CHAPTER 2: REVIEW OF LITERATURE

The review of literature for the present study "**Calcium and vitamin D supplementation in pregnancy in three different settings**" undertaken is presented under the following headings:

2.1 Introduction

2.2 Requirements for Calcium and Vitamin D in Indian pregnant women

2.3 Nutrition transition and Nutritional status of pregnant women in India

2.4 Dietary intake of calcium by Indian population

2.5 Dietary consumption of calcium by pregnant women in India

2.6 Vitamin D status of adult Indian population

2.7 Vitamin D status of pregnant women and neonates in different parts of India

2.8 Importance/ role of calcium and vitamin D (on mother-child dyad)

2.9 Impact of calcium and vitamin D deficiency on mother-child dyad

2.10 Vitamin D and/ or calcium supplementation during pregnancy

2.11 National Guideline laid by Government of India

2.1 Introduction

Pregnant women have been recognized as the most vulnerable group from nutritional point of view. During pregnancy, many physiological and metabolic changes happen to support the growth of the foetus. During the intrauterine stage, the foetus stores many of the nutrients in the liver, which it utilizes in the postnatal stage. Nutrient requirement, thus increases during pregnancy as the woman has to provide not only for herself but also for the growing foetus.

Significant changes in the calcium and vitamin D metabolism have been seen during pregnancy (Abrams.,2007). Intestinal absorption of calcium increases during pregnancy to meet the increased demand of the growing foetus (Ritchie et al.,1998). The absorption is maximum during the third trimester (Cross et al.,1995). Calcium and vitamin D acts hand in hand in the body. For the absorption of calcium, a binding protein is required. The calcium-binding protein is induced by calcitriol (the active form of vitamin D). Calcitriol concentration increases during pregnancy to facilitate calcium absorption (Hacker et al., 2012).

WHO/FAO Expert consultation has stated that in most of the locations of the world in the broad band around the equator i.e. between 42°N latitude and 42°S latitude, the most physiologically relevant and efficient way to acquire Vitamin D is to synthesize it under the skin from 7-dehydrocholesterol by UV rays in the sunlight. Approximately, 30 minutes of exposure of the skin of the arms and the face, to the sunlight can provide the amount of vitamin D required daily. However, several factors can contribute to vitamin D deficiency like traditional lifestyle, clothing, pollution, geographical location, seasons of the year, skin types (Indian skin type is V) etc. All these factors reduce exposure to sunlight and, hence, result in vitamin D deficiency especially in pregnancy, infancy and childhood (WHO/FAO Expert consultation, 2004).

Vitamin D is a prohormone which primarily required for the absorption of calcium and bone formation along with several other conventional and non-conventional functions. Vitamin D deficiency during pregnancy has negative impact on both the mother and the child; pre-eclampsia (Bener et al., 2013), insulin resistance (Asemi et al., 2013) and gestational diabetes mellitus (Zhang et al. 2018 and 2008) are some of the maternal consequences of vitamin D deficiency. Foetal consequences of maternal vitamin D deficiency has both short- and long-term impacts; neonatal hypocalcaemia (Brooke et al., 1980), small for gestational age infants (Leffelaar et al., 2010), impaired skeletal growth leading to development of rickets (Ingole et al., 2014), reduced bone mass density (Mahon et al., 2010), increased risk of metabolic and autoimmune disease (Mulligan et al., 2010).

Deficiency of vitamin D leads to poor absorption of calcium which in turn leads to calcium deficiency. Calcium is a mineral which is abundantly found in the human body and is very important for different physiological functions like bone formation, muscle contraction, blood coagulation, and is necessary for the functioning of enzymes and hormones (WHO/FAO Expert consultation, 2004).

Villar et al. reported that there is an adverse effect of inadequate maternal consumption of calcium during pregnancy, on the mother-child dyad (Villar et al., 2004). Several studies have reported calcium supplementation in pregnancy has favourable impact on lowering the pregnancy induced hypertension (PIH); calcium supplementation or high dietary calcium intake can reduce high blood pressure in pregnant women which in turn may reduce the development of toxaemia (Villar et al.,2004 and 1983). Villar et al. have reported that the prevalence of pre-eclampsia was higher in women whose calcium intake was low (Villar et al.,2003). Supplementing 1.5 g calcium/day reduced the severity of pre-eclampsia, maternal morbidity, and neonatal mortality as secondary outcomes (Villar et al.,2006).

2.2 Requirements for Calcium and Vitamin D in Indian pregnant women

Calcium and vitamin D are nutrients that work hand in hand in bone health. Vitamin D is required for calcium absorption and calcium deficiency may lead to secondary vitamin D deficiency. Thus, optimal intake of calcium is required to avoid secondary vitamin D deficiency so that both calcium and vitamin D can work towards maintaining bone health (Harinarayan, 2014).

The foetus depends on the mother for its nutritional needs, thus the pregnant woman has to provide for the foetus along with fulfilling her nutritional requirements. Several nutrient requirements increase during pregnancy. The NIN-ICMR recommends the RDA of all the macro and microminerals for the Indian population; it takes into account, all the nutritional requirements of the pregnant women along with all the other age groups of both genders. As the present study is focused on calcium and vitamin D supplementation in pregnancy, the requirement of calcium and vitamin D is discussed.

NIN-ICMR-RDA had recommended 1200mg/day calcium as RDA for pregnant women in the year of 2010 (NIN-ICMR-RDA, 2010). According to IOM, there is no requirement of extra calcium during pregnancy if the intake of the same is sufficient (IOM, 2011). According to the available evidences, calcium absorption increases during pregnancy which may lead to an increased risk of kidney stones.

The most recent recommendation of the NIN-ICMR-RDA has recommended 800 mg of calcium as EAR and 1000 mg of calcium as RDA per day for pregnant women (NIN-ICMR, 2020).

Vitamin D is a prohormone which is predominantly synthesized in the human body. The 7-dehydrocholesterol is the precursor of vitamin D which is present under the skin (in the epidermis layer) and is converted to cholecalciferol (vitamin D) with the help of sunlight (ultraviolet rays of 290 -315nm length). The plant origin of vitamin D is known as ergocalciferol which is derived from ergosterol present in the plants (Srilakshmi, 2012). Vitamin D content in most of the foods are negligible, egg yolk, butter, milk etc. are some poor sources of vitamin D, as the vitamin D content varies with the diets and breeds of animals concerned. Studies carried out in NIN, Hyderabad have reported plants belonging to the S*olanaceae* family and *c.diurnum* leaves can be used as inexpensive plant sources of vitamin D (Srilakshmi, 2012). Thus, the most physiologically relevant and efficient way to acquire vitamin D is to convert the 7-dehydroclosterol by approximately, 30 minutes of exposure of the skin of the arms and the face, to the sunlight daily (WHO/FAO Expert consultation, 2004).

In 1988, the WHO committee recommended 100 IU of vitamin D per day for adult male which was then revised and increased to 200 IU/day by the joint FAO/WHO committee (WHO/FAO Expert consultation, 2004). In the year of 2011, the Institute of Medicine (US) recommended 600 IU/ day for adult male taking minimal sun exposure. In India, the NIN-ICMR-2020 guideline recommends adequate exposure to sunlight during 11 am to 3 pm in all seasons as this is the most desirable as well as an effective way to increase vitamin D level. In case of minimal sun exposure, and unlikely situations the recommendations of the IOM should be considered; RDA of vitamin D for all the age groups in both sexes is 600 IU/ day except for infants of 0-12 months of age (400 IU/ day). The EAR is 400 IU/day for all the age groups in both sexes except for infants of 0-12 months of age. Along with this adequate intake of calcium is to be ensured (NIN-ICMR, 2020).

2.3 Nutrition transition and Nutritional status of pregnant women in India

Currently, India is going through an economic, social, demographic, health and nutritional transition. India is presently experiencing the dual nutrition burden (Ramachandran, 2006 and Ramachandran & Kalaivani, 2018) and its associated problems of NCDs (Srinath Reddy & Katan, 2004 and Prabhakaran et al., 2007). The double burden of malnutrition is characterized by the coexistence of undernutrition along with overweight, obesity or diet-related NCDs, within individuals, households and populations, and across the life course (WHO, 2017).

Data on the magnitude of the dual nutrition burden in the Indian population from different states and segments are available from different national surveys. NNMB surveys show a decline in under-nutrition over time from 1970s to 2000 (NNMB, Technical Report No: 26 and 27). Data from NFHS (IIPS-NFHS-1,2,3,4 and 5), DLHS (IIPS-DLHS-2 and 4) and AHS CAB (RGI-AHS-CAB, 2011) show decline in under-nutrition and an increase in over-nutrition rates in Indian population.

Initially, the prevalence of over-nutrition was commonly observed among the urban affluent population (Ramachandran & Kalaivani, 2018); however, the above-mentioned recent surveys indicate over-nutrition is high even in poor in urban areas and rural areas in all income groups. National survey data shows India has experienced the steepest fall in the prevalence of under-nutrition, morbidity due to communicable diseases and steep improvement in maternal child health between 1990 and 2015; but during this period over-nutrition and non-communicable diseases (NCDs) increased simultaneously (Ramachandran & Kalaivani, 2018 and Goel et al., 2020).

Over-nutrition rate has increased in both men and women, however; recent national surveys indicate over-nutrition rate is higher in women (IIPS-NFHS-4 and 5). A study carried out on the same urban community population of the present study has observed that, in women, the prevalence of overnutrition was high and progressively increased with increasing age; around 70% of the above 50 years of women were over-nourished (Goel et al., 2020). Another study undertaken in the urban low-middle-income group of lactating women from Delhi reported prevalence of over-nutrition in lactating women especially in the ≥30-year age group was high; over-nutrition rates increased with waning lactation (Goel et al., 2020).

In India, the majority of low-income group households experienced food insecurity in the 1970s. Women were undernourished, had limited nutritional intake, and had short statures (NNMB 1975-79 and Krishnaswamy et al., 1997). Mean pregnancy weight gain was around 5-6 kg with a mean birth weight of 2.7 kg (Ramachandran, 1989; Ramachandran, 2002). India is experiencing a double burden of malnutrition where both maternal under-nutrition and over-nutrition are major public health problems (NNMB reports, Ramachandran P and Kalaivani, 2018, NFHS-3 & 4 and Goel et al, 2020). Maternal weight prior to pregnancy and during pregnancy has increased though no improvement in birth weight has been observed (Sharma et al., 2008). A study, taken up in the same population as this present study i.e. pregnant women from urban low-middle-income families, to assess weight gain during pregnancy, birth weight and magnitude of residual post-pregnancy weight retention had reported that, though women were heavier before and during pregnancy and there had been improvement in pregnancy weight gain, there was no change in mean birth-weight and post-pregnancy weight retention of about 2 kg (Pramanik, Ramachandran & Kalaivani, 2022). In comparison to the study carried out in the 1980s (Ramachandran, 1989; Ramachandran, 2002), a recent study showed an increased maternal weight by about 10 kg whereas the increase in maternal height is below 2 cm (Goel et al.,2020). Currently, mean height of women (18-29 years) from low-middle-income group families in Delhi is 151.7 cm and the weight is 54 kg; with a steep fall in the under-nutrition rate and increased prevalence of overnutrition (Goel et al.,2020). There is some improvement in pregnancy weight gain with an unaltered birth weight (Sharma et al., 2008 and Pramanik et al., 2022). This might be attributable to the fact that; there is any change in the maternal height which is an important determinant of birth length and birth weight, over-nutrition in 1/3rd of the women may have an adverse impact on the course of pregnancy and lead to gestational diabetes and pregnancy induced hypertension which intern has adverse impact on the birth weight and there has not been substantial reduction in the anaemia and other obstetric problems associated with low birth weight (Pramanik et al., 2022).

Several available studies have shown the adverse effects of calcium and vitamin D deficiency during pregnancy on the course and outcome of pregnancy. Calcium deficiency during pregnancy might lead to pregnancy-induced hypertension and pre-eclampsia (Kumar et al., 2009) which intern may adversely affect the birthweight of the infant and may lead to preterm delivery (Ye et al., 2010), stillbirth and neonatal mortality (Ananth & Basso, 2010). Other studies have shown calcium supplementation improved the course and outcome of pregnancy by reducing the PIH, pre-eclampsia, eclampsia (Belizán & Villar, 1980, Villar et al., 2006, Imdad et al.,2011, Kanagal et al., 2014 and Hofmeyr et al., 2018) and improving the birth weight (Imdad and Bhutta, 2012) and improved foetal skeletal development (Young et al., 2012) BMD of the infant (Raman et al., 1978). Vitamin D deficiency had been associated with adverse course of pregnancy like, insulin resistance (Maghbooli et al., 2008), gestational diabetes (Clifton-Bligh et al., 2008, Zhang et al., 2008 and 2018), pre-eclampsia, etc (Aghajafari et al., 2013, Wei et al., 2013, Agarwal et al., 2018, Bodnar et al., 2007, Baker et al., 2010 and Sing et al., 2016) and lead to impaired innate immunity function in childhood; infants born severely vitamin D deficient mothers may develop tetany due to severe neonatal hypocalcaemia (Harinarayan, 2014, Mehrotra et al., 2010 and Do et al., 2014), pre-term delivery, low birth weight, small of gestational age babies (Aghajafari et al., 2013, Wei et al., 2013, Agarwal et al., 2018, Gernand et al., 2014, Wang et al., 2018, Chen et al., 2017, Arora et al., 2018 and Fang et al., 2021). Intrauterine exposure to vitamin D deficiency adversely affects the foetal skeletal development and bone mineral accumulation leading to low bone mineral content/ density (Javaid et al., 2006, Viljakainen et al., 2011 and Sarma et al., 2018). A systemic review had reported vitamin D supplementation during pregnancy increases the birth weight, and birth length of the offspring (Pérez-López et al., 2015).

Therefore, the unaltered birthweight (Pramanik et al., 2022) might be a result of calcium and vitamin D deficiency also other than the points mentioned earlier. However, the present study is focused on the availability and compliance of calcium and vitamin D supplementation in pregnancy. The present study is a part of a project undertaken by the organization where the researcher was working. The main project has a biochemical component also along with other parameters discussed in the present study.

2.4 Dietary intake of calcium by Indian population

At the time of independence, India was not self-sufficient in food production. In 1970s the Green Revolution made India self-sufficient in food production though poverty, low dietary intake and undernutrition rate were high (Ramachandran, 2006). To overcome the burden of poverty and undernutrition, India identified poor families based on the energy consumption (Ramachandran, 2007). To improve the purchasing power employment was provided, to improve household food security subsidized food grains were made available and food supplementation through ICDS was initiated to bridge the gap in the dietary intake of the children and pregnant and lactating women from poor families. National Food Security Act (NFSA, 2013) distributed subsidized food grain to 2/3rd of all Indian families (75% of the rural population and up to 50% of the urban population) in addition to providing food grains for ICDS and MDM food supplement programmes. Despite this, NNMB and NSSO surveys had reported a reduction in the energy intake and consumption of cereals along with other food items over the last three decades.

There is a steep reduction in physical activity in the work, household and transport domains due to mechanization therefore, the recent guideline laid by ICMR-NIN recognized the problem of increasing over-nutrition and advocated that the current energy intake is sufficient to meet the EAR for the short-statured sedentary Indians (NIN-ICMR, 2020). This in turn leads to the fact that majority of the current Indian families are food secured. A recent study undertaken on low-middle-income families from North Indian urban community reported these families to be food secure in terms of energy intake (Kumari, Kalaivani, & Ramachandran, 2022).

The focus of the present study is the calcium and vitamin D supplementation in pregnant women, therefore here the consumption of the vitamin D and calcium will only be discussed.

Despite being a tropical country with abundant sunshine, several studies from India reported high prevalence of vitamin D deficiency across age groups, and physiological status, in both genders from all over India (Kamboj, Dwivedi and Toteja, 2018 and Trilok Kumar, Chugh & Eggersdorfer, 2015). Most of the food contains negligible amounts of vitamin D, even the best source of vitamin D is not a reliable source as the vitamin content depends on the diet and the breed of the animal (Srilakshmi, 2012). The most physiologically relevant and efficient way is to synthesize it in the body by adequate sun exposure (WHO/FAO Expert consultation, 2004). Hence it is not feasible to estimate the dietary consumption of vitamin D. Whereas it is readily possible to estimate the dietary intake of calcium by converting the food items consumed to their nutrient content.

National Nutrition Monitoring Bureau (NNMB) surveyed household consumption patterns of nutrition in rural, tribal and urban areas of India. Data from these surveys provide information regarding the time trend (from 1975 to 2017) of consumption of calcium along with other nutrients and food items.

A. NNMB Rural Survey (2012):

Data from this survey showed that there was a decline in calcium consumption in both adult men and women; pregnant and lactation women also showed a similar trend. The pooled data from the rural areas of the 10 survey states showed mean calcium consumption was 419±320 mg/CU/day whereas the RDA was 600mg/day. The median intake of calcium was 331 mg/CU/day (NNMB, Rural-Third Repeat Survey 2011-2012).

Table 2.1: Average consumption of Calcium (CU/day): TIME TRENDS (NNMB Rural Survey)

	Year	Kerala	Tamil Nadu	Karna-taka	Andhra Pradesh	Maha-rashtra	Gujarat	Orissa	Pooled	RDA
Calcium (mg)	1975-79	507	552	946	565	512	551	*	606	400
	1988-90	608	472	869	432	461	550	346	565	
	1996-97	728	451	764	418	555	530	313	521	
	2011-12	501	468	493	388	297	470	416	433	

Source: NNMB, Rural-Third Repeat Survey 2011-2012

Table 2.2: Calcium intake in adults (NNMB Rural Survey)

Adults	Year	n	Calcium (mg)
Men	1996-97	1349	683
	2011-12	4774	453
Women	1996-97	1477	593
	2011-12	9519	414
Pregnant	1996-97	79	575
	2011-12	322	418
Lactating	1996-97	429	553
	2011-12	693	411

Source: NNMB, Rural-Third Repeat Survey 2011-2012

Data from the survey showed a gradual reduction in calcium intake in the adults of both genders and in different physiological conditions in all the states. The main source of calcium is milk and milk products and cereal & millets. Over the time there was a reduction in milk and milk product consumption and cereal consumption in the population (NNMB, Rural-Third Repeat Survey 2011-2012).

B. NNMB Tribal Survey (2009):

The data shows there is a decrease in the consumption of dietary calcium over time. The average calcium consumption of all the states was well below the RDA set by the ICMR;

with the average consumption of calcium being 223mg/day whereas the RDA was 400mg/day. The lowest average consumption (161mg/day) was reported in Madhya Pradesh though the average consumption of calcium none of the state was meeting the RDA. The average consumption of milk and milk products was only 14.1% of the RDA. The time trends from 1998-99 to 2007-08 had shown decrease in the median calcium consumption from 394mg/day to 315mg/day. This decrease is evident in all the states included in the survey except Gujarat where it almost remained the same (NNMB, Tribal-Second Repeat Survey 2008-2009).

Table 2.3: Interstate differences in calcium intake (NNMB Tribal Surveys)

Year		Kerala	Tamil Nadu	Karna taka	Andhra Pradesh	Maha-rashtra	Gujarat	Madhya Pradesh	Orissa	West Bengal	Pooled	RDA
1998-99	N	1140	956	801	739	940	950	799	1084	627	**8036**	400
	Ca (mg)	421	312	380	445	354	316	247	573	480	**394**	
2007-08	N	1197	1162	1065	1188	1175	1197	1186	1195	712	**10077**	
	Ca (mg)	326	265	336	311	287	322	196	450	365	**315**	

* Ca=Calcium

Source: NNMB, Tribal-Second Repeat Survey 2008-2009

C. NNMB Urban Survey (2017):

Consumption of calcium in the urban population was low, only 67% of RDA. Household consumption of milk and milk products which are the main source of calcium was low, 81.3% of the RDI was met (NNMB, Brief Urban Nutrition Report 2017).

Along with the national-level survey data, several other studies from all over India had reported a high prevalence of low calcium consumption.

A cross-sectional study on the adolescent girl observed low calcium intake in symptomatic adolescents with osteomalacia (Rajeswari et al., 2003).

Harinarayan, Ramalakshmi & Venkataprasad (2004) observed low calcium intake in the rural population of 5 villages near Tirupati and hospital staff from a south Indian urban area. The rural population had a lower calcium consumption than the urban population and the phytate-to-calcium ratio was higher in the rural population which hindered calcium absorption in the gut.

Harinarayan C.V. had reported daily dietary intake of calcium in the postmenopausal women, was lower than the RDA issued by ICMR for the Indian population (Harinarayan, 2005).

A study on healthy adults from urban and rural areas were conducted in Tirupati, South Andhra Pradesh, India had observed daily dietary intake of calcium was low both in urban and rural populations in comparison to the RDA issued by ICMR. Dietary calcium and phosphorus were significantly lower in the rural population than the urban population, and the phytate-to-calcium ratio was significantly higher in the rural population than the urban population. (Harinarayan et al., 2007).

A cross-sectional study on adult males and females residing in Kashmir, North India, reported dietary calcium intake was lower than the ICMR-RDA. Females were consuming significantly lower dietary calcium than the male counterparts of the study population. The author also reported calcium intake was significantly lower in the subjects with vitamin D deficiency (Zargar et al., 2007).

Harinarayan et al., (2008) reported low consumption of calcium, both in urban and rural areas across the age groups in comparison to recommended daily/dietary allowances (RDA) for calcium issued by the Indian Council of Medical Research (ICMR); but the phytate-to-calcium ratio was higher in the rural population.

Similar findings were reported from a community-based cross-sectional study on post-menopausal women (≥50 years) in a semi-urban region of South India; low calcium consumption in contrast to the recommended intake of the same was also recorded in these women (Paul et al., 2008).

Goswami et al., (2008) reported low calcium intake in the residents of a North Indian village. Diets of the females were more deficient than their male counterpart.

A supplementation study on apparently healthy North Indian subjects had shown their dietary intake of calcium was lower than the RDA laid by ICMR (Goswami et al., 2008).

Puri et al. (2008) undertook a study on school girls of upper and low socioeconomic status and found that the dietary calcium intake of the girls from low socioeconomic status was lower than the RDA. The dietary intake of calcium along with other macro-nutrients i.e. energy, protein and fat were lower in the girls from low socioeconomic status than that of the girls from upper socioeconomic status. Consumption of milk and milk-based products was higher in the girls from upper socioeconomic status.

A cross-sectional study undertaken in adolescent girls majorly form economically undeveloped families had reported low dietary intake of calcium (Sahu et al., 2009). Another Randomized controlled trial on school girls from Government school (government-aided) and Private school (fee paying) in Delhi observed a similar trend of higher dietary calcium consumption in girls from the upper socioeconomic strata than the girls from low- socioeconomic strata (Marwaha et al., 2010).

Similar findings were reported from a cross-sectional study undertaken in adolescent school-going girls and boys from both upper and lower socioeconomic strata from Pune, Maharashtra. There was significant difference in dietary calcium consumption amongst the girls and boys from the different socioeconomic strata, intake of calcium in girls from the low socioeconomic strata were the lowest in all and was also lower than the ICMR RDA (Sanwalka et al., 2010).

A pilot study undertaken in toddlers from crèche in Pune for young children of underprivileged mothers reported low intake of dietary calcium in the study population; the mean calcium intake of the toddlers was only 47% of Indian Recommended Dietary allowances (Ekbote et al., 2011).

A cross-sectional study on healthy volunteers, aged between 25-35 years, of both the sex from Mumbai, western India had reported low calcium intake in comparison to the RDA issued by ICMR in both the sex and consumption of phytate was noted to be higher than the calcium in the study population (Shivane et al., 2011).

Data from a study on healthy female college-going students in two categories, sportswomen and controls in the age group of 18-21 years, residing in New Delhi, North India had revealed that dietary calcium intake is significantly better in the sportswomen than the control group, the calcium intake in the control group was way below the RDA. Only 24% of the sportswomen consumed calcium below the RDA in contrast to 99% in the control subjects (Marwaha et al., 2011).

A randomized control trial on children in the age group of 6 months to 5 years with nutritional rickets attending an outpatient department of a tertiary care teaching hospital in North India noted dietary calcium intake lower than the ICMR-RDA in all the subjects (Aggarwal et al., 2013).

In a cluster randomized trial in Andhra Pradesh, 60 villages were randomized into three groups namely, the control group (received routine Integrated Child Development Services); the complementary feeding group (received the ICDS plus the World Health Organization recommendations on breastfeeding and complementary foods); and the responsive complementary feeding and play group (received the same intervention as the CFG plus skills for responsive feeding and psychosocial stimulation). The data from this study reported the median dietary calcium intake of the subjects was way lower than the ICMR-RDA (Vazir et al., 2013).

A prospective cohort study undertaken in young (18-23 years) men and women in rural Hyderabad had shown that the dietary calcium intake was lower in the female than the male counterpart of the study population and the dietary calcium intake in the women was lower than the ICMR-RDA (Matsuzaki et al., 2014). Another study from Western India confirmed a similar trend of lower dietary calcium intake by women than men (Kamalanathan et al., 2014).

A household survey carried out in 3 urban slum areas of Delhi, North India had reported inadequate consumption of calcium along with other micronutrients in adult women who had delivered a child recently; only 52.8% of the women consumed adequate dietary calcium (Ghosh-Jerath et al., 2015).

A cross-sectional study undertaken among postmenopausal women from urban Tamil Nadu, South India observed that 74.5% of the study subjects were consuming dietary calcium below the ICMR-RDA (Raj, Oommen & Paul, 2015).

A study on dietary intake was carried out in healthy subjects from Bengaluru, a metropolitan city, and compared the dietary calcium intake of healthy subjects from rural areas around Tirupati and urban Tirupati, South India. The study reported that consumption of milk and milk products and the dietary calcium intake were significantly lower in the rural population than in the urban and metropolitan populations; a significantly higher dietary phytate/calcium ratio in the rural subjects in contrast to the urban and metropolitan city group (Harinarayan and Ramalakshmi, 2016).

A community-based cross-sectional study; carried out by the National Nutrition Monitoring Bureau (NNMB), during 2005-06 among the rural population of nine major states of India observed that the consumption of milk and milk products were low in comparison to the RDI, in the study population, with a mean consumption below RDA set by ICMR in the women subjects (Arlappa et al., 2016).

A cross-sectional study was conducted in urban postpartum primiparas mothers attending a tertiary level health care hospital in Pune city, Western India had found that dietary calcium intake was lower than the ICMR-RDA in women immediately postpartum, 1 year postpartum, 3 years postpartum and decreases gradually with time, i.e. the mean dietary calcium intake was highest in the immediately postpartum women and lowest in the 3 years postpartum women (Kajale et al., 2016).

To assess dietary patterns of 2 to 16 year old children with special reference to calcium, a study was undertaken in the schoolchildren (2–16 years) around Pune city, Western India had observed that the diet of the majority of the children was cereal‑pulse‑based; overall, around 76% children and 80% adolescents did not meet the RDA for calcium and the mean calcium intake was 57% of the RDA in children and 53% in adolescents. Milk and milk product consumption was reduced with increasing age (Ekbote et al., 2017).

Low dietary intake of calcium had been reported in North Indian men working indoors as well as outdoors (Goswami et al., 2017).

A cross-sectional study amongst adolescents (10 to <14 years) from lower, middle, and upper socioeconomic strata from Patan, Gujarat had observed dietary calcium intake in the adolescents from lower and middle socioeconomic strata was way below the ICMR-RDA whereas the same was close to the RDA in the adolescents from upper socioeconomic strata (Patel et al., 2017).

A cross-sectional study in peri- and post-menopausal women from low socioeconomic group living in a slum area of Mumbai, Western India reported dietary calcium intake of the study subjects was very low in comparison to the ICMR-RDA (Shaki et al., 2018).

A pilot survey on adolescent girls residing in the KOKAN region of western India revealed that diet of 98.8% of the subjects were deficient in dietary calcium and the median dietary calcium intake of the study subjects was way below the RDA (Patil et al., 2018).

A cross-sectional study carried out among inpatients and normal relatives of orthopaedics department of a tertiary care teaching hospital observed the mean dietary calcium intake was lower than the RDA; the diet of around 3/4th of the subjects was deficient in dietary calcium (Raj et al., 2018).

Poor dietary calcium intake had been reported in the children of 6 to 12 years of age attending Government schools in a semirural area near Pune, western India. Only 34% of the RDA for dietary calcium was met; the diet of the girls was more deficient in calcium than the boys (Mandlik et al., 2018). Another subsequent study in the same population had again confirmed the low dietary calcium intake in the school-going children attending Government schools in the semirural area near Pune, western India (Mandlik et al., 2020).

To assess the nutrient intakes a total of pregnant women, lactating mothers, newly married women, and adolescent girls from 4 districts of each region of modern India- Delhi, Karnataka, Bihar, and Rajasthan from the North, South, East, and West regions, were interviewed for a community-based, cross-sectional study. Adolescents and newly married women on average consumed less than three-fourths of the recommended intakes of energy, iron, calcium, folic acid, protein, and zinc in one day but newly married women consumed 140% of the recommended intake for fat. The percentage of subjects consuming adequate level of calcium was lowest in the lactating mothers compared to the other groups though dietary calcium was inadequate in all 4 groups (Sharma et al., 2020).

Harinarayan, Akhila and Shanthisree (2021) documented the dietary calcium intake drawn from various studies from 1999–2019 which shows intake less than the RDA for various age groups, genders, and physiological states.

2.5 Dietary consumption of calcium by pregnant women in India

Evidence suggests that during pregnancy demand of calcium increases; the metabolism of calcium is regulated by a complex of hormones and vitamin D. Dietary calcium intake plays an important role. Inadequate calcium intake increases the catabolism of vitamin D and vitamin D deficiency leads to hypocalcaemia and rickets (Pettifor, 2004).

Over time, poverty reduced and household food security improved. Despite, readily available food grains at a subsidized rate, data from both NSSO and NNMB surveys have shown a progressive reduction in dietary energy and cereal intake along with other food items. These surveys also indicate a reduction in physical activity especially in urban areas. Data from national-level surveys like NNMB and NFHS have reported a progressive reduction in the under-nutrition rate and an increase in the over-nutrition rate in women both in urban and rural areas. In view of these facts, the Expert Group on Nutrient Requirements of Indians has recommended energy and nutrient intake should depend on the EAR (ICMR-NIN, 2020). A diet survey undertaken on pregnant women from low-income group in Delhi has shown that the pregnant women were consuming adequate energy and were from food-secure households (Pramanik, Kalaivani & Ramachandran, 2021). The purpose of the present study is to assess the availability of supplements, coverage, acceptance, and compliance rates of ongoing Calcium and Vitamin D supplementation in pregnancy. Evidence suggests increased absorption of calcium during pregnancy and IOM, 2011 has recommended that no extra calcium is required during pregnancy if the dietary intake of the same is adequate. Hence, it is important to assess the dietary calcium intake in the study group to comprehend if the diet of these pregnant women were actually calcium deficient.

NNMB surveys in tribal, rural and urban areas show the time trend of dietary calcium intake by pregnant women.

A. NNMB Rural Survey (2012):

NNMB rural survey had observed consumption of dietary calcium is way below the RDA set by ICMR, in the pregnant women from rural India. Average consumption was only 418 mg/ day whereas the RDA was 1200 mg/day. The time trend of calcium consumption in pregnant women shows a decline from 575mg/day in 1996-97 to 418 mg/day in the 2011-12 survey (NNMB, Rural-Third Repeat Survey 2011-2012).

More than 60% of the pregnant women from rural areas of all the states were consuming calcium <50% of the RDA, pooled data shows 76.1% of the pregnant women were consuming <50% of the RDA and only 7.5% were consuming ≥70% of the RDA (NNMB, Rural-Third Repeat Survey 2011-2012).

Table 2.4: Dietary calcium intake in rural pregnant women (NNMB Rural Survey)

% RDA	States										
	Kerala	**Tamil Nadu**	**Kar-nataka**	**Andhra Pradesh**	**Maha-rashtra**	**Gujarat**	**Madhya Pradesh**	**Orissa**	**West Bengal**	**Uttar Pradesh**	**Pooled**
n	34	38	47	29	34	22	26	22	25	45	322
<50	64.7	78.9	70.2	75.9	97.1	72.7	96.2	68.2	68	71.1	76.1
50-70	14.7	15.8	21.3	17.2	2.9	18.2	3.8	18.2	28	22.2	16.5
≥70	20.6	5.3	8.5	6.9	0	9.1	0	13.6	4	6.7	7.5

Source: NNMB, Rural-Third Repeat Survey 2011-2012

B. NNMB Tribal Survey (2009):

Data from the NNMB Tribal survey had shown low intake of dietary calcium by the pregnant women from all the states, the average intake of pregnant women from all the states included in the survey was 313mg/day though the RDA was 1000mg/day. Pooled data from all the states showed more than 80% of pregnant women were consuming calcium <50% of the RDA and only 10% were consuming calcium ≥70% of the RDA (NNMB, Tribal-Second Repeat Survey, 2008-2009).

Table 2.5: Dietary calcium intake in tribal pregnant women (NNMB tribal survey)

% of RDA	States									Pooled
	Kerala	Tamil Nadu	Karna-taka	Andhra Pradesh	Mahara-shtra	Gujarat	Madhya Pradesh	Orissa	West Bengal	
	n=20	n=36	n=24	n=14	n=7	n=11	n=7	n=24	n=15	n=158
<50	85.0	100.0	62.5	78.6	85.7	90.9	85.7	58.3	86.7	**81.0**
50-70	10.0	0.0	12.5	14.3	14.3	0.0	14.3	20.8	0.0	**8.9**
≥70	5.0	0.0	25.0	7.1	0.0	9.1	0.0	20.8	13.3	**10.1**

Source: NNMB, Tribal-Second Repeat Survey 2008-2009

C. NNMB Urban Survey (2017):

As the data from the NNMB report shows low consumption of calcium in the urban households it is obvious that there was inadequate consumption of the same in the pregnant women from the same group.

In company with the NNMB reports, there are studies documenting low intake of calcium in pregnant Indian women.

A study carried out on subjects from 6 distinct groups- physician & nurses group, soldier group, de-pigmented group, pregnant women with low socioeconomic status, newborns from the previous pregnant women, had reported that, in the physician & nurses' group, there were no changes in the composition of diet between summer and winter. Energy, carbohydrate, protein and fat intake of the physician & nurses' group, the soldier group and the de-pigmented group were adequate in comparison to the RDA issued by ICMR.

The intake of energy, protein and calcium were significantly low in the pregnant group; the phytate-to-calcium ratio was significantly higher than in other groups. The carbohydrate and fat intake were lower in the pregnant group in comparison to the other groups. (Goswami et al., 2000).

A study undertaken on pregnant women recruited from Queen Mary's Hospital, King George Medical University, Lucknow had observed calcium intake lower than the RDA both in rural and urban populations but the intake of the same was even lower in the rural population (Sachan et al., 2005).

Another study carried out on pregnant women from six rural villages near the city of Pune observed calcium intakes in pregnant women were low in comparison to the ICMR-recommended daily allowances (Ganpule et al., 2006).

A cross-sectional study conducted on pregnant women majorly from low-socioeconomic households in the Barabanki district, near Lucknow reported low intake of dietary calcium in the study population (Sahu et al., 2009).

A cross-sectional study on pregnant women in the third trimester observed low dietary calcium intake in the study population. Two-thirds (66%) of the study population had low dietary calcium intake (Darwish et al., 2009).

A cross-sectional study by Jani et al., (2014), enrolled healthy pregnant women, in their third trimester from Mumbai, Western India. Mean calcium intake was much lower than the recommended dietary allowances of calcium by ICMR.

A household survey carried out in 3 urban slum areas of Delhi, North India had reported inadequate consumption of calcium along with other micronutrients in pregnant women; only 47.3% of the women consumed adequate dietary calcium (Ghosh-Jerath et al., 2015).

A cross-sectional descriptive study undertaken on pregnant women attending PHCI, Lucknow, Uttar Pradesh reported low consumption of calcium in pregnant women.

Dietary intake of milk and milk products in the third trimester of pregnancy and calcium intake was lower than the RDA (Sahu et al., 2015).

A community-based cross-sectional study was conducted in Haryana, North India on pregnant women between 28 weeks and 36 weeks of gestational age. The mean dietary calcium intake was 858.4mg/day in contrast to the RDA of 1,200 mg/day. More than ¾th of the study population were consuming calcium below the RDA and only 23.5% of the pregnant women consumed more than or equal to the RDA (Gupta et al., 2016).

A community-based, cross-sectional study was carried out to assess the nutrient intakes of pregnant women, lactating mothers, newly married women, and adolescent girls from 4 districts of each region of modern India-Delhi, Karnataka, Bihar, and Rajasthan from the North, South, East, and West regions. Consumption of dietary calcium was inadequate in all the 4 groups. Low calcium consumption was observed in pregnant women; only 27.8% of the subjects were consuming adequate amount of dietary calcium; 76.7% of the pregnant women were consuming calcium below 50% of the RDA (Sharma et al., 2020).

2.6 Vitamin D status of adult Indian population

Osteomalacia in *purda*-wearing north Indian women, congenital rickets due to severe maternal vitamin D deficiency was a well-recognized clinical entity in the early part of the last century (Teotia, & Teotia, 1972, Teotia, Teotia & Singh, 1979, Teotia, Teotia & Nath, 1995, Teotia & Teotia, 1997 and Teotia & Teotia, 2008). However, by the mid-20th century, as physicians did not report osteomalacia in women and congenital rickets in infants, it seemed as if these were no longer a clinical problem, and the vitamin D status of pregnant women became less of a concern (Gopalan, & Ramachandran, 2008). The vitamin D deficiency was attributed to low intake of vitamin D and low exposure to sunshine; the high prevalence of rickets and osteomalacia in Asians residing in Britain was attributed to the changing food and cultural habits (Hodgkin et al., 1973 and Brook et al., 1980). India being a tropical country it was believed that vitamin D deficiency in India is not common. Later, with the availability of the technology for vitamin D estimation, several investigators estimated the prevalence of Vitamin D deficiency using plasma vitamin D levels (Hollis, 2005).

Vitamin D assays:

Initially, the estimation of serum vitamin D had methodological issues. Vitamin D_2 from plant origin or D_3 from animal origin or synthesized from 7-dehydrocholesterol present under the skin by adequate exposure to the UV rays from sun gets hydroxylated at C-25 position in the liver to form the 25-hydroxyvitamin D [25(OH)D] and then another hydroxylation takes place at C-1 position, in the kidney to form the biologically active form of vitamin D i.e. 1,25-dihydroxyvitamin D [1,25$(OH)_2$D]. In appreciation of this fact, a binding protein assay using the vitamin D binding protein (DBP) to measure circulating levels of 25(OH)D or 1,25$(OH)_2$D in the circulation was developed (Holick, 2009). The 25(OH)D is the major metabolite circulating in the blood, which is directly dependent on both skin and oral sources and is the best determinant of vitamin D status is the concentration of 25(OH)D in the serum (Harinarayan & Joshi, 2009). There are several more advantages of measuring the concentration of the 25(OH)D instead of 1,25$(OH)_2$D. The circulating half-life of 1,25$(OH)_2$D is only 4-6 hours and the circulating level is a thousand-fold less than 25(OH)D. In vitamin D deficient subjects, intestinal absorption of calcium decreases which in turn increases the secretion of PTH (parathyroid hormone). The increased level of PTH in turn increases the renal reabsorption of calcium, resorption of bone and renal conversion of 1,25$(OH)_2$D, the active form of vitamin D from 25(OH)D. Thus, measuring circulating 1,25$(OH)_2$D, in the deficient subjects would give a falsely normal or elevated level, making it unreliable determinant of vitamin D status (Holick, 2009). The advantage of binding protein assay using the vitamin D binding protein (DBP) to measure circulating levels of 25(OH)D was that DBP efficiently recognized both 25(OH)D from plant and animal sources; however, the major limitation was the assay measured 25(OH)D in a serum sample that contained other vitamin D metabolites (Holick, 2009). Harinarayan (2014) reported that the first ever assay carried out by them was a titrated assay (Harinarayan, Gupta & Kochupillai, 1995).

In 1985, radioimmunoassay (RIA) was developed for 25(OH)D. This procedure had similar advantages and disadvantages as of the binding protein assay (Hollis, 2004). With the availability of the RIA, it became possible to compare the values, which increased the concordance between inter-laboratory values of vitamin D assay (Harinarayan, 2014). Currently, there are antibodies co-specific to both 25(OH)D_2 and 25(OH)D_3, thus the laboratories use the term 25(OH)D assay and not 25(OH)D_2 and 25(OH)D_3 (Hollis, 2000 and Harinarayan, 2004). In order to remove the interfering vitamin D metabolites, simple preparative chromatography was developed in which 25(OH)D was separated from more polar metabolites that interfered with the assay (Holick, 2009). RIA has been replaced by ELISA (enzyme-linked immunoassay), because of the simplicity in usage; in this assay 25(OH)D and its products get measured. LCMS (Liquid Chromatography Mass tandem Spectrophotometry) is the gold standard method of measuring vitamin D; in this method, 25(OH)D_2 and 25(OH)D_3 are measured separately and added to get the "total 25(OH)D" (Harinarayan, 2014).

Between 1995 to 2000 studies started to report vitamin D deficiency in the Indian population (Harinarayan, Gupta & Kochupillai, 1995 and Goswami et al., 2000). Later, several epidemiological studies carried out in India reported vitamin D deficiency across age groups (Kamboj, Dwivedi and Toteja, 2018) and in both sexes from all over India (Trilok Kumar, Chugh & Eggersdorfer, 2015 and Goswami, Mishra & Kochupillai, 2008).

Some of the factors assumed to be responsible for this high prevalence of vitamin D deficiency are:

- *Modernization:* India is going through India is going through an economic, social, demographic, health and nutritional transition (Ramachandran & Kalaivani, 2018). This change in the work culture had resulted in a reduction in adequate sun exposure and increased hours spent indoors, especially in the urban areas (Babu, & Calvo, 2010).
- *Sun-fleeing behavior:* Either to avoid tanning or simply because of the heat, Indians avoid the sun (Harinarayan, 2014).

- *Clothing habit:* Indians traditionally wear clothes that fully cover the body even when exposed to the sun. This tradition is especially observed in the women wearing the "Burqa" or "Pardah" which further reduces skin exposure to sunlight (Harinarayan, 2014).
- *Skin pigmentation:* Melanin content of the skin is inversely proportional to the conversion of 7-dehydrocholesterol in the skin to cholecalciferol. Indians have darker complexion and thus require a longer duration of sun exposure to synthesize an adequate amount of vitamin D (Harinarayan, 2014).
- *Atmospheric pollution:* Vitamin D photosynthesis gets hampered due to atmospheric pollution as pollution scatters short UVB wavelengths. There are reports of a high incidence of vitamin D deficiency rickets in toddlers living in high atmospheric pollution in Delhi, India (Agarwal et al., 2002 and Tiwari & Puliyel, 2004).
- *Food habits:* Food fads and habits lead to low calcium and vitamin D intake. Low calcium and high fiber diet with phosphates and phytates deplete vitamin D stores and increase calcium requirement (Harinarayan, Ramalakshmi & Venkataprasad, 2004).
- *Pregnancy related:* Repeated, unplanned and frequent pregnancies in women with low dietary calcium intake may lead to vitamin D deficiency in the mother-child dyad (Harinarayan, 2014).
- *Heritability:* Heritability of the vitamin D binding protein determines the improvement of 25(OH)D in response to treatment (Harinarayan, 2014).

In the year of 2000, Goswami et al. reported vitamin D deficiency is prevalent in medical personnel like doctors and nurses from North India (Delhi).

Arya et al., (2004) had shown vitamin D deficiency is common in urban north Indian hospital staff; 78.3% of subjects had serum 25(OH)D level $\leq$20ng/ ml, which may be attributable to inadequate sun exposure and Indian skin pigmentation. The author found a correlation between 25(OH)D level and daily sun exposure.

Harinarayan, Ramalakshmi & Venkataprasad (2004) reported similar findings in a previous study carried out in 5 villages near Tirupati and hospital staff from south Indian urban area; 69% of the population were either deficient or had insufficient level of vitamin D along with low calcium intake. The rural population had a lower calcium consumption than the urban population and the phytate-to-calcium ratio was higher in the rural population which hindered calcium absorption in the gut.

Harinarayan C.V. reported that 82% of the study group had vitamin D deficiency. The study was carried out on postmenopausal women from South India and found that only 18% had adequate level of vitamin D (Harinarayan, 2005).

Vuputturi et al., (2006) reported 94.3% vitamin D deficiency in adults, including both males and females, in a study population from Delhi, North India.

Vitamin D deficiency has been seen in all parts of India (Beloyartseva et al., 2012), both in urban and rural areas, in both males and females.

A study carried out in Tirupati, South Andhra Pradesh, India reported a high deficiency of vitamin D in terms of 25(OH)D concentration in blood, in the South Indian population. In this study, healthy adults from urban and rural areas were recruited. The urban population were predominantly involved in indoor jobs, working indoors from 10 am to 5 pm, and who were not working predominantly stayed inside, fully dressed, only face and forearm were exposed to sunlight; in contrast to the rural population who were agricultural workers working in the field from 8 am to 5 pm, exposing the chest, back, arms, forearms, legs to the sunlight. The 25(OH)D concentration was higher in rural populations; deficiency in women was higher in females both in rural and urban populations. Rural men were 44%, 39.5% and 16.5% deficient, insufficient and sufficient respectively in 25(OH)D concentration whereas the rural women were 70%, 29% and 1% deficient, insufficient and sufficient respectively. Urban men were 62%, 26% and 12% deficient, insufficient and sufficient respectively in 25(OH)D concentration whereas the rural women were 75%, 19% and 6% deficient, insufficient and sufficient respectively (Harinarayan et al., 2007).

Vitamin D deficiency is prevalent in Kashmir valley despite abundant sunshine; the author of a study reported that 83% of the overall adult subjects were vitamin D deficient, with women being more prone to vitamin D deficiency (Zargar et al., 2007).

A study carried out in a North Indian village had shown 70% deficiency in the rural population despite abundant sunshine; female counterparts were more vitamin D deficient than male counterparts. The authors compared the value with that of the urban population and reported that the rural population is less deficient than the urban population though only around one-third of the population was vitamin D sufficient (Goswami et al., 2008).

Harinarayan et al., (2008) reported vitamin D deficiency in both rural and urban populations, in both adults and children. The urban population had higher vitamin D deficiency than the rural population. Calcium consumption was low, both in urban and rural areas across age groups in comparison to recommended daily/dietary allowances (RDA) for calcium issued by the Indian Council of Medical Research (ICMR); but the phytate-to-calcium ratio was higher in the rural population. Similar findings were reported from a community-based cross-sectional study on post-menopausal women (≥50 years) in a semi-urban region of South India; low calcium consumption in contrast to the recommended intake of the same was also recorded in these women (Paul et al., 2008).

A prospective, cross-sectional study conducted in a tertiary healthcare centre in Mumbai on young otherwise healthy resident doctors has shown 87.5% insufficiency of vitamin D in the subjects (Multani et al., 2010).

Women, both reproductive and post-menopausal, have vitamin D deficiency. Lower bone mass density was reported in these women. More than 70% of the study women from both reproductive and post-menopausal age from South India had circulating 25(OH)D level of <20ng/ ml and only around 7% in both age groups had sufficient circulating 25(OH)D level i.e. >30ng/ml and the remaining had an insufficient level of the same (Harinarayan et al.,2011).

A study carried out in healthy North India elderly subjects, reported vitamin D deficiency and insufficiency in a large proportion of the study group irrespective of gender and age

(50yrs - <65yrs vs ≥65 years). Vitamin D deficiency (25(OH)D: <20ng/ ml) was seen in 91.2% and vitamin D insufficiency (25(OH)D: 20 to <30ng/ ml) was seen in 6.8% of the subjects (Marwaha et al., 2011).

Ramakrishnan et al., (2011) carried out a study on 329 young adults from Chandigarh, North India, in the summer and 237 subjects from the same cohort in the winter and found out 27.5% and 49.5% vitamin D deficiency in summer and winter; the vitamin D level was positively correlated to sun exposure and calcium intake in the summer.

A cross-sectional study on healthy volunteers, aged between 25-35 years, of both sexes from Mumbai, western India reported low level of 25(OH)D in the overall study population; 70% were vitamin D deficient. Hypovitaminosis D was more prevalent in females (Shivane et al., 2011).

A cross-sectional study on middle-aged medical and paramedical personnel from 18 Indian cities across 4 regions (North, South, East and West) of India reported a high prevalence of vitamin D deficiency. Only 6% of the study population had sufficient level of vitamin D, 79% had deficiency and 15% had insufficient level of 25(OH)D level (Beloyartseva et al., 2012).

An observational cross-sectional study carried out in the winter on physicians and diabetologists from Kolkata, East India, reported 92.5% deficiency and 5% insufficiency amongst the subjects (Baidya et al., 2012).

Another study carried out on adult males (≥50 years) from Varanasi, North India, had shown a high prevalence of vitamin D deficiency; only 13.5% of the subjects had normal vitamin D levels (Agrawal & Sharma, 2013).

Overall, 90% of vitamin D deficiency/ insufficiency was reported from a study carried out on a healthy population of 17-68 years of age from Punjab, North-West India. The study found a significant difference between the prevalence of vitamin D in urban and rural populations though both the rural (81.25%) and urban (94.12%) populations had a high prevalence of vitamin D deficiency (Bachhel, Singh and Sidhu, 2015).

Gunjaliya et al., (2015) showed a high prevalence of hypovitaminosis D in the populations of Ahmedabad, Gujarat, West India; more than 85% of the subjects across all age groups and genders from higher socioeconomic class had hypovitaminosis D.

A cross-sectional study conducted among the healthy population of Cuttack, a coastal district of Odisha, East India reported that 84.9% of the study population were vitamin D deficient and females (78.7%) were more deficient than males (Rattan, Sahoo & Mahapatra, 2016).

A retrospective cross-sectional study was conducted in Gurgaon, North India on apparently healthy adult subjects of both genders had reported that 93% of the subjects were either vitamin D deficient or insufficient; the vitamin D level was significantly lower in the females. Seasonal variations of the vitamin D levels were also observed; vitamin D levels were significantly lower in winter-spring seasons than in summer-autumn seasons (Shukla et al., 2016).

Pal et al., (2016) reported a high prevalence of hypovitaminosis D in adults (20-80 years) of Agra, North India; 91.3% had 25(OH)D level <30ng/ mL; older subjects were shown to have more deficiency than the younger.

Misra et al., (2017) carried out a cross-sectional study on women (20-60 years) residing in rural areas of Ballabgarh, North India; 90.8% vitamin D deficiency and 8.9% vitamin D insufficiency had been reported by the author.

A cross-sectional study, conducted among post-menopausal women from the village of Singur Block, West Bengal, India reported a high vitamin D deficiency in post-menopausal women (Srimani, Saha & Chaudhuri, 2017).

Bawaskar et al., (2017) undertook a hospital-based cross-sectional study on subjects from an OPD of a rural secondary level hospital in Maharashtra, West India and showed 65.4% Vitamin D deficiency (<20 ng/ml) and 23.5% insufficiency in the study population; dark complexion, wearing “Burkha”, inadequate exposure to sunlight, and presence of diabetes were identified as statistically significant predictors of Vitamin D deficiency by the authors.

A community-based cross-sectional study on the urban elderly population (≥60 years) of Hyderabad, South India, reported a high prevalence of vitamin D deficiency which was significantly related to body mass index, metabolic syndrome and hypertension (Suryanarayana et al., 2018).

A prospective observational-study carried out in elderly (>50years of age) subjects of fragility fractures including both genders from Chandigarh, North-west India, reported an overall 74.2% vitamin D deficiency. Female subjects were more deficient than the male subjects, 75.7% of the female subjects were deficient in contrast to 72.4% of male subjects. The authors found 59% of the subjects had inadequate sun exposure (Dadra et al., 2019).

A cross-sectional, community-based study on adults from rural West Bengal, East India documented more than two-thirds of the study population had hypovitaminosis D (Garg et al., 2019).

Dik and Kaur, (2020) undertook a cross-sectional study in adult males and females of the age between 30 to 70 years from Chandigarh, North-west India and found that 28.52% of males and 63.38% of females were vitamin D deficient. Vitamin D deficiency was higher in the oldest age group in comparison to the youngest age group; the authors reported a significant difference in vitamin D deficiency between male and female groups.

A cross-sectional study carried out in healthy athletes of the age group 18 to 45 years from North India showed that 69.9% had vitamin D deficiency, 13.8% had vitamin D insufficiency and only 16.3% had sufficient levels of vitamin D (Gupta et al., 2021).

Nagaraja et al., (2021) undertook a cross-sectional study on 198 female nursing students of a college located in the urban area of Northeast India who was attending the gynaecology outpatient department of a tertiary care centre, and reported 75.3% of the subjects had less than an hour daily exposure to the sun. Out of 198, 126 subjects were tested for vitamin D levels and 95.2% were found out to be vitamin D deficient, 3.2% had vitamin D insufficiency; only 1.6% had sufficient levels of vitamin D.

A hospital-based cross-sectional study carried out in apparently healthy adults of both genders from Bihar, Eastern India, showed 67.2% of subjects were vitamin D deficient, 16.6% were vitamin D insufficient and only 16.2% had normal vitamin D levels. The prevalence of vitamin D deficiency increases with age irrespective of gender. The prevalence of the deficiency was more in females (89%) than in males (79%) subjects (Singh, Mishra & Shekhar, 2021).

A study carried out on subjects (both males and females) from rural Karnataka, South India, reported 75.7% vitamin D deficiency/ insufficiency; with females being significantly more deficient than males (85.5% vs. 64.7%). The highest prevalence (94.3%) of low vitamin D levels was seen in the females ≥75 years of age (Sundarakumar et al., 2021).

A cross-sectional study conducted in perimenopausal women from two districts of Kerala by Vasudevan et al., (2021) showed that 89.1% of the subjects were vitamin D deficient, 9.8% had insufficient vitamin D and only 1.1% had sufficient vitamin D levels. According to the study, the prevalence of deficiency was higher in younger age group, Hindu religion, and middle and upper socioeconomic status. The study showed that Vitamin D deficiency was less common among women who were exposed to sunlight for more than 45 min.

A study carried out in rural Uttarakhand, North India, showed 86% of the subjects had either vitamin D deficiency or insufficiency (Mirza et al., 2022).

Hinduja et al., (2022) undertook a cross-sectional observational study on adult subjects attending a tertiary care hospital in Mumbai, Western India and found that 57% of participants were deficient, 25% had insufficient, and 18% had adequate vitamin D levels. The authors found that upper‑middle‑class participants had a higher prevalence of vitamin D deficiency.

2.7 Vitamin D status of pregnant women and neonates in different parts of India

Vitamin D deficiency across the Indian population is well documented in all age groups and both genders. Several epidemiological studies have reported that women have more vitamin D deficiency. A cross-sectional study carried out on non-pregnant non-lactating women from Delhi, North India, showed that 88% deficiency in the women of reproductive age (20-49 years) (Sofi et al., 2017).

Vitamin D deficiency in females during reproductive age may lead to vitamin D deficiency in pregnancy which can affect the health of the mother-child-dyad.

Osteomalacia in *purda*-wearing north Indian women in the early part of the last century was a well-recognized clinical entity (Teotia & Teotia, 1999). However, by mid-twentieth century, it looked as if osteomalacia in women, and babies with congenital rickets was no longer a clinical problem and interest in vitamin D status in pregnant women waned (Gopalan, & Ramachandran, 2008). In the seventies neonatal hypocalcaemia among Asian immigrants in UK was attributed to poor maternal exposure to sunlight among the immigrants and vitamin D supplementation during pregnancy to the 'at risk' Asian mothers in UK was suggested as the remedy (Brooke et al., 1980). As obstetricians in India did not see osteomalacia and paediatricians did not report hypocalcaemia in neonates, it was assumed that Indians in India did not face these problems.

Later with the availability of technology for vitamin D estimation, several investigators estimated the prevalence of Vitamin D deficiency using plasma vitamin D levels (Hollis, 2005 and Harinarayan et al., 2008). Prevalence of vitamin D deficiency ranged from 40% to 99%; with majority of the study reporting 80% to 90% deficiency (Aparna et al., 2018).

A study carried out by Goswami et al. showed that despite abundant sunlight in Delhi, India healthy adults are deficient in vitamin D. This may be attributed to the pigmentation of the Indian skin and inadequate exposure to the sun. In this study, healthy adults without metabolic bone disease, chronic hepatic & renal disorders, or any other mineral or vitamin deficiency; who were not on any drugs or vitamin/ mineral supplementation or using sunscreen were enrolled. The subjects were from 6 distinct groups- men and women in the physician & the nurses group (assessed both in summer and winter), men in the soldier group (estimated in winter), men and women in the de-pigmented group (estimated in winter), pregnant women with low socioeconomic status (estimated in summer), newborn from the previous pregnant women (estimated in summer). In the physician & nurses' group, there were no changes in the composition of the diet between summer and winter. Energy, carbohydrate, protein and fat intake of the physician & nurses' group, the soldier group and the de-pigmented group, were adequate in comparison to the RDA issued by ICMR. The intake of energy, protein and calcium were significantly low in the pregnant group; the phytate-to-calcium ratio was significantly higher than in other groups. The carbohydrate and fat intake were lower in the pregnant group in comparison to the other groups. Mean 25(OH)D concentration was higher in the soldier group due to the highest exposure to the sunlight, second was the de-pigmented group which can be attributed to the absence of pigmentation, the physician & nurses group came in the third position. There was not much difference in the mean 25(OH)D concentration between the physician & nurses' group and the pregnant group. Cord blood mean concentration of 25(OH)D were significantly lower in the newborn than the pregnant group. A positive correlation was seen between the mother and the newborn in the 25(OH)D concentration and total calcium (Goswami et al., 2000).

Sachan et al. carried out a study to determine the prevalence of vitamin D deficiency and osteomalacia in pregnancy and 25(OH)D concentration in cord blood and to correlate maternal 25(OH)D concentration with sun exposure, daily calcium intake, and intact PTH concentration. Fullterm pregnant women were recruited in Queen Mary's Hospital, King George Medical University, Lucknow, India. The subjects were predominantly from low and middle socio-economic groups, both from nearby urban and rural areas. Total 157 subjects were Hindu and 50 were Muslims. Of the Muslim subjects, 29 women practiced purdah, in which the veil covers the whole body except the hands and the face. The study reported a high prevalence of physiologically significant deficiency of vitamin D in pregnant women as well as their newborns. The prevalence of hypovitaminosis D in the neonates was 95.7%; 84.3% of the urban pregnant women and 83.6% of the rural pregnant women had 25(OH)D concentration below the cutoff. Maternal serum 25(OH)D concentration had a strong positive correlation with the cord blood concentration of 25(OH)D and had a moderate negative correlation with the PTH level of the mother. Sun exposure was significantly higher in the rural subjects in the last trimester of pregnancy;

wherever there was no difference between the maternal 25(OH)D concentration. There was no significant difference in the 25(OH)D concentration, daily calcium intake, or PTH level between the women practising purdah and women who were not practising purdah (Sachan et al., 2005).

A longitudinal study carried out on healthy pregnant women between 20 to 35 years of age, weighing >45 kg, with a normal pregnancy resulting in the birth of term neonates weighing >2.5 kg, at a referral private hospital in Mumbai, western India observed 50% of the mothers were vitamin D deficient, 62% of the cord blood samples collected from these mothers were vitamin D deficient. Out of these neonates, only the exclusively breastfed were followed up at 3 months and 80% of them were vitamin D deficient (Bhalala et al., 2007).

Sahu et al. reported a high prevalence of vitamin D deficiency in pregnant women and adolescent girls from rural India. A cross-sectional study was carried out for 18 months in a rural Indian community; adolescent girls and pregnant women in second trimesters were enrolled. In the study subjects, 88% of the adolescent girls and 74% of the pregnant women were deficient in vitamin D [25(OH)D<50nmol/L]. In a subsample of the adolescent girls, the vitamin D level of 34 brothers was estimated and found that 25(OH)D concentration of the adolescent girls was lower than that of their brothers. The study also reported seasonal variation of the 25(OH)D concentration; the mean 25(OH)D concentration of the girls and the pregnant women was 55.5±19.8 nmol/L in summer which was significantly higher than the concentration in winter i.e. 27.3±12.3 nmol/L (Sahu et al.,2009).

A cross-sectional study on pregnant women in their third trimester who delivered at the Holdsworth Memorial Hospital, Mysore, South India, reported that two-thirds (66%) of the pregnant women were vitamin D deficient (Farrant et al., 2009).

Marwaha et al. reported a high prevalence of vitamin D deficiency in pregnant women, lactating women, and infants. The study was carried out on apparently healthy pregnant women free from any complication, with single intrauterine gestation across trimesters in both summer and winter seasons. The study showed 96.3% of the pregnant women were deficient in vitamin D; 36.8% were mildly deficient [25(OH)D 25-50nmol/l], 41.8% were moderately deficient [25(OH)D 12.5-25nmol/l], 17.7% were severely deficient [25(OH)D <12.5nmol/l]. The concentration of 25(OH)D in pregnant women was lower in winter in the second and the third trimesters; however, there were no significant differences between different trimesters. Intake of energy total calcium and calcium from dairy sources were significantly lower than the RDA issued by ICMR. Vitamin D intake was higher in winter but the difference was not statistically significant. Intake of energy increases with trimesters of pregnancy but the changes were not statistically significant. Data from the mother-infant pairs, re-estimated six weeks postpartum showed 99.7 % of the lactating women and 98.8% of the exclusively breastfed infants were deficient in vitamin D. There was a strong positive correlation on 25(OH)D concentration, ionized calcium and PTH between mother and their infants (Marwaha et al.,2011).

Dasgupta et al., (2012) undertook a study on pregnant women in the 20-40-year age group in their first trimester from North Eastern part of India. Nearly 42% of the pregnant women had vitamin D deficiency and 14% had vitamin D insufficiency.

A cross-sectional study undertaken by Jani et al., (2014), enrolled healthy pregnant women, aged 20-35 years, with singleton pregnancies, in their third trimester (32-36 weeks of gestational age), from two medical centres, a Government hospital (non-affluent subjects) and a private nursing home (affluent subjects) located in Mumbai, Western India. All of the study subjects had 25(OH)D levels <30ng/ml; 94% had vitamin D deficiency and the remaining 6% had insufficiency and no subjects had vitamin D sufficiency. The subjects with vitamin D deficiency had lower sun exposure index. Mothers of neonates with low birth weight had lower vitamin D levels in comparison to the mothers with neonates weighing ≥2.5 kg. Non-affluent pregnant women had lower 25(OH)D levels than their affluent counterpart.

A study carried out on mothers in labour and cord blood from the newborns, reported there was a strong correlation between maternal and newborn vitamin D levels; 70.7% of the mother and 83% of the newborns had low vitamin D levels. Ninety-three percent of the newborns from the mothers with hypovitaminosis D had low vitamin D levels (Kumar et al., 2015).

A study was carried out to assess the prevalence of vitamin D deficiency in burka-wearing pregnant women in Delhi, India. Pregnant women (18-40 years) across all the gestational ages were recruited from the ANC OPD/ward of Kasturba Hospital. The study reported a high prevalence of vitamin D deficiency which was associated with adverse foeto-maternal outcomes; 37.5 % of the subjects were vitamin D deficient, 39% of the subjects had inadequate vitamin D levels and only 23.55 of the subjects had sufficient levels of vitamin D in their body. Pregnant women who had developed preeclampsia (7.5%) were vitamin D deficient. Six percent of the subjects delivered prematurely; out of them 2% had vitamin D deficiency. Babies of 6% of the subjects were admitted to NICU; 2.5% of the mothers were vitamin D deficient. Twelve babies had an APGAR score <7 at 5 min; mothers of 2% of the babies were vitamin D deficient (Ajmani et al.,2016).

Sharma et al. undertook a study on women with primigravida and single live pregnancy, without any chronic disease, enrolled between October 2011 to April 2013 attending the antenatal clinic in Lok Nayak Hospital, Delhi, India. The study reported that 93.5% of the pregnant women were deficient; 34.44% were severely deficient and only 6.45% had adequate vitamin D (Sharma et al.,2016).

Sathis et al. undertook a cross-sectional study on healthy, singleton pregnant women, admitted to the labour ward of the obstetrics and gynaecology department of SRM Medical College Hospital and Research Centre (tertiary care hospital, majorly catering low socioeconomic group), Kanchipuram, South India. The study observed a high prevalence of vitamin D in South Indian pregnant women and in their newborns. Maternal vitamin D deficiency was seen in 57.41% of the subjects, 22.22% of the subjects were insufficient, 5.56% were severely vitamin D deficient and only 14.81% were sufficient in vitamin D. Amongst the newborns 7%, 56%, 20% and 17% were severely deficient, deficient, insufficient and sufficient in vitamin D level respectively. There was a strong positive correlation in vitamin D levels between the pregnant women and their new born. A statistically significant association had been observed between cord blood vitamin D level and birth weight, birth length, head circumference and chest circumference of the newborn (Sathis et al.,2016).

A case-control study carried out in North Indian pregnant women reported that 78% of the subjects were vitamin D deficient (Kumari et al., 2017).

Arora et al. reported a high prevalence of vitamin D deficiency in the mother-child dyad. Pregnant women with singleton pregnancy and free from any systemic diseases were consecutively enrolled for the study when they were admitted to the labour ward of a tertiary care centre in Northern India. Eighty-six percent of the pregnant women were deficient in vitamin D level, 9.5% had insufficiency and only 4.5% of the pregnant women had sufficient levels of vitamin D. The mean maternal calcium level was 8.6±1.2 mg/dl, 9.3±1.1 mg/dl and 10.0±2.7 mg/dl in vitamin D deficient, insufficient and sufficient group consecutively. Twenty-six percent of the pregnant women developed preeclampsia; vitamin D deficiency was higher in those pregnant women who developed preeclampsia in comparison to the pregnant women with normal blood pressure though the difference was not statistically significant. Cesarean section delivery rate was higher in women with vitamin D deficiency/ insufficiency. Nine percent of the pregnant women underwent cesarean section delivery out of them 92% were vitamin D deficient and 6% were vitamin D insufficient. 85.6% of the pregnant women were deficient and 10.8% of the pregnant women were sufficient in vitamin D that underwent normal vaginal delivery. This difference was statistically significant. The study reported there was a strong positive correlation between maternal serum 25(OH)D level and cord blood 25(OH)D level in their newborns. In cord blood, 85%, 11.5% and 3.5% were deficient, insufficient and sufficient in vitamin D levels. Mothers who had hypovitaminosis D had no cord blood sufficient in vitamin D level. The mean birth weight of the newborns was 2.7(0.5) kg, 2.9(0.5) kg and 3.0(0.5) kg of the mothers with vitamin D deficiency, insufficiency and sufficiency consecutively. A significant association was observed between maternal vitamin D deficiency and low birth weight of the baby; mothers of low birth weight babies were 94% deficient and 5.3% insufficient in vitamin D level whereas mothers of babies with birth weight >2.5 kg had 80.5% deficient, 12.2% insufficient and 7.3% sufficient level of vitamin D (Arora et al.,2018).

A prospective study undertaken on pregnant women of gestational age <16 weeks with singleton pregnancy an attending antenatal clinic of Shillong, Meghalaya, East India, observed a high prevalence of vitamin D deficiency/ insufficiency in the eastern region of India which was associated with preeclampsia, low birth weight and cesarean delivery. The authors reported 84.18% of vitamin D deficiency and 12.44% of vitamin D insufficiency in pregnancy (Sharma, Nath & Mohammad, 2019).

Sharma, Minhas & Shrama, (2021) undertook a prospective observational study on singleton apparently healthy pregnant women in their second and third trimesters (gestational age >16weeks) attending an OPD in Himachal Pradesh, North India observed a very high prevalence of vitamin D deficiency/ insufficiency in the study population (91.6%); 29.24% deficiency (<20ng/ml), 62.26% insufficiency (<32ng/ml) and only 8.4% had sufficient level of vitamin D (>32ng/ml).

Data from a cross-sectional study undertaken in Chennai, Tamil Nadu, South India, on singleton, non-smoker pregnant women between 20-40 years of age during 6-38 weeks gestational age showed vitamin D deficiency level is highest in the first trimester and gradually the deficiency level reduces throughout the second and third trimesters of pregnancy. The mean 25(OH)D level was lowest in the first trimester and then gradually increased in second and third trimester. The reason behind the low level of vitamin D in the first trimester of pregnancy has been attributed organogenesis and after the formation of the placenta, the level of vitamin D gradually increases (Christy, Perumal & Sumathy, 2021).

Another study by Hemlatha (2021) on pregnant women attending antennal OPD at a medical college in Telangana, India, showed a high prevalence of vitamin D deficiency in pregnancy. More than 90% of the subjects were either vitamin D deficient or insufficient (62.7% deficient and 28.2% insufficient) and only 9.1% had normal of vitamin D levels.

A prospective cohort study conducted on adult women, aged between 18 to 45 years with singleton pregnancy at term (37 to 40 completed weeks), attending antenatal ward, labour room of Obstetrics and Gynaecology Department, Assam Medical College and Hospital, Dibrugarh, Assam, North East India had shown a high prevalence of vitamin D deficiency, 61.43% of the study population was vitamin D deficient, 22.86% had insufficient and only 15.71% had a sufficient level of vitamin D. Authors had reported positive correlation between maternal vitamin D level with the birthweight, birth length, head & chest circumference of the newborn, cord blood vitamin D level and other perinatal outcomes like Neonatal Intensive Care Unit admission and Respiratory Distress Syndrome (Sonowal et al., 2021).

A cross-sectional comparative study, carried out on 100 pregnant women with pre-eclampsia in labour and 100 normotensive pregnant women in labor in the Department of Obstetrics and Gynaecology, Dr Rajendra Prasad Government Medical College in Kangra, Himachal Pradesh, observed vitamin D level of the pregnant women with pre-eclampsia was significantly lower than the normotensive pregnant women. The study reported that none of the pregnant women having pre-eclampsia had vitamin D sufficiency whereas 27% of the normotensive pregnant women had sufficient vitamin D levels; 97% of the pre-eclamptic group was vitamin D deficient and only one-fourth of the normotensive women had vitamin D deficiency. The mean 25(OH)D level was 8.87±4.66 ng/ml and 25.83±7.07 ng/ml in the pre-eclamptic and normotensive pregnant women groups respectively; this difference was highly significant. Mean cord blood level of vitamin D and the level of the same in the newborn were significantly lower in the pregnant women with pre-eclampsia than of the normal pregnant women; the number of vitamin D deficient neonates was also higher in the mothers with pre-eclampsia (Karpa et al., 2022).

A cross-sectional study carried out in healthy pregnant women, aged 20-35 years, from Chennai, Tamil Nadu, South India, reported, that 62% of study group pregnant women had hypovitaminosis D (25(OH) D level <20 ng/mL) and 38% of the pregnant women had 25(OH) D level >20 ng/mL. Less physical activity, decreased sun exposure, skin complexion, low socioeconomic status, and lack of awareness were the major risk factors associated with hypovitaminosis D in the study population by the author (Ravinder et al., 2022).

Data from these studies indicate that biochemical deficiency is common in both south and north India. Studies carried out in Lucknow have shown very high levels of vitamin D deficiency in pregnant women (Sachan et al.,2005); vitamin D deficiency as defined by low circulating 25(OH)D concentrations is common during infancy (Agarwal et al., 2002; Pettifor, 2008; Balasubramanian & Ganesh, 2008, Jain et al., 2011 and Chacham et al., 2020) and childhood (Marwaha et al., 2005; Dhillon et al., 2015; Sharawat, & Dawman, 2019; Joshi & Bhatia, 2014; Puri et al, 2008; Chowdhury et al, 2017; Kapil et al., 2017; Basu et al., 2015; Garg et al., 2014; Angurana et al., 2014; Tiwari & Puliyel, 2004; Balasubramanian et al., 2003 and Ekbote et al., 2010).

However, it is not possible to compare the findings of these studies because of the methodological, geographical and seasonal differences amongst these studies and all of these factors individually can impact the vitamin D level. Along with these factors, there is controversy regarding the normal vitamin D level in pregnancy which also makes it difficult to bring all the results from the studies into line. The Institute of Medicine (2011) has suggested 20 ng/ ml to be the normal level whereas the Endocrine Society (2011) recommended >30 ng/ ml to be the normal level of vitamin D in pregnancy. On the basis of the data from a study carried out by Luxwolda et al., (2012) on African tribal pregnant women who achieved the level of 60 ng/ml serum vitamin D concentration and the non-pregnant women from the same tribe had the level of 46 ng/ml serum vitamin D concentration, Hollis & Wagner, (2013) had suggested that a higher concentration of vitamin D to be maintained during pregnancy. Harinarayan, (2014) suggested vitamin D concentration of >30 ng/ml is to be considered normal, however, had emphasized on “population based reference value” and “functional health based reference value” to avoid the confounding factor in assessing vitamin D deficiency.

2.8 Importance/ role of calcium and vitamin D (on mother-child dyad)

It is well known that the pregnancy period is one of the most demanding phases of human life from the nutritional point of view. Nutrients play important role in the optimum growth of the unborn child and in maintaining the nutritional status of the mother.

Calcium and vitamin D are two nutrients which are predominantly required for the bone formation of the growing foetus and for maintaining maternal bone health along with other activities (Gopalan, 2007). Vitamin D maintains the level of calcium in the bloodstream, maintaining the muscle strength, 1,25-dihydroxy vitamin D (active form of vitamin D) bind to different receptor proteins and controls the activity like insulin secretion, PTH hormone secretion, operation of the immune system, development of the reproductive system and skin (Harinarayan, 2014). Calcium helps in tooth formation, blood clotting, contraction of muscle, regulation of heartbeat, activation of enzymes, sending nerve signals etc. (Das, 2009 & Park, 2007).

Approximately 30 gm of calcium transfers from the mother to the foetus during the last trimester of pregnancy, two third of the foetal calcium transfers after 30th weeks of gestation at a rate of 300mg per day (Srilakshmi, 2012). Vitamin D is very essential to increase maternal calcium absorption and plays an important role in calcium metabolism of the foetus. Vitamin D deficiency causes hypocalcaemia in the infants (Srilakshmi, 2012).

Calcium supplementation reduces the risk of pre-eclampsia, and pregnancy induced hypertension, maternal calcium deficiency may affect the cardiovascular development of the foetus and predispose the newborn to the risk of high blood pressure (BP); maternal calcium deficiency may affect the health of the children in different ways like increased body fat percentage, elevated triglyceride and insulin resistance (Christian et al., 2010).

Bone mineral density of the foetus and the newborn is affected by the level of maternal calcium. A study carried out on calcium deficient mothers; a group of mothers with low calcium levels were given calcium supplements and another group of mothers with low calcium levels were given placebos; the infants of the mothers who received the calcium supplements had higher bone mineral composition than that of the infants from the mother received placebos (Specker, 2004).

Foetal vitamin D concentration is determined by the maternal vitamin D concentration (Ramji, 2016). Maternal vitamin D deficiency may lead to less muscle mass and insulin resistance in the foetus and infants (Krishnaveni et al., 2011). Intrauterine exposure of the foetus to vitamin D deficiency may adversely affect the bone development and innate immunity function in childhood; infants born severely vitamin D deficient mothers may develop tetany due to severe neonatal hypocalcaemia (Harinarayan, 2014).

2.9 Impact of calcium and vitamin D deficiency on mother-child dyad

In maintaining the optimum growth of the foetus and maternal nutritional status, during pregnancy sound nutrition plays the most important role.

During pregnancy requirement of different nutrients increases. Calcium is one of them; approximately 30gm of calcium is deposited in the foetal skeleton by the end of the pregnancy. During the third trimester, 250 to 350 gm calcium is transported from the mother to the foetus per day (Kovacs & Kronenberg, 1997; Prentice, 2003 and Ryan et al., 1988).

Deficiency of calcium may affect both maternal and foetal wellbeing. Reports are available on the impact of calcium supplementation in pregnancy, to avoid the negative consequences of calcium deficiency both on the mother and the child.

Various studies have shown there is an inverse relationship between pregnancy-induced hypertension and calcium intake (Belizán & Villar, 1980). PIH complicates the course of pregnancy and leads to preterm delivery (Ye et al., 2010), stillbirth and neonatal mortality (Ananth & Basso, 2010). A meta-analysis of studies carried out in 10 developing countries has shown a reduction in PIH, pre-eclampsia and related complications like preterm delivery and neonatal mortality with calcium supplementation during pregnancy (Imdad et al.,2011). A study carried out on 524 healthy primi-gravidas, with low calcium intake, in North India, has reported calcium supplementation during pregnancy has reduced the risk of pre-eclampsia (Kumar et al., 2009). A study from a South Indian coastal area reported significantly low maternal serum calcium levels in pregnant women with pre-eclampsia; and calcium supplementation may reduce the risk of pre-eclampsia especially in those with poor nutrition (Kanagal et al., 2014). A supplementation study conducted by WHO on pregnant women with low calcium intake (<600mg/day) reported that calcium supplementation reduced the relative risk of severe gestational hypertension and eclampsia (Villar et al., 2006). A Cochrane review of 13 trials on pregnant women reported calcium supplementation was beneficial in reducing the average risk of preeclampsia and consuming 1000mg extra calcium as supplements was helpful for the pregnant women consuming lower calcium (<900mg/day). The risk of developing PIH may also be reduced with calcium supplementation, especially for those pregnant women with low calcium intake (Hofmeyr et al., 2018). Pooled analysis from 15 randomized control trials had shown calcium supplementation during pregnancy is associated with reducing gestational hypertensive disorder and pre-term birth; and increases birth weight (Imdad and Bhutta, 2012). Another study reported maternal bone turnover was found to be greater in pregnant women with preeclampsia. This indicates that to preserve maternal bone health, calcium supplementation in pregnancy with preeclampsia is necessary (Kumar et al., 2012).

The calcium supplementation study carried out by WHO on pregnant women with low calcium intake reported that with 1000mg calcium supplementation, the risk of preterm delivery and maternal and neonatal morbidity was reduced (Villar et al., 2006). Previously mentioned Cochrane review also reported similar findings of reduction in preterm delivery with 1000mg calcium supplementation, in pregnant women routinely consuming low calcium (Hofmeyr et al., 2018). Kumar et al., (2009) and Imdad and Bhutta, (2012) also reported a reduction in the risk of preterm birth with calcium supplementation.

A study carried out on Mexican pregnant women reported, that calcium supplementation of 1200mg/day is associated with a reduction in the resorption of calcium from the maternal skeleton thus reducing skeletal bone turnover in the third trimester of pregnancy (Janakiraman et al., 2003). Another study indicated that 1000mg calcium supplementation in multiparous women with habitual low calcium intake may reduce pregnancy-induced bone degradation and reduce the stress on calcium homeostasis during pregnancy (Laboissiereet al., 2000).

The foetal requirement of calcium is met by maternal transfer to the foetus. Some observational studies have reported a positive relationship between maternal dietary intake of calcium and bone outcomes of the foetus and child. An increase in maternal dietary calcium in terms of dairy items is beneficial for maternal bone mass and foetal bone development (Chang et al. 2003). Optimal calcium intake and vitamin D status of the mother is important for foetal skeletal development; increasing calcium intake during pregnancy may improve foetal skeletal development (Young et al., 2012). A study from Pune, India had reported Children of mothers who had a higher frequency of intake of calcium-rich foods during pregnancy had higher bone mineral content and bone mineral density (Ganpule et al., 2006).

Supplementation studies reported that calcium supplementation during pregnancy was positively associated with the bone mineral content and bone mineral density of the infant (Raman et al., 1978); the positive impact of calcium supplementation during pregnancy was observed in pregnant women with basal low calcium intake (Koo et al., 1999).

Calcium plays an important role during pregnancy; during intrauterine life, the skeletal development of the foetus is determined by the maternal calcium consumption and the development during this period impacts the growth in childhood and the bone health throughout the life span. Thus, adequate calcium consumption during pregnancy is very important and the benefit of the calcium supplementation is specifically observed in those with habitual low calcium intake.

Bone formation of the growing foetus and maintaining maternal bone health, calcium and vitamin D are two important nutrients (Gopalan, 2007). Approximately 30 gm of calcium is transferred from the mother to the foetal skeleton in the third trimester of pregnancy (Srilakshmi, 2012). Vitamin D is required for calcium absorption. The intestinal calcium absorption reduces to 10 to 15% whereas in vitamin D sufficient states calcium absorption is 30 to 80% (Misra et al., 2008). Hypovitaminosis D in pregnancy affects both maternal and foetal bone health as foetal vitamin D status is dependent on that of the mother; and affects the innate immunity function in childhood; infants born severely vitamin D deficient mothers may develop tetany due to severe neonatal hypocalcaemia (Harinarayan, 2014).

Systemic review and meta-analysis carried out by Aghajafari et al. (2013) and Wei et al. (2013) reported that vitamin D deficiency during pregnancy had adverse maternal and neonatal outcomes; like increased risk of gestational diabetes (GDM), pre-eclampsia, small for gestational age (SGA) and low birth weight (LBW) infants. Another review of available observational and interventional studies had also shown similar adverse effects of low maternal vitamin D levels during pregnancy on maternal and neonatal outcomes and found primarily preeclampsia, GDM, low birth weight and preterm births are the most common adverse effects that are predominantly reported along with several other impacts for which further research is required (Agarwal et al., 2018).

Studies reported low levels of serum 25(OH)D in pregnant women who developed preeclampsia later in the pregnancy and concluded hypovitaminosis D was an independent factor responsible for the development of pre-eclampsia during pregnancy (Bodnar et al., 2007, Baker et al., 2010 and Sing et al., 2016). Robinson et al. (2010) reported pregnant women who developed severe pre-eclampsia before 34 weeks of gestational age had lower vitamin D; in a subsequent study, Robinson et al. (2011) reported pregnant women with SGA in early-onset severe pre-eclampsia had significantly lower vitamin D level than that of women with only EOSPE without foetal growth retardation. Another case-control study reported that both, serum calcium and vitamin D were low in the pregnant women with PIH; thus the researcher suggested to increase low-fat dairy products, fruits and vegetables along with sufficient sun exposure during pregnancy to prevent PIH and promote better maternal health and foetal growth (Sharma et al., 2014). A case-control study from India on pregnant women showed that hypovitaminosis D is high in Indian pregnant women; and the pregnant women with pre-eclampsia had significantly lower vitamin D levels than the control group (Singla et al., 2015). A comparative study carried out in Himachal Pradesh reported, that vitamin D and calcium levels were significantly lowered in women with pre-eclampsia as compared to those of the normotensive pregnant women; 100% of the pregnant women with pre-eclampsia in the study population were either vitamin D deficient or had insufficient level of the same whereas 73% the normotensive pregnant women were vitamin D deficient/ insufficient (Karpa et al., 2022).

Vitamin D deficiency during pregnancy is related to insulin resistance (Maghbooli et al., 2008). A case-control study carried out in North India on 274 pregnant women reported 78% of the subjects were vitamin D deficient; mean serum vitamin D was lower in women with gestational diabetes and women with pre-eclampsia and thus the deficiency of vitamin D had been reported as a factor associated with an elevated risk of GDM and pre-eclampsia in pregnancy by the researcher (Kumari et al., 2017). Maternal 25-hydroxyvitamin D level was identified to be inversely proportional to the risk of developing GDM by several researchers (Clifton-Bligh et al., 2008, Zhang et al., 2008 and 2018). A cohort study carried out in the Middle East reported maternal vitamin D deficiency is significantly associated with an increased risk of GDM, anaemia and pe-eclampsia (Bener et al., 2013).

A study showed that vitamin D deficiency may increase the risk of cesarean section (C-sec) (Merewood et al., 2009 and Hubeish et al., 2018). Another recent Swedish prospective population-based cohort study reported that vitamin D deficiency in late pregnancy was associated with doubled odds of birth asphyxia and emergency cesarean deliveries (Augustin et al., 2020).

Maternal vitamin D status is associated with foetal growth; the risk of SGA (Small for Gestational Age) increases with maternal vitamin D deficiency (Gernand et al., 2014). Maternal vitamin D deficiency is an independent factor associated with elevated risk of LBW and SGA in term infants (Wang et al., 2018 and Chen et al., 2017). A study carried out in North India reported a high prevalence of maternal vitamin D deficiency which was associated with pre-eclampsia, increased rate of caesarean delivery and LBW (Arora et al., 2018). A systemic review and meta-analysis reported that maternal vitamin D deficiency in pregnancy increases the risk of low birth weight infants (Fang et al., 2021).

Maternal vitamin D levels have been correlated with the neonatal vitamin D level, maternal vitamin D deficiency increases the risk of vitamin D deficiency in the neonates (Bowyer et al., 2009 and Thomas et al., 2011).

Maternal vitamin D deficiency is associated with neonatal vitamin D deficiency which is the major cause of hypocalcaemic seizures in neonates; infants born to mothers with hypovitaminosis D are at higher risk of developing hypocalcaemic seizures (Mehrotra et al., 2010). Maternal severe vitamin D deficiency poses the infant at the risk of developing tetany due to severe hypocalcaemia and may manifest craniotabes, a condition in which thinning of the skull is observed (Harinarayan, 2014). Maternal vitamin D deficiency or insufficiency increases the risk of neonatal late-onset hypocalcemia (Do et al., 2014).

Maternal vitamin D deficiency is associated with impaired foetal growth and skeletal development (Mahon et al., 2010 and Robinson et al., 2011). A systemic review reported that maternal vitamin D deficiency leads to adverse pregnancy outcomes like SGA and LBW infants (Aghajafari et al., 2013). A systemic review by Pérez-López et al., (2015) reported vitamin D supplementation during pregnancy increased circulating 25(OH)D levels, birth weight, and birth length of the offspring. Maternal vitamin D deficiency is prevalent and intrauterine exposure to low vitamin D levels leads to reduced bone mineral accumulation in the offspring in childhood (Javaid et al., 2006). Similarly, Viljakainen et al., (2010) reported intrauterine bone mineral accrual and bone size are affected by maternal vitamin D deficiency; bone mineral content (BMC) of the infants born to mothers with low vitamin D was lower (Viljakainen et al., 2011). A recent prospective cohort study from North East India reported maternal vitamin D deficiency leads to adverse skeletal growth of the newborn, fetal femur length and birth length were significantly shorter in mothers with low vitamin D (Sarma et al., 2018). Recently, some studies have demonstrated a complex interplay between vitamin D and the placenta to ensure that they can both play optimal roles in supporting fetal growth and maternal adaptations to pregnancy (Ashley et al., 2022, Ganguly et al., 2018 and Hollis & Wagner, 2017). Vitamin D plays an important role in maintaining the health of the placenta and reducing the chance of placental inflammation and infection during pregnancy (Shin et al., 2010).

Studies reported maternal vitamin D is important for foetal lung development (Ramji, 2016). Low cord blood level of 25 hydroxyvitamin D is associated with a risk of respiratory infection and childhood wheezing (Camargo et al., 2011). Maternal vitamin D deficiency increases the risk of neonatal hypovitaminosis D which in turn is associated with an increased risk of RSV (Respiratory Syncytial Virus) LRTI (Lower Respiratory

Tract infection) in the first year of life (Belderbos et al., 2011). Another study reported, all of the pre-term study-infants had low vitamin D levels and respiratory distress syndrome was more common in severely vitamin D-deficient pre-terms in comparison to those with mild or moderate vitamin D deficiency (Ataseven et al., 2013). A meta-analysis by Zang et al., (2022) reported vitamin D deficiency is very likely to be a high-risk factor for NRDS (Neonatal Respiratory Distress Syndrome). A birth cohort study carried out by Hart et al., (2015) reported, that maternal vitamin D deficiency during pregnancy was associated with impaired lung development in 6-year-old offspring, neurocognitive difficulties at age 10, increased risk of eating disorders in adolescence, and lower peak bone mass at 20 years; vitamin D may have an important, multifaceted role in the development of fetal lungs, brain, and bone.

In consideration of the foregoing, this is apparent that there have been reports linking low vitamin D levels to pregnancy-induced hypertension, gestational diabetes, poor intrauterine growth, and preterm births; however, these associations might not be causally related to vitamin D deficiency (Roth et al., 2018) and need further investigation (Cross et al., 1995, Abrams, 2007, Holick et al., 2011 and Hollis & Wagner, 2017).

2.10 Vitamin D and/ or calcium supplementation during pregnancy

Rickets and osteomalacia are characterized pathophysiologically by a failure of normal mineralization of bone and epiphyseal cartilage and clinically by skeletal deformity. Rickets are commonly seen in children while osteomalacia is common in adults. Vitamin D and/or calcium deficiency possess the risk of developing these two (Steinbock, 1993).

Rickets is one of the oldest diseases. Reference of rickets are found as early as 300 BC.; later, a more specific description can be seen seventh and eighth centuries A.D., and Chien-i, the Father of Chinese paediatrics, described many cases of rickets in the tenth century (Lee, 1940). The references of rickets were found in the first and second centuries when the Greek physicians Soranus of Ephesus and Claudius Galenus reported observations of a bone deformity similar to those associated with rickets in Roman children (WHO, 2019). English physician, Dr Daniel Whistler, described rickets in his thesis for the degree of M.D. in the year1645 before the year 1650 in which a more detailed description was published by Francis Glisson (Cone, 1980). The term “Rickets” was first coined in the year of 1634 (Steinbock, 1993). In the late 18th century and the beginning of the 19th century, cases of rickets increased in England and later in other European countries and in the United States of America (USA), simultaneously with the Industrial Revolution and in the 20th Century it became endemic, particularly in the industrialized cities of northern Europe. In the 1800s, physicians and scientists observed inadequate sun exposure was related to an increase in the cases, as rickets were more common in urban areas, extreme latitudes and seasonal variation was observed. During this period only the deficiency of calcium also was found to be related to the condition. Later, McCollum and colleagues identified vitamin D as the anti-rachitic substance which was necessary from the prevention and treatment point of view. By this time, it was known that vitamin D is necessary for absorption and utilization of calcium (WHO, 2019, McCollum et al, 1922, McCollum et al, 1925 and McCollum, 1957).

In the last few years cases of vitamin D deficiency have been observed to be increasing in UK (Belton, 1986, Pal & Shaw, 2001 and Ashraf & Mughal, 2002), Europe (Dagnelie et al., 1990, Garabedian & Ben-Mekhbi, 1989, Park et al., 1987, Benichou, Sallière & Labrune, 1985, Hellebostad, Markestad & Seeger Halvorsen,1985, Freycon et al., 1983, Pedersen, Michaelsen & Mølgaard, 2003, Bonet Alcaina et al., 2002 and López Segura, Bonet Alcaina & García Algar, 2002) and North America (Feldman, Marcuse & Springer, 1990, Kruger, Lyne & Kleerekoper, 1987, Hayward, Stein & Gibson, 1987, Haworth & Dilling, 1986 and Bachrach, Fisher & Parks, 1979) in a variety of ethnic group, specifically in the dark-skinned or Asian population. The wheat being the staple food, the high phytate content of the bread was held responsible for the vitamin D deficiency in the Asian immigrants (Reinhold, 1976 and Shany, Hirsh & Berlyne, 1976).

In the seventies neonatal hypocalcaemia among Asian immigrants in UK was attributed to poor maternal exposure to sunlight among the immigrants and vitamin D supplementation during pregnancy to the ‘at risk’ Asian mothers in UK was suggested as the remedy (Hodgkin et al., 1973 and Brook et al., 1980). Data from these studies implied that Indians/ Asians do not face the problem of vitamin D deficiency in India but due to lower sun exposure and inadequate diet in Britain was responsible for the vitamin D deficiency of these Asian immigrants. Thus, Asian pregnant women, living in Britain, were suggested to be supplemented with 1000 IU vitamin D. However, it was documented in the UK Government report and other researchers, that rickets, osteomalacia and vitamin D deficiency were present in India even after being a tropical country (Rickets and osteomalacia, 1980 and rickets in India, 1922). Inadequate exposure to sunlight along with calcium deficiency is the cause behind (Uday & Högler, 2019). Initially, only vitamin D deficiency was thought to be the cause of rickets and osteomalacia which is aggravated in the presence of calcium deficiency but later it was found that only nutritional deficiency of calcium is potent enough to lead to the conditions (Thacher et al., 1999). Calcium deficiency can be observed in Asian (Balasubramanian et al., 2003 and Fischer et al., 1999) and African (Thacher et al., 2012) countries. An increased number of cases with vitamin D deficiency are being reported from across the world (Hilger et al., 2014), mostly from Europe and Asia followed by mild prevalence in North and South America, and Oceania (Cashman, 2022). Vitamin D deficiency is surging in developed countries (Robinson et al., 2006, Wheeler et al., 2015, Munns et al., 2012, Beck-Nielsen et al., 2009, Amrein et al., 2020) mainly due to a lack of sun exposure (Cashman et al., 2016), lack of food fortification (Hayes & Cashman, 2017), ineffective supplementation programmes (Uday et al., 2017) and global immigration (Thacher et al., 2016). Inadequate dietary calcium intake can readily be reversed by increasing calcium-rich foods but it is not the case in vitamin D deficiency. To acquire vitamin D sun exposure is the most physiologically relevant and effective way which in turn can be affected by various factors like skin colour, clothing, altitude, season, excessive use of sunscreen, sun avoidance and repeated unplanned, unspaced pregnancy (Harinarayan, 2014). These are the factors responsible for the increasing cases of vitamin D deficiency in tropical countries like India where an abundance of sunshine is present (G and Gupta, 2014).

Maternal calcium and vitamin D deficiency pose a risk on both the mother and the unborn child which in turn may affect the well-being of the child in the long run. Thus, curing maternal deficiencies is very important. There are several reports available from all over the world on calcium and vitamin D supplementation during pregnancy to avoid the adverse consequences on the mother-child dyad. Previously undertaken randomized control trials on vitamin D supplementation were of short duration of 3 to 4 months whereas the more recent data reports the efficacy and safety of supplementing 4000 IU vitamin D supplementation daily for a duration of 6 months in pregnancy (Mithal & Kalra, 2014). A randomized controlled trial on singleton pregnant women demonstrated vitamin D supplementation during pregnancy decreased complications of pregnancy like PIH and cesarean section delivery though the study did not find any correlation between maternal supplementation and the birth weight. The subjects of the study received 400, 2000 or 4000 IU vitamin D3/day from 12–16 weeks onwards till delivery and no adverse effect related to the high dose of vitamin D supplementation was observed, thus the author concluded that 4000 IU vitamin D_3 supplementation in pregnancy is safe and the most effective way to correct maternal vitamin D deficiency/ insufficiency and impart wellbeing to the mother-child dyad (Hollis et al., 2011). Similarly, another study on pregnant women from Arab, also reported that the 4000 IU vitamin D3 supplementation during pregnancy was the most effective way to improve maternal vitamin D level without any adverse effect (Dawodu et al., 2013). A study from New Zealand reported a similar finding that maternal supplementation with 1000/ 2000 IU vitamin D and 400/ 800 IU in infancy respectively was effective in improving the vitamin D levels in infants (Grant et al., 2014). In view of the high prevalence of vitamin D deficiency, The International Federation of Gynecology and Obstetrics, (2015) recommended 400 IU of vitamin D supplementation along with dietary vitamin D consumption to a total consumption of 1,000–2,000 IU/day along with adequate sun exposure. The Maternal Vitamin D Osteoporosis Study (MAVIDOS) was a multicentre, double-blind, randomised, placebo-controlled trial undertaken in UK had observed that maternal supplementation of 1000 IU vitamin D was able to cure vitamin D deficiency in pregnancy and is safe (Cooper et al., 2016).

In the year 2020, WHO antenatal care recommendations for a positive pregnancy experience Nutritional interventions update: Vitamin D supplements during pregnancy was published and regarding vitamin D supplementation WHO suggested that not all pregnant women be supplemented with vitamin D for better maternal and perinatal outcome though all the pregnant women must be encouraged for adequate sun exposure to synthesize the required amount of vitamin D in the body and in places where sun exposure is limited and/ or prevalence of vitamin D deficiency during pregnancy is high, 200 IU of vitamin D is to be given as oral supplementation on a daily basis (WHO, 2020).

Evidence from a Cochrane review (Palacios, Kostiuk & Peña-Rosas, 2019) which included 30 RCTs from all over the world most of which were from the low-middle-socioeconomic countries like- India, China, Bangladesh, Brazil, the Islamic Republic of Iran & Pakistan; and the remaining 8 from the high-income countries like Australia, France, New Zealand, the Russian Federation and the United Kingdom had been used to draw the guideline by WHO (2020). Three types of RCTs were included; vitamin D versus no vitamin D (or placebo) (22 trials), vitamin D + calcium versus no vitamin D + calcium (or placebo) (9 trials) and vitamin D + calcium + other micronutrients versus calcium + other micronutrients (one trial) supplementations were given to pregnant women. WHO guideline methodologists revised the groups into two groups namely, Comparison 1: Oral vitamin D supplement versus no vitamin D (placebo or no supplement); and Comparison 2: Oral vitamin D + calcium supplement versus no vitamin D (placebo or no supplement) + calcium. Vitamin D supplements compared with no vitamin D supplements are that vitamin D supplements may reduce the risk of pre-eclampsia & GDM; however, the evidence is of low certainty and probably makes little or no difference to the risk of caesarean section, maternal mortality, risk of preterm birth or stillbirth. vitamin D plus calcium supplements compared with no vitamin D plus calcium also suggests, with low certainty, that vitamin D plus calcium supplements may reduce the risk of pre-eclampsia; evidence on the effect of vitamin D plus calcium on GDM, low birthweight and neonatal mortality is of very low certainty and has little or no effect on caesarean section rates (WHO, 2020).

Marya, Rathee & Manrow, (1987) demonstrated that 1200 IU/ day of vitamin D with 375 mg/ day calcium supplementation in second trimester of pregnancy onwards was able to reduce the blood pressure of pregnant subjects in the third trimester when compared to the non-supplemented group. In a previous study, 1200 U/ day vitamin D supplementation throughout the third trimester was observed to be associated with increased foetal birthweight. The same study also showed a high dose of vitamin D supplementation (600,000 U) in the 7th and 8th month of pregnancy was more effective (Marya et al., 1981). Data from another study suggest that supplementation of 60,000 IU vitamin D_3 in the 6th and 7th month was associated with improved placenta growth with intern accelerated fetal growth and improved birthweight (Kaur et al., 1991). Sahu et al., (2009) undertook a supplementation study on rural pregnant women and supplemented with either 60 000 U in the fifth month or 120 000 U each in the 5th and 7th months of pregnancy and reported the higher dose was effective in raising maternal 25(OH)D level without any adverse effect. Another more recent study on pregnant women in the second trimester who were given either one oral dose of 1500 µg (60,000 IU) vitamin D3 or two doses of 3000 µg (120,000 IU) vitamin D3 each in the second and third trimesters had observed a beneficial effect of the supplementation on infant anthropometry, the larger dose was able to improve maternal 25(OH)D level (Kalra et al., 2012). A study carried out in primigravida pregnant women reported supplementation with 60,000 IU vitamin D, every fortnight from 28 to 36 weeks of gestational age was effective in reducing the risk of preeclampsia by increasing the therapeutic effectiveness of calcium supplementation in pregnant women (Singla et al., 2012). A recent randomized controlled trial on maternal vitamin D supplementation compared 1000 IU daily, 30,000 IU monthly, 2000 IU, 60,000 IU monthly and concluded vitamin D supplementation with 2000 IU/day or 60,000 IU/month is the effective and safe way to attain vitamin D sufficiency in pregnant women (Mir et al., 2016).

In India, most of the supplementation studies have shown higher dose of vitamin D (60,0000 IU) weekly along with 1000 mg elemental calcium is safe and effective in correcting vitamin D deficiency. Available evidences lead to the fact that a loading dose is required to improve the vitamin D level, particularly ‘at risk’ group and sustained long-term fortification/ supplementation is required (Harinarayan, 2014). As vitamin D and calcium are two micronutrients whose actions are intertwined, supplementation of both should go hand in hand to get the overall health benefits. With regard to calcium supplementation, WHO, 2018 recommended 1.5-2 gm of oral calcium to be given as supplements to pregnant women with low dietary calcium intake from 20 weeks of pregnancy till delivery, to reduce the risk of pre-eclampsia.

2.11 National Guideline laid by Government of India

Pregnancy is the physiological condition when woman develops a foetus and supports its growth for 40 weeks in the uterus. Maternal nutritional status is very important in this stage as it determines the nutritional status of the growing foetus as well. During pregnancy nutritional requirements increase as the woman has to support both, her own and the foetal requirements; calcium is one of such nutrients, the requirement of which increases during pregnancy. There are several reports on low calcium intake during pregnancy and high prevalence of biochemical vitamin D deficiency; maternal deficiency of vitamin D and low level of calcium consumption has adverse effects on the mother-child dyad.

As the demand of calcium increases during pregnancy, vitamin D sufficiency becomes increasingly important for the best outcomes for the mother and foetus. Numerous prenatal health issues, including small stature, newborn hypocalcaemia and seizures, impaired growth, skeletal issues such as rickets, and low BMD are associated with low vitamin D levels. Numerous maternal health issues, like preeclampsia, premature labour, and an increased caesarean section rate, are associated with low levels of vitamin D (Maladkar, Sankar & Kamat 2015).

Given the high prevalence of biochemical vitamin D deficiency, low calcium intake, and known adverse consequences of poor vitamin D status on the mother-child dyad, calcium and vitamin D supplementation during pregnancy has been advocated. Studies from UK had reported a reduction in neonatal tetany following calcium and vitamin D supplementation during pregnancy (Brooke et al., 1980). As discussed earlier, there have been reports suggesting that calcium and vitamin D supplementation may reduce the prevalence of Pregnancy induced hypertension. The Government of India laid down the National Guidelines for “Calcium Supplementation During Pregnancy and Lactation” under the Maternal Health Division, Ministry of Health & Family Welfare in December 2014 (MOHFW, 2014). According to the guidelines pregnant women are to be supplied with calcium supplementation starting from 14weeks of gestational age till six months postpartum. Two oral swallowable tablets containing 500 mg elemental calcium (as calcium carbonate salt) and 250 IU vitamin D are to be taken twice daily just after meal. IFA tablets are not to be taken simultaneously with calcium tablets but should be taken at least 2 hours after meals for better absorption of both the supplements. Along with the supplementations the pregnant women are to be given basic nutrition and health education regarding the importance of calcium and vitamin D supplementation, the protocols to be followed during consuming the supplements; are to be counseled regarding consumption of calcium-rich foods, proper sun exposure and reassured regarding any of the side effects they face during consumption of the calcium supplements.