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Original Article

Prevalence of Vitamin D Deficiency among Kashmiri Pregnant Females and its Impact on Maternal Outcome

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Abstract

Background: Vitamin D is a fat-soluble vitamin that is naturally present in few foods, added to others, and available as a dietary supplement. It is also produced endogenously when ultraviolet rays from sunlight strike the skin and trigger Vitamin D synthesis. The prevalence of Vitamin D deficiency has been reported to range from 15% to 80%. Research suggests that some of the damage done by Vitamin D deficiency is done in utero while the fetus is developing. Much of the damage may be permanent which cannot be fully reversed by taking Vitamin D after birth. In maternal Vitamin D deficiency, the maternal skeleton is also used as source of calcium for the developing fetus. This process is mediated by parathyroid hormone, which mobilizes calcium in a Vitamin D-dependent mechanism. Northern latitude especially winter or spring, limited sun exposure, regular use of sunscreens, African American or dark skin, obesity, extensive clothing cover, and malabsorptive syndromes (cystic fibrosis, cholestatic liver disease, inflammatory bowel disease, and short gut syndrome) are some of the risk factors for Vitamin D deficiency.

Aims and Objectives: This study aimed to find the prevalence of Vitamin D deficiency in pregnant women more than 28 weeks gestational age attending obstetric outpatient department (OPD) at Lalla Ded hospital for antenatal checkup and the cases were followed during antenatal, intrapartum, and neonatal period to find any fetomaternal correlation with Vitamin D deficiency and to know the prevalence of Vitamin D deficiency in pregnant Kashmiri women attending tertiary care hospital.

Materials and Methods: The study, entitled "The prevalence of Vitamin D deficiency in Kashmiri pregnant women and its impact on fetomaternal outcome – A tertiary care center study," is an observational study conducted in the Postgraduate Department of Obstetrics and Gynecology, Lalla Ded Hospital, an associated hospital of Government Medical College, Srinagar for 1½ years after obtaining clearance from the Institutional Ethical Committee. Based on the confidence level of 95%, the minimum sample size is 550. Proper written and informed consent was taken from pregnant women who were willing to participate in the study. They were requested to complete a questionnaire in their local language that covered sociodemographic data, obstetric history, lifestyle, dietary habits, and sunlight exposure. All singleton pregnant Kashmiri women aged between 18 and 35 years and more than 28 weeks of gestational age attending obstetric OPD at L.D Hospital for antenatal checkup were taken in study.

Results: The prevalence of Vitamin D deficiency was 60.2% (n = 331), 20.5% (n = 113) patients were Vitamin D sufficient while insufficient Vitamin D was observed in 19.3% (n = 106) patients. In patients aged between 26 and 30, Vitamin D deficiency was seen in 187 (59.9%) patients, insufficiency was observed in 60 (19.2%) patients while 65 (20.8%) had sufficient Vitamin D. In patients with 31–35 years of age, Vitamin D deficiency was observed in 93 (66.4%) patients, Vitamin D insufficiency was seen in 24 (17.1%) while 23 (16.4%) women were found to be Vitamin D sufficient. In women with <25 years of age, 51 (52%), 22 (22.4%), and 25 (25.5%) were Vitamin D deficient, insufficient, and sufficient. There were 189 (56.3%) primigravida compared to 142 (66.4%) multigravida women with Vitamin D deficiency. Vitamin D was insufficient in 65 (19.3%) primigravida compared to 41 (19.2%) multigravida. Sufficient Vitamin D was observed in 82 (24.4%) primigravida against 31 (14.5%) multigravida women. Statistically insignificant association was observed when Vitamin D status was compared with gestational age at delivery (P = 0.678) and gestational diabetes mellitus (P = 0.141). Mode of delivery, gestational hypertensive disorders, and maternal hypocalcemia had significant association with Vitamin D status.

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Conclusion: The present study provided significant information about the Vitamin D status of the Kashmiri pregnant women. Vitamin D deficiency has adverse effects on both mother and fetus, primarily preeclampsia, and maternal hypocalcemia. Increasing hours of sun exposure, Vitamin D supplementation during pregnancy could prevent some of the consequences. Effective educational programs should be initiated to elevate awareness among pregnant females about the importance of this vitamin and deficiency-associated complications.

Keywords: Maternal hypocalcemia, Preeclampsia, Vitamin D

INTRODUCTION

Vitamin D is a fat-soluble vitamin that is naturally present in a few foods, added to others, and available as a dietary supplement. It is also produced endogenously when ultraviolet rays from sunlight strike the skin and trigger Vitamin D synthesis. Vitamin D promotes calcium absorption in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal bone mineralization and prevent hypocalcemic tetany. It is also needed for bone growth and bone remodeling. Vitamin D deficiency is an unrecognized epidemic which is common among children, adults, and pregnant women throughout the world.

The prevalence of Vitamin D deficiency has been reported to range from 15% to 80%. Research suggests that some of the damage done by Vitamin D deficiency is done in utero while the fetus is developing. Much of the damage may be permanent which cannot be fully reversed by taking Vitamin D after birth.[1,2] Its biological actions include an increase in intestinal calcium absorption, transcellular calcium flux, and opening gated calcium channels allowing calcium uptake into cells such as osteoblasts and skeletal muscle. Vitamin D has an increasingly recognized repertoire of non-classical actions such as promoting insulin action and secretion, immune modulation, and lung development. It inhibits parathyroid hormone (PTH) secretion and adaptive immunity while promoting insulin secretion and innate immunity. It also inhibits cell proliferation and stimulates their differentiation.[3]

Vitamin D Metabolism in Pregnancy

The most important source of Vitamin D is skin synthesis of Vitamin D from 7-dehydrocholesterol by UV – irradiation. It is transported in the blood by Vitamin D-binding protein. Vitamins D2 and D3 are 25-hydroxylated in the liver to produce major circulating Vitamin D metabolite in blood 25-hydroxy Vitamin D3 which undergoes further hydroxylation mainly in the kidneys to form the steroid hormone 1-alpha 25-dihydroxy Vitamin D. This hormone binds to intracellular Vitamin D-regulated genes all across the genome through epigenetic mechanisms. During pregnancy, maternal Vitamin D metabolism is altered to enable transfer of calcium across placenta to enable fetal skeletal development. Extra calcium is obtained mainly from increased maternal intestinal calcium absorption, a Vitamin D-dependent process, and increased renal hydroxylation. Transplacental transfer of calcium to the fetus is also facilitated by the expression of all key mediators of Vitamin D metabolism in the placenta.[4,5] In maternal Vitamin D deficiency, the maternal skeleton is also used as source of calcium for the developing fetus. This process is mediated by PTH, which mobilizes calcium in a Vitamin D-dependent mechanism. Further, adaptation occurs involving maternal PTH, PTH-related protein, and interaction of prolactin, estradiol, and some other hormones during breastfeeding after loss of placental influence on Vitamin D metabolism.[6]

A number of maternal health problems have been associated with maternal Vitamin D deficiency. In mother spontaneous preterm birth, an increased rate of cesarean section, preeclampsia, gestational diabetes mellitus (GDM), and muscle weakness have been described. Risk factors for Vitamin D deficiency: Northern latitude especially winter or spring, limited sun exposure, regular use of sunscreens, African American or dark skin, obesity, extensive clothing cover, and malabsorptive syndromes (cystic fibrosis, cholestatic liver disease, inflammatory bowel disease, and short gut syndrome).

The hallmark of preeclampsia is marked changes in Vitamin D and calcium metabolism as compared to normal pregnancy. Normotensive pregnant women have high 25(OH) Vitamin D levels than women suffering from preeclampsia.[7,8] The placenta itself expresses 1 alpha-hydroxylase and, thus, produces active metabolite 1,25 (OH)2D3.[9] In syncytiotrophoblasts from pre-eclamptic pregnancies, the expression and activity of 1 alpha-hydroxylase is limited implying a significant role of Vitamin D in placenta.[10] Vitamin D is a key regulator of target genes associated with implantation, trophoblast invasion, and implantation tolerance.[11] Vitamin D regulates the angiogenic processes through direct effects on angiogenesis by gene transcription, including vascular endothelial growth factor.[12]

The need of primary cesarean section is demonstrated to have an inverse association with the status of Vitamin D. Severely, Vitamin D-deficient women with levels of Vitamin D below 37.5 nmol/l delivered nearly 4 times as often by cesarean section than those with values more than 37.5nmol/l.[13]

Vitamin D is known to influence insulin secretion. Vitamin D regulates insulin secretion by pancreatic beta-cells and, thereby, affects circulating glucose levels, glucose intolerance, and features of metabolic syndrome in normoglycemic subjects. Vitamin D deficiency in early pregnancy sufficiently increases the risk of gestational diabetes in later pregnancy.[14]

Aims and Objectives

This study aimed to find the prevalence of Vitamin D deficiency in pregnant women more than 28 weeks gestational age attending the obstetric outpatient department (OPD) at Lalla Ded hospital for antenatal checkup and the cases were followed during antenatal, intrapartum, and neonatal periods to find any fetomaternal correlation with Vitamin D deficiency, to know the prevalence of Vitamin D deficiency in pregnant Kashmiri women attending tertiary care hospital, and to know the maternal outcome in these women.

MATERIALS AND METHODS

The study, entitled "The prevalence of Vitamin D deficiency in Kashmiri pregnant women and its maternal outcome – A tertiary care center study," is an observational study conducted in the Postgraduate Department of Obstetrics and Gynecology, Lalla Ded Hospital, an associated hospital of the Government Medical College, Srinagar for 1 ½ years after obtaining clearance from the Institutional Ethical Committee. Based on confidence level of 95%, minimum sample size is 550.

Proper written and informed consent was taken from pregnant women who were willing to participate in the study. They were requested to complete a questionnaire in their local language that covered sociodemographic data, obstetric history, lifestyle, dietary habits, and sunlight exposure. All singleton pregnant Kashmiri women aged between 18 and 35 years and more than 28 weeks of gestational age attending obstetric OPD at L.D Hospital for antenatal checkup were taken in study.

Exclusion Criteria

The following criteria were excluded from the study:

1. Pregnant women with pre-existing medical disorders such as chronic hypertension, diabetes mellitus, renal disorder, and skin disorder
2. Previous history of lower-segment cesarean section (LSCS)
3. History of use of drugs interfering with Vitamin D metabolism such as anticonvulsants and corticosteroids.

Methodology

For this study, a 2 mL venous blood sample was taken during routine blood collection irrespective of fasting status. The sample for Vitamin D3 was protected from light, centrifuged, and stored at −20°C until analysis. Reliable Vitamin D3 was measured using a quantitative chemiluminescent immunoassay method (CLIA). Vitamin D status is best determined by measuring 25(OH) Vitamin D as it is the major circulating form and has longer half-life (2–3 weeks) than 1,25 dihydroxy vitamin D (5–8 h).

Results of the above laboratory investigations were recorded along with clinical data of the patient in pro forma. Subjects were classified as vitamin D insufficient, deficient, and sufficient. Values <20 ng/mL were the cutoff to define vitamin D deficiency.

The cases were followed in the antepartum period for any of these complications such as pregnancy induced hypertension (PIH), GDM, and maternal hypocalcemia. Gestational age at the time of delivery and mode of delivery was recorded in pro forma. The following parameters were calculated Vitamin D3 levels and maternal calcium levels.

Statistical Analysis

Data were entered in a Microsoft Excel spreadsheet. Results on continuous measurements were presented as mean±SD and results on categorical measurements were present in number (%). Chi-square test was used to find the significance of study parameters.

RESULTS AND OBSERVATIONS

The study patients were aged between 19 and 35 years with a mean age of 28.9 ± 3.64 years. Most common age group affected was 26–30 years in 312 (56.7%) patients followed by 31–35 years in 140 (25.5%) patients while 98 (17.8%) patients were aged <25 years [Table 1].

Out of 550 patients studied, 336 (61.1%) were primigravida while rest 214 (38.9%) were multigravida [Table 2].

Prevalence of vitamin D deficiency was 60.2% (n = 331), 20.5% (n = 113) patients were vitamin D sufficient while insufficient vitamin D was observed in 19.3% (n = 106) patients [Table 3].

In patients aged between 26 and 30, Vitamin D deficiency was seen in 187 (59.9%) patients, insufficiency was observed

in 60 (19.2%) patients while 65 (20.8%) had sufficient vitamin D. In patients with 31–35 years of age, Vitamin D deficiency was observed in 93 (66.4%) patients, Vitamin D insufficiency was seen in 24 (17.1%) while 23 (16.4%) women were found to be Vitamin D sufficient. In women with <25 years of age, 51 (52%), 22 (22.4%), and 25 (25.5%) were Vitamin D deficient, insufficient, and sufficient. The statistically insignificant association was observed between vitamin D status and age with $P = 0.269$ [Table 4].

Significant statistical difference was observed when patients were compared on the basis of vitamin D status and gravidity with $P = 0.014$. There were 189 (56.3%) primigravida compared to 142 (66.4%) multigravida women with Vitamin D deficiency. Vitamin D was insufficient in 65 (19.3%) primigravida compared to 41 (19.2%) multigravida. Sufficient vitamin D was observed in 82 (24.4%) primigravida against 31 (14.5%) multigravida women [Table 5].

Table 1: Age distribution of study patients

Age (years)	Number	Percentage
≤25	98	17.8
26–30	312	56.7
31–35	140	25.5
Total	550	100

Mean±SD (range)=28.9±3.64 (19–35 years)

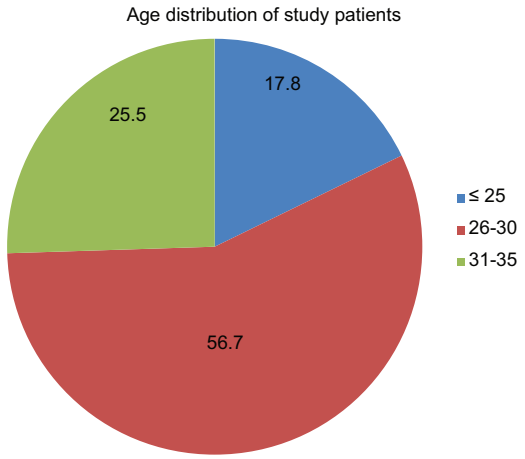

Table 2: Distribution of study patients as per gravid

Gravida	Number	Percentage
Primigravida	336	61.1
Multigravida	214	38.9
Total	550	100.0

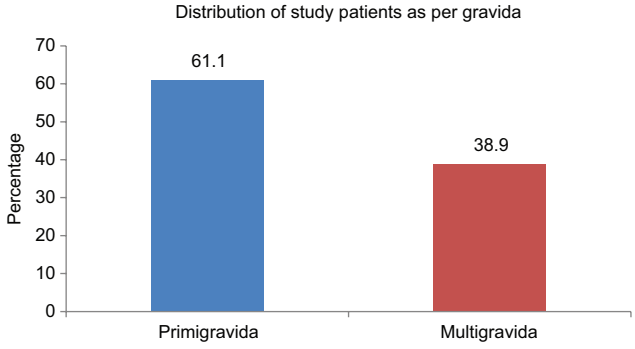

Table 3: Prevalence of Vitamin D deficiency in study patients

Vitamin D status	Number	Percentage
Deficiency	331	60.2
Insufficiency	106	19.3
Sufficiency	113	20.5
Total	550	100

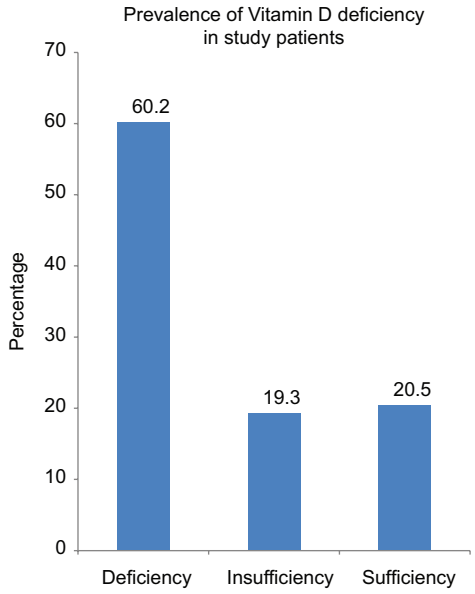

Table 4: Association of Vitamin D status with maternal age

Age (years)	Deficiency		Insufficiency		Sufficiency		*P*-value
	No.	%age	No.	%age	No.	%age	
≤25	51	52.0	22	22.4	25	25.5	0.269
26–30	187	59.9	60	19.2	65	20.8	
31–35	93	66.4	24	17.1	23	16.4	
Total	331	60.2	106	19.3	113	20.5	

Table 5: Association of Vitamin D status with gravid

Gravida	Deficiency		Insufficiency		Sufficiency		*P*-value
	No.	%age	No.	%age	No.	%age	
Primigravida	189	56.3	65	19.3	82	24.4	0.014*
Multigravida	142	66.4	41	19.2	31	14.5	
Total	331	60.2	106	19.3	113	20.5	

In patients with a gestational age of 37–40 weeks, majority, that is, 291 (59.9%) were vitamin D deficient, 91 (18.7%) had vitamin D insufficiency while 104 (21.4%) had vitamin D sufficiency.

In women with 34–36 weeks of gestation, 29 (63.0%), 11 (23.9%), and 6 (13.0%) were Vitamin D deficient, insufficient, and Vitamin D sufficient.

Vitamin D deficiency was observed in 11 (61.1%) patients, 4 (22.2%) had Vitamin D insufficiency while 3 (16.7%) were Vitamin D sufficient with gestational age of <33 weeks. The association between preterm delivery and vitamin D deficiency was insignificant. Moreover, as the majority of patients contacted the tertiary hospital near term, this association could not be made out.

Gestational hypertensive disorder was present in 132 (66.2%) patients with Vitamin D deficiency, 27 (16.0%) patients with Vitamin D insufficiency, and 30 (17.8%) patients with sufficient Vitamin D. GDM was present in 65 (65.7%) patients with Vitamin D deficiency, 12 (12.1%) patients with Vitamin D insufficiency, and 22 (22.2%) patients with sufficient Vitamin D.

Maternal hypocalcemia was present in 227 (76.9%) patients with Vitamin D deficiency, 38 (12.9%) patients with Vitamin D insufficiency, and 30 (10.2%) patients with sufficient Vitamin D [Table 6].

DISCUSSION

The present study entitled "Prevalence of Vitamin D deficiency in Kashmiri pregnant women and its impact on Fetomaternal outcome – A tertiary care center study" was a prospective observational study which was carried out in Lalla Ded Hospital, Government Medical College, Srinagar over a period of 1½ years from 2020 to 2021. Five hundred and fifty cases who fulfilled the criteria were recruited for the study.

The mean age of our study population was 26+3.64 years. The most common age group affected was 26–30 years in 56.7% of patients. In the study conducted by Al-Shaikh *et al.*,[15] 52% of Vitamin D deficient belonged to age group of 25–35 years which is comparable to our study. In study conducted by Gupta *et al.*,[16] the majority of patients were in age group of 21–25 years of age which is not comparable to our study. Yadav *et al.*,[17] in their study, found that mean age group affected with Vitamin D deficiency is 28.3 years which is comparable with the findings of the present study.

In our study, Vitamin D deficiency, insufficiency, and sufficiency were found in 60.2%, 19.3%, and 20.5% of subjects, respectively. Our study findings were consistent with the findings of Sharma *et al.*,[16]

Wherein Vitamin D deficiency was present in 84.8% of pregnant women and Vitamin D insufficiency was present in 12.44%. Dar *et al.*,[18] found Vitamin D deficiency in 68.5% of Kashmiri pregnant women and only 18% of subjects were Vitamin D sufficient which is comparable to our study. Kaur *et al.*,[19] in their study, found the prevalence of Vitamin D deficiency in pregnant women to be 79.8% which is comparable with the findings of the present study.

In our study, Vitamin D deficiency was more common in multigravidas (66.4%) as compared to primigravida (56.3%). These results were comparable with the study

Table 6: Association of Vitamin D status with maternal outcome

Variable	Deficiency		Insufficiency		Sufficiency		*P*-value
	No.	%age	No.	%age	No.	%age	
Gestational age at delivery (weeks)							
<33	11	61.1	4	22.2	3	16.7	0.678
34–36	29	63.0	11	23.9	6	13.0	
37–40	291	59.9	91	18.7	104	21.4	
Mode of delivery							
NVD	143	53.2	61	22.7	65	24.2	0.004*
LSCS	188	66.9	45	16.0	48	17.1	
Gestational hypertensive disorders							
Present	132	66.2	27	16.0	30	17.8	0.008*
Absent	199	52.2	79	20.7	103	27.0	
GDM							
Present	65	65.7	12	12.1	22	22.2	0.141
Absent	266	59.0	94	20.8	91	20.2	
Maternal hypocalcemia							
Present	227	76.9	38	12.9	30	10.2	<0.001*
Absent	104	40.8	68	26.7	83	32.5	

LSCS: Lower-segment cesarean section, GDM: Gestational diabetes mellitus

conducted by Al-Shaikh *et al.*,[15] who found that 66.8% of Vitamin D-deficient women were multiparous.

In our study, pregnant females who delivered at 37–40 weeks of gestation, 291 (59.9%) were Vitamin D deficient, 91 (18.7%) were Vitamin D insufficient while 104 (21.4%) were Vitamin D sufficient. In those pregnant women who delivered at <33 weeks gestation, Vitamin D deficiency was observed in 11 (61.1%) patients, 4 (22.2%) had Vitamin D insufficiency while 3 (16.7%) were Vitamin D sufficient. There was no significant correlation between Vitamin D deficiency and preterm birth. Yang *et al.*,[18,20,21] in their study, found that pregnant women with lower vitamin D (<20 ng/mL) had no significant increase in preterm birth risk which is comparable with our study.

In our study, gestational hypertensive disorder was present in 66.3% of Vitamin D-deficient pregnant women, 16 % of Vitamin D insufficient, and 17.8% of Vitamin D sufficient women. These results were comparable with the study conducted by Talukdar and Joshi[22] where hypertensive disorder was present in 63.6% of Vitamin D-deficient pregnant women and only 26.6% of Vitamin D-sufficient women. In study conducted by Bodnar *et al.*,[7] a positive correlation was found between Vitamin D deficiency and development of preeclampsia which is in accordance with our study.

In our study, only 65 out of 331 Vitamin D-deficient pregnant women had GDM which is comparable to a study conducted by Talukdar and Joshi[22] where only 9.1% of Vitamin D-deficient women had GDM while 90.9% were having normal sugars. The study conducted by Baker *et al.*,[19] showed no significant association of GDM with vitamin D deficiency which is in accordance with our study. The study findings of Hauta-Alus *et al.*,[23] were also consistent with our findings showing no significant association of GDM with Vitamin D deficiency. Rekha *et al.*, (2019) in their study, found that mean Vitamin D levels were lower in women with GDM as compared to normal pregnant women.

There is a strong association between Vitamin D deficiency and maternal hypocalcemia. In our study, 227 (76.9%) of Vitamin D deficient had hypocalcemia while 104 (40.8%) had normal calcium levels. In Vitamin D-sufficient group, 30 (10.2%) had hypocalcemia. Almaghamsi *et al.*,[24] found vitamin D deficiency as an important cause of maternal hypocalcemia. They found that vitamin D, calcitonin, and PTH interact to steadily maintain homeostatic ionic calcium control during pregnancy.

In our study, out of 331 women who were Vitamin D deficient, 188 (66.9%) delivered through LSCS while 143 (53.9%) delivered through normal vaginal delivery. In the study conducted by Prasad *et al.*,[25] 54% of study subjects who were Vitamin D deficient delivered through LSCS and 34% had normal vaginal delivery which is similar to our study. Our study findings were in accordance with Merewood *et al.*,[26] where they found that there exists an inverse association between cesarean section and serum Vitamin D levels. In their study, 28% pregnant women with Vitamin D deficiency had cesarean section compared to 14% pregnant women with sufficient Vitamin D levels.[27]

CONCLUSION

Vitamin D deficiency is an unrecognized epidemic that is increasing worldwide both in the general population as well as in pregnant women. Vitamin D is an important vitamin for the regulation of calcium metabolism and maintaining good health.

The present study provided significant information about the vitamin D status of Kashmiri pregnant women. Vitamin D deficiency has adverse effects on both mother and fetus. In our study of Kashmiri pregnant women, statistically significant association was observed between Vitamin D deficiency and mode of delivery, gestational hypertensive disorders, and maternal hypocalcemia. A statistically significant association was observed when Vitamin D status was compared with birth weight ($P = 0.002$), 1 min Apgar score ($P = 0.008$), respiratory infection, and neonatal hypocalcemia.

Increasing hours of sun exposure and Vitamin D supplementation during pregnancy could prevent some of the consequences. Effective educational programs should be initiated to elevate awareness among pregnant females about the importance of this vitamin and deficiency-associated complications.

As the majority of patients in our study contacted the tertiary care center for the 1st time near term (≥37 weeks) maternal and fetal outcome could not be prevented; therefore, serum analysis of Vitamin D should be done in pregnant females early in pregnancy and Vitamin D supplementation provided to prevent adverse maternal and fetal outcome.

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