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Relationship among Hypovitaminosis D, Maternal Periodontal Disease, and Low Birth Weight

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ABSTRACT

Objective: To determine if low birth weight is associated with hypovitaminosis D and periodontal disease among a sample of Pakistani women residing in district Jhelum, Punjab.

Study Design: Cross-sectional study nested in a large community-based longitudinal study.

Place and Duration of Study: Tehsil Pind Dadan Khan, District Jhelum, Pakistan from August 2012 to October 2015.

Methodology: Women during 12-16th week of pregnancy were selected. Dental examination was performed. Probing depth ≥ 3 mm was labeled as periodontal disease, whereas serum level < 20.0 ng/mL was taken as hypovitaminosis D. Mothers of low birth weight babies (< 2500 g) were compared to mothers who gave birth to normal weight (≥ 2500 g) babies. Odds ratio was applied to measure the strength of association of low birth weight with maternal hypovitaminosis D and also for maternal periodontal disease.

Results: There were 62 participants in the study. The mean age of mothers was 26.7 ± 4.5 years. It was alarming to observe that 53 (85%) participants had vitamin D deficiency. However, periodontal disease was only seen in four participants (6%). Out of the 62 mothers, eighteen (29%) gave birth to low birth weight babies. None of the variables were found to be associated with the low birth weight.

Conclusion: The present study did not find any significant association of low birth weight with hypovitaminosis D or maternal periodontal disease in the studied sample.

Key Words: Low birth weight. Periodontal disease. Pregnant women. Vitamin D.

INTRODUCTION

In the developing world, over 20 million infants ($> 15\%$ of all live births) are born annually with low birth weight (LBW). According to the World Health Organization (WHO) global estimates on LBW, the prevalence of LBW in the developed part of the world is around 7%; whereas, in developing countries it is nearly 16.5%.¹ Highest prevalence of LBW is reported in South Asia, i.e. 27%. The prevalence of LBW in Pakistan ranges between 12-25%.² The WHO report estimates it to be at least 19%.¹

Periodontal disease is a persistent source of bacterial infection that can induce systemic inflammation, which in turn, exacerbates the risk of adverse pregnancy outcomes.^{3,4} Considerable research has been done to study this relationship but to date the findings on this relationship have been varied. A systemic review done on 25 studies showed that 18 studies, showing the risk of adverse pregnancy outcomes, is associated with periodontal disease [odds ratio: 1.10 - 20.0], while seven studies indicated no evidence of such association [odds ratio: 0.73 - 2.50].⁵

Adverse pregnancy outcomes are also linked with maternal hypovitaminosis D.⁶ A systematic review, performed on 31 studies, indicated that hypovitaminosis D is significantly associated with LBW but the substantial heterogeneity among studies made the reliability of that association questionable.⁷ Another systematic review and meta-analysis, conducted on 24 studies, clearly demonstrated that pregnant women with vitamin D levels < 20 ng/mL had a higher risk of developing preeclampsia [odds ratio: 2.09]; pre-term birth [odds ratio: 1.58]; small for gestational age [odds ratio: 1.52]; and gestational diabetes [odds ratio: 1.38].⁸

As hypovitaminosis D is a prevalent condition among pregnant in south Asian countries, particularly India and Pakistan,⁹⁻¹¹ a large proportion of pregnant women (35-100%) are affected with periodontal disease,¹² and one out of every five live-births in Pakistan is a LBW.¹ Thus, it is imperative to study the factors related to the LBW.

The objective of the present study was to assess if low birth weight is associated with maternal hypovitaminosis D and periodontal disease.

METHODOLOGY

A cross-sectional study that was nested in a large longitudinal study was done from August 2012 to October 2015 at Tehsil Pind Dadan Khan, District Jhelum, Pakistan. The Women and Child Health Division of the Aga Khan University with the help of Pakistan

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Initiative for Mothers and Newborns has established an outreach community research center in that area. The study participants were pregnant women who were resident of that area. Participants were selected using convenience sampling that was done within the sampling frame of the primary study whose objectives were different from the present study. The present study focused on the mothers who gave birth to low birth weight babies (<2500g). These mothers were compared with the mothers with newborns of normal weight (birth weight \geq 2500g).

Subjects with less than 20 standing teeth or history of dental surgery or antibiotic consumption within six weeks of delivery were excluded. Similarly, mothers whose vitamin D status were not available or could not

be measured were also excluded. The study protocol was approved by the ethics review committee (ERC) of the Aga Khan University, Ref # 147-Ped-ERC-2010.

The sample size was calculated using WHO calculator by Lwanga and Lemeshow.¹³ A population prevalence of 20% was taken for low birth weight babies with an absolute precision of 10% at 95% level of confidence to reach a final sample size of 62 mothers.

The interviews of the study participants took place at the outreach community data collection center and at the study subjects' residence. All study participants underwent a physical examination during 12-16th week of pregnancy. The study participants were dentally examined in daylight by a trained dentist using sterilized dental examination instruments. The subjects were examined while seated on a house chair. A standard periodontal probe (William's probe with graduated marking at 1mm interval) was used for recording following parameters: clinical attachment loss (AL), periodontal probing depth (PD), and gingival bleeding on probing (BoP). A six-point probing approach was followed for AL and PD readings (only Ramfjord's teeth were included). Thus, of 36 probing sites per individual were obtained. The periodontal readings were rounded off to the nearest millimeter. The oral hygiene was assessed using Silness-Loe Index,¹² and dental caries was assessed using DMFT index on the six teeth identified above. Serum samples (10 ml) were also obtained for assessing the hemoglobin levels for anemia and vitamin D levels (analyzed using DiaSorin kit, USA). The samples were later tested at the Aga Khan University, nutrition research laboratory, Karachi.

Table I: Characteristics of study participants (n=62).

Variables	Range	Mean	SD
Age (years)	19-36	26.8	4.4
*Vitamin D level (ng/mL)	4-27.3	10.8	IQR: 8.2-15.2
*Weight in Kg (12-16th week of pregnancy)	38-101.3	58.7	IQR: 49.8-66.7
Height (in cm)	145-170	155.3	5.2
Hb (gm/dL)	6.5-15	10.2	2.9
Number of teeth	23-32	30.1	2.3
Probing depth (mm)	1-3	1.8	0.6
Attachment loss (mm)	0-4	1.2	0.9
Birth weight (kg)	2.0-5.5	2.9	0.6
Gestation period (weeks)	37-44	38.4	1.7
Parity status		n	%
<2		43	69.4
\geq 3		19	30.6

*Owing to lack of normal distribution of vitamin D levels and weight of the study participants, the median and interquartile ranges (IQR) were reported rather than the mean and standard deviation.

Table II: Variables associated with low birth weight among study participants (n=62).

Variables	Categories	n	LBW count (%)	Odds ratio (95% CI)	p-value
All	-	62	18 (29.0)	-	-
Age in years	<26	32	6 (18.75)	1.0	0.35
	\geq 26.1	30	12 (40.0)	0.35 (0.11-1.09)	
Vitamin D levels	<20.0 ng/mL	53	16 (30.1)	1.51 (0.29-8.10)	1.00
	\geq 20.1 ng/mL	9	2 (22.2)	1.0	
School education	<5 years	22	7 (31.8)	1.23 (0.40-3.83)	0.78
	\geq 6 years	40	11 (27.5)	1.0	
Parity status	<2	43	12 (27.9)	0.84 (0.26-2.72)	0.77
	\geq 3	19	6 (31.6)	1.0	
Anemia	<10.0 gm/dL	40	11 (27.5)	0.81 (0.32-1.81)	0.81
	\geq 10.1 gm/dL	22	7 (31.8)	1.0	
Bleeding on probing	Absent	29	6 (20.6)	0.46 (0.15-1.43)	0.26
	Present	33	12 (36.4)	1.0	
Probing depth	<3 mm	55	14 (25.4)	0.25 (0.05-1.29)	0.18
	\geq 3.1 mm	7	4 (57.1)	1.0	
Attachment loss	<2 mm	44	13 (29.5)	1.0	1.00
	\geq 2.1 mm	18	5 (27.8)	1.09 (0.32-3.69)	
DMFT index	<4	55	16 (29.1)	1.0	1.00
	\geq 4.1	7	2 (28.5)	1.03 (0.18-5.85)	
Oral hygiene	high plaque \geq 1.1	22	6 (27.3)	0.87 (0.28-2.78)	1.00
	low plaque <1	40	12 (30.0)	1.0	

Odds ratio was calculated. LBW refers to low birth weight (\leq 2500 gm). DMFT index was used for assessing decayed, missing and filled teeth (on Ramfjord teeth only) Silness-Loe Index was used for the assessment of oral hygiene.

For case definitions, newborns with known birth weight <2500 g were labeled as LBW. Study participants exhibiting at least one periodontal site with probing depth ≥ 3 mm were signified as having periodontal disease. For vitamin D levels, the cutoff value of <20.0 ng/mL was taken for hypovitaminosis D.

Data was analyzed on SPSS version 19.0 and Graph Pad Prism 6.0. The frequency distribution and percentages of the categorical variables and means and SD of continuous variables were computed. Odds ratio was applied to determine the strength of association between LBW and other variables including maternal periodontal disease and hypovitaminosis D. Logistic regression was planned to be applied while keeping the LBW as an outcome variable; whereas mother's age, periodontal disease, and vitamin D status were taken as independent variables. The level of significance for the statistical test was kept at 0.05.

RESULTS

There were 62 mothers in the study. The mean age of the participants was 26.7 ± 4.5 years. All participants were otherwise healthy; no diabetics or smokers were reported in the study sample. Similarly, none of them has ever received a dental implant or fixed bridge. Nearly one-third of the participants ($n=22$) had no formal education beyond secondary school. Sixteen mothers (25.8%) were primi-para and 19 mothers (30.6%) had a parity status of three or more. The demographic details of the participants are shown in Table I.

Fifty-three (85%) participants were vitamin D deficient. However, periodontal disease was only seen in four (6%) subjects. Out of the 62 mothers, eighteen (29%) gave birth to low birth weight babies. None of the variables (vitamin D status, age, education, anemia, parity status, periodontal probing depth, bleeding on probing, clinical attachment loss, oral hygiene and DMFT status etc.) were found to have any association with the LBW (Table II). Hence, logistic regression analysis could not be performed.

DISCUSSION

Birth weight of the newborn is primarily determined by the health and nutrition of the female before conception and during pregnancy. The other risk factors known to be associated with LBW are poor maternal nutrition, anemia, smoking, primi-parity, low socioeconomic status (SES), mental stress during pregnancy, abuse in family, lack of antenatal visits, short maternal height and low maternal weight etc.¹⁴ The frequency of LBW in the present study turned out to be 18/62 (29%). This proportion is alarmingly high. A probable explanation would be the fact that the studied sample belonged to a rural setting, which has a number of risk factors simultaneously present for LBW. These include low education, low SES, lack of antenatal care, and above all anemia. It's imperative to note that two third of the mothers in the study were anemic (Table I).

The present study was attempted to explore a possible relationship of LBW with maternal hypovitaminosis D and periodontal disease. In addition to serve as an essential micronutrient for calcium balance, vitamin D is a modulator of immunity (through induction of defensins such as Cathelicidin LL-37) and through its bone mineral density effect.¹⁵ Thus, it can potentially play a part in the inflammation caused by periodontal disease.

Considerable amount of research has been done on exploring the relationship of adverse pregnancy outcome and periodontal disease. Ide and Papapanou inferred in a meta-analysis that low birth weight and preterm birth are significantly linked to maternal periodontitis.¹⁶ Despite the substantial evidence in favor of that association, the presence of substantial heterogeneity among the studies warranted the researchers to interpret the evidence with caution.

The relationship between adverse pregnancy outcomes and hypovitaminosis D has also been established.⁶ Aghajafari *et al.* carried out a systematic review on 31 studies and reported that hypovitaminosis D in mothers is associated with adverse pregnancy outcomes such as preeclampsia, small for gestational age, gestational diabetes, and low birth weight.⁷ Wei *et al.* in their meta-analysis of 24 studies confirmed that maternal hypovitaminosis D is linked with adverse outcomes such as preeclampsia, pre-term birth, small for gestational age and gestational diabetes.⁸

Nearly 85% mothers in the present study had vitamin D deficiency. Presence of maternal hypovitaminosis D among pregnant is a disturbing situation. Vitamin D deficiency or insufficiency is now recognized as a public health problem. A local study reported that >90% Pakistani females of child bearing in certain geographical areas of country, are deficient in their plasma vitamin D concentration.¹⁷

It is interesting to note that although periodontal disease has been identified as a risk factor for low birth weight,¹⁸⁻²⁰ but the effectiveness of periodontal treatment such as non-surgical periodontal scaling on improving the birth outcomes has been inconsistent.^{8,20} This has made the management of periodontal diseases, among pregnant women, a challenge for dentists, obstetricians and related public health professionals.

Females with periodontal disease or hypovitaminosis D are at a higher risk of delivering low birth weight babies. Moreover, evidence also suggests that periodontitis and maternal hypovitaminosis D are associated with each other.²¹ Therefore, finding a simple and cost-effective nutritional intervention that could improve the pregnancy outcomes as well as periodontal and bone health would be a highly desirable endeavor. In this context, attempts have been made to use vitamin D supplementation among pregnant to improve periodontal,²² or maternal outcomes,²³ but without any major success.

No significant association of LBW with other variables could be detected in the present study (Table II). This is

probably due to low frequency of periodontal disease in the present sample. This is the most important limitation of the present study. Out of the 62 participants in the study, only seven had periodontal disease, and of which only four exhibited LBW. This can be explained by the fact that study participants were selected irrespective of their periodontal status. Other limitation of the present study includes a cross-sectional study design where no biological plausibility of maternal hypovitaminosis D or periodontal disease could be detected on the occurrence of LBW.

As an ethical responsibility of providing oral health education and required dental care to the study participants, a two-week dental camp was set up by the investigators at the study site after the conclusion of the study. Basic clinical dental care, such as teeth extraction and scaling, was provided free of cost to the study participants by trained dentist. The details of those services are documented elsewhere.²⁴

CONCLUSION

No association was observed between low birth weight and hypovitaminosis D among study participants. Similarly, maternal periodontal disease was also not found to be associated with the low birth weight.

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