5	102		20.2	16		VACCUM			3.6
Vidhya	27	I17025228	HW	12TH	26.1	prom	37+4	6	98		8.2	18		VACCUM			2.3
Angel	32	I17025305	HW	B.B.M	24.8	induced	40+1	1	93		29.4	16	NVD				2.77
Valli	31	I17025249	HW	9TH	29.5	induced	40+1	4	86		14.22	6	NVD				3.5
Ananthavalli	28	I17024772	HW	10TH	27.6	abdominal pain	38	5	100		14.5	18	NVD				2.6
Geetha	29	I17029522	HW	B.COM	22.8	induced	40+1	6	101		20.8	10			LSCS	NPL	2.7
Surya	25	I17029524	HW	B.TECH	29.9	prom	37	3	89		7.72	17	NVD				2.6
Kowsalya	19	I17030163	HW	10TH	18.7	abdominal pain	39	5	104		15.49	11		VACCUM			3.2
Thasleema	19	I17030604	I.T	I.T	19.3	abdominal pain	38+4	4	86		6.13	15	NVD				2.51
Kalaiyarasi	28	I17030609	HW	B.TECH	28.01	prom	39+1	4	105		7.8	18	NVD				2.98
Govindammal	22	I17031875	Farmer	4TH	30	prom	38+3	9	100		32.4	19	NVD				3.2
Sugandhi	29	I17031693	HW	B.COM	18.5	induced	40+1	1	104		16.18	19	NVD				2.66
Anbarasi	27	I17031126	TEACHER	B.ED	22.2	abdominal pain	39+6	3	118		32.48	10		FORCEPS			2.8
Nithya	26	I17029662	HW	12TH	24.6	prom	37	4	85		20.9	6			LSCS	BREECH	2.7
Poongothai	26	I17032720	manager	M.Phil	24.6	prom	38+4	4	106		22.8	5	NVD				2.88
Karthika	26	I17032759	HW	8th	29.7	abdominal pain	38	5	99		7.17	12			LSCS	NPL	3
Kirubashini	25	I17033032	HW	BBM	19.8	induced	40	4	97		8.84	5	NVD				2.9
Punitha Baby	28	I17033567	HW	12TH	27.2	abdominal pain	40	4	118		12.05	23		VACCUM			2.87
Hema	23	I17044735	HW	12TH	26.5	induced	40	5	102		16.36	12	NVD				3.28