Pattern of Vitamin D among Pakistani Pregnant Women
Jamal Abdul Nasir\textsuperscript{1}, Muhammad Imran\textsuperscript{2} and Syed Arif Ahmed Zaidi\textsuperscript{3}

ABSTRACT
Vitamin D deficiency is an emerging health concern around the world, highly prevalent in south Asian population, despite abundant sunlight. In Pakistan, all age groups are vulnerable to Vitamin D deficiency including pregnant women. This systematic review aimed to determine the pattern of Vitamin D deficiency among Pakistani pregnant women as well as exploring the causes and possible interventions that have had a substantial effect on improving the vitamin D level. Three databases (PubMed, Pub Get and Google Scholar), for the present review up to 2016, were used for the identification of published peer reviewed original relevant studies regarding Vitamin D deficiency among Pakistani pregnant women with the keywords Vitamin D or 25-hydroxyvitamin D or 25(OH)D in combination with pregnant women. Five studies were included for the final analysis. Vitamin D deficiency was common and highly prevalent among Pakistani pregnant women and their neonates. The main reasons for this were found to be avoiding sun exposure, quality of diet, and lower intake of calcium. Maternal vitamin D supplementation was found to be a key intervention to improve the maternal and neonatal vitamin D status. These review findings can be emerging in ensuring the adequate vitamin D level for Pakistani pregnant women during pregnancy, ultimately to achieve positive maternal and neonate’s health outcomes.


INTRODUCTION
Vitamin D is a steroid hormone which is responsible for regulating the calcium and phosphorus in the body. There are five different kinds of vitamin D: D1, D2 (ergocalciferol), D3 (cholecalciferol), D4 (dihydro-ergocalciferol), and D5 (sitocalciferol). Vitamin D2 and D3 are more prevalent in human. The value of 25[OH]D level <20 ng/ml is labelled as the severe deficiency of vitamin D. In addition, insufficiency and sufficiency of vitamin D is defined at the value of 25[OH]D between 21-29 ng/ml and ≥30 ng/ml respectively. Vitamin D deficiency is an emerging health concern around the world. Literature showed about one billion people across the globe suffered from Vitamin D deficiency or insufficiency.\textsuperscript{1,2}

Vitamin D deficiency is common during pregnancy, and associated to its outcomes.\textsuperscript{3,4} Approximately 14 million pregnant women per year suffer from acute maternal complications worldwide.\textsuperscript{5,6} Studies showed that vitamin D maintains the required ranges of serum calcium and phosphorus by improving calcium absorption from the intestine and supporting the utilization of calcium and other minerals from the skeleton for pregnant women.\textsuperscript{7-10} Studies suggested that low levels of vitamin D lead to higher rates of gestational and low birth-weight in infants.\textsuperscript{11,12} Fetal concentrations of vitamin D are dependent on maternal concentrations, so children born to mothers deficient in vitamin D are at risk of neonatal hypocalcemia and infantile rickets.\textsuperscript{11} In addition, complications for offspring of vitamin D-deficient mothers can last beyond the neonatal period. Studies suggest that these children are at an increased risk of developing asthma, type 1 diabetes, upper-respiratory infections, dental caries, and language impairment.\textsuperscript{13-15} Several studies suggested that vitamin D deficiency during pregnancy can contribute to adverse maternal outcomes, including higher rates of preeclampsia, gestational diabetes, bacterial vaginosis, primary cesarean section and postpartum depressive symptoms.\textsuperscript{12,16-20} Bio-social factors have great impact in reducing the levels of vitamin D including poverty, illiteracy, poor exposure to sunlight, cultural bounds, religious and social customs. It could significantly be hypothesized in this research that there would be variation of bio-social factors between developed and developing countries. Fertility transition of developed and developing countries is different. Keeping in view the high fertility levels, this study was aimed to explore the status of vitamin D deficiency in Pakistan. In addition, the study presents a systematic review having a definite objective to determine the pattern of vitamin D deficiency among Pakistani pregnant women as well as exploring the causes and possible interventions that have had a substantial effect on improving the vitamin D level.

METHODOLOGY
Three databases (PubMed, Pub Get and Google Scholar) were used for the identification of published...
articles regarding vitamin D deficiency among Pakistani pregnant women for systematic review up to 2016. Specific terms of search were vitamin D or 25-hydroxyvitamin D or 25(OH)D in combination with pregnant women. Further, manually all appropriate original and other related articles were searched. Twenty-two peer reviewed original articles were identified after the initial search of record. After screening the record and excluding duplicates literature about pregnant women having specific diseases during pregnancy, reproductive-age women but not married or currently not pregnant, and the studies which did not meet the criteria of peer reviewed original articles were excluded. Finally, five studies were included for extraction of data for final analysis.

Among the selected five articles, four were cross-sectional studies and the remaining one was an open label, randomised controlled trials, the study emphasis the obstetric and neonatal outcomes of maternal vitamin D supplementation. The four cross-sectional studies deal with vitamin D deficiency among pregnant women – three conducted in Pakistan and one from Oslo, Norway among Pakistani migrant pregnant women. Information from five shortlisted articles was enlisted into a predesigned data extraction form.

**RESULTS**

Results for literature search for systematic review were presented in Figure 1. Five studies were selected for the final analysis, including four cross-sectional and one randomized controlled trial.

The most recent was a cross-sectional study which focused on the comparison of Vit D status between urban and rural Pakistani pregnant women and their neonates. The study was conducted at urban Karachi and rural Jhelum with 390 women and 266 neonates. The average Vit D status among mothers and their neonates respectively from Karachi being 13.37 and 19.87 nmol/L and from Jhelum being 28.65 and 29.55 nmol/L. The study concluded that the prevalence of vitamin D deficiency (<50 nmol/L) was higher among mothers and their neonates in urban Karachi (20%; 99.5% and 19.87; 97.3%) than in rural Jhelum (55; 89% and 37; 82%). The study also exhibited that Gc genotypes had no association with serum 25(OH)D concentrations for both women and their neonates.

In a cross-sectional study, there was a comparison of Vit D status among pregnant women and non-pregnant women. A sample of 71 women (36 pregnant at 12 weeks of gestation and 35 non-pregnant) was used from Jhelum, Pakistan. Approximately 89% (severely deficient 12; 33.4% and deficient 20; 55.5%) pregnant women were found to be vitamin D deficiency compared to 54% (severely deficient 1; 2.8% and deficient 18; 51.5%) non-pregnant (p <0.001). Further, the study investigated that blood indices (hemoglobin, hematocrit, mean corpuscular volume) were significantly lower among the pregnant compared to the non-pregnant group (p < 0.001), and no association between low vit D levels and periodontal disease was seen in the studied population.

The third study come up with conclusion that the maternal and neonatal vitamin D status can be improved by using vitamin D supplementation during pregnancy. It was a single centre, open label, randomised controlled trial study conducted at University Hospital Karachi, Pakistan with definite objective to examine the supplementation of vitamin D during pregnancy effect obstetric and neonatal outcomes. Two groups (group A, 200 mg ferrous sulphate and 600 mg calcium daily vs. supplementation of Vit D (group B, 4000 IU Vit D3 daily) of pregnant women were compared started at 20 weeks and continued till delivery. At delivery, group B had significantly higher Vit D status (improved maternal vitamin D status with supplementation) compared to group A. Further, the effect of maternal Vit D supplementation on pregnancy outcomes were compared; maternal Vit D supplementation failed to impact on risks for preterm delivery, gestational hypertension, preeclampsia, GDM, or the incidence of delivery by caesarean section (p >0.05). The study also compared the effect of maternal Vit D supplementation
The review findings showed that vitamin D deficiency was common and highly prevalent among Pakistani pregnant women and their neonates, avoiding sun exposure; and lower dietary intake of vitamin D found to be main reason. Maternal vitamin D supplementation was found to be an effective intervention to improve the vitamin D status among mothers and their neonatal.

Despite ample sunlight in Pakistan, the high prevalence of vitamin D deficiency is reported,21-25 not only in pregnant women but also in general population of various age groups. In Asian countries, sun exposure is supposed to be a major natural mode of vitamin D. Several studies revealed that avoiding sun exposure and lower consumption of vit D in diet considered to be key reasons to vitamin D deficiency. A study conducted at various hospitals in Karachi from April to September 2007 among 244 healthy adults (193 female) to underline the prevalence of vitamin D deficiency and its predictors showed that about 76.2% respondents had vitamin D deficiency and significantly correlated with sunlight exposure duration, large area of skin exposed, consumption of vit D in diet and colour of clothes worn.26 Several studies from our neighbouring countries confirmed the vitamin D deficiency; for instance, two cross-sectional studies conducted in Shanghai, China found that majority of the PW (69%) had vitamin D deficiency with mean level of 17.57 ±11.44 ng/ml.27 A study from India found that high prevalence of physiologically significant hypovitaminosis D among PW and their newborns.28 In Bangladesh, hypovitaminosis D is common in women regardless of age, lifestyle and clothing.29

Pakistan is the second most populated Muslim country after Indonesia; cultural, social and religious norms might be the reason of vitamin D deficiency among females as they are not exposed properly to sunlight and mostly housewives stay at home or if they go out, mostly cover their bodies except face and hand. The other factors for vitamin D deficiency are lack of balanced diet containing Vit D in the daily diet as well as Vit D supplementation during pregnancy.

In Pakistan, about 70% population dwell in rural areas and about 90% of the births are conducted by untrained dais (traditional birth attendants) at home.30 The traditional birth attendants are unable to effectively diagnose the pregnancy related complications. A study

**DISCUSSION**

The fifth study emphasized on vitamin D deficiency in Pakistani and Norwegian pregnant women (PW) and also underlined the possible causes of vitamin D deficiency. Pakistani women had a significantly lower 25-hydroxyvitamin D3 level as compared to Norwegian and a higher level of serum parathyroid hormone. Further, the pregnant women from Pakistan had lower dietary intake of vitamin D, lower supplementation and lower intake of calcium than Norwegian women. The study documented that Pakistani women dwellers of Oslo were more prone to develop vitamin D deficiency during pregnancy. Avoiding sun exposure, low dietary intake of vitamin D and no or little use of supplementation was found to be main reasons.

**Table I: Comparative studies showing vitamin D deficiency among pregnant women.**

<table>
<thead>
<tr>
<th>Place</th>
<th>Year</th>
<th>Study design</th>
<th>Sample size</th>
<th>Main finding</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rural Jhelum and urban Karachi</td>
<td>2016</td>
<td>Cross-sectional</td>
<td>Women=290 and neonates=266</td>
<td>The prevalence of vitamin D deficiency was higher among mothers and their neonates in urban Karachi (99.5% and 97.3%) and rural Jhelum (89% and 82%), respectively.</td>
<td>21</td>
</tr>
<tr>
<td>Jhelum, Pakistan</td>
<td>2016</td>
<td>Cross-sectional</td>
<td>Pregnant women=36 and non-pregnant women=35</td>
<td>Vitamin D deficiency was highly prevalent in pregnant women compared to non-pregnant group. Further, periodontal disease and low level of vitamin D had disassociated.</td>
<td>22</td>
</tr>
<tr>
<td>Karachi, Pakistan</td>
<td>2014</td>
<td>Randomized controlled trials</td>
<td>193 completed the trial</td>
<td>Maternal vitamin D supplementation improved the maternal and neonatal vitamin D status.</td>
<td>23</td>
</tr>
<tr>
<td>Karachi, Pakistan</td>
<td>2011</td>
<td>Cross-sectional</td>
<td>50 pregnant women</td>
<td>High prevalence of vitamin D deficiency noticed among mothers (46%) and their new-borns (88%). Further, direct correlation observed between the vitamin D level in maternal and cord blood. However, sun exposure and quality of diet significantly affecting the maternal vit D level.</td>
<td>24</td>
</tr>
<tr>
<td>Oslo, Norway</td>
<td>1995</td>
<td>Cross-sectional</td>
<td>38 Pakistani and 38 Norwegian pregnant women</td>
<td>Pakistani women dwellers of Oslo were more prone to develop vitamin D deficiency during pregnancy. Avoiding sun exposure, low dietary intake of vit D, no or little use of supplementation was found to be main reasons.</td>
<td>25</td>
</tr>
</tbody>
</table>
conducted in Islamabad, Pakistan, showed that 80% of maternal deaths occurred at home and only one out of 20 reaches a facility with emergency obstetrical care.\textsuperscript{31} A study finding from India revealed that there is still a wide gap between provision and utilization of maternal care services. Since most of the deliveries are conducted at home by untrained traditional birth attendants, the people must be educated to utilize the services of trained personnel.\textsuperscript{32}

Government and other health related NGOs can play a vital role to combat this epidemic by promoting the public awareness programs and food fabrication policies.

These review findings can be emerged in ensuring the adequate vitamin D level for Pakistani pregnant women during pregnancy, ultimately to achieve positive maternal and neonate’s health outcomes.

Limited literature related on this subject was found on vitamin deficiency among Pakistani pregnant women. Other important variables, for instance socioeconomic and demographic factors of pregnant women, are lacking to draw a temporal decision regarding vitamin D deficiency in pregnant women.

**CONCLUSION**

It is concluded that vitamin D deficiency was common and highly prevalent among Pakistani pregnant women and their neonates, due to lack of sun exposure; and lower dietary intake of vitamin D is found to be main reason. Maternal vitamin D supplementation is an effective intervention to improve the vitamin D status among mothers and their neonates.

**REFERENCES**


