

Evaluation of Relation between Maternal Periodontal Infection and Preterm Low Birth Weight: A Case- Control Study

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ABSTRACT:

Introduction: Newborns weighing under 2500 gram are referred to as 'Low Birth Weight' infants and delivery before 37 weeks of gestation is regarded as 'Preterm' delivery. Preterm Low Birth Weight of newborn is a major public health concern worldwide. A number of factors have been attributed to this complication of pregnancy, among which role of remote infection has got popularity recently. Now, periodontal disease is prevalent during pregnancy; and as a chronic infection, it has potential to induce preterm labor. Hence, it is important to introspect for the relationship between maternal periodontal infection and preterm labor; and to aid in prediction and prevention of premature birth.

Aim: To establish a correlation between maternal periodontal infection and PLBW.

Materials and Methods: The case-control study was conducted on 60 post-partum women in Kolkata during 2016-17. Mothers having preterm low birth weight newborn were referred to as cases, while mothers having full term, normal weight newborn were regarded as controls. Within 72 hours of delivery, the mothers were examined for periodontal status (OHI-S, PBI, PPD, CPI), with standard tools and protocols; and data of both group were then compared.

Results: all periodontal indices were found significantly higher in case population relative to control one, indicating that female having PLBW neonates, had worse periodontal status than female with healthy neonates.

Conclusion: There lies a definite correlation between maternal periodontal infection and PLBW.

Key-words: periodontal infection, preterm low birth weight.

INTRODUCTION

Preterm Low Birth Weight presents a major public health concern worldwide with high morbidity and mortality (WHO, 2008), as infants' birth weight is a vital determinant of chance of survival, and future growth and development [1]. Newborns weighing under 2500 gram are referred to as 'Low Birth Weight' infants and delivery before 37 weeks of gestation is regarded as 'Preterm labor. By definition, preterm labor, resulting in low birth weight of infant, (i.e. born before 37 weeks and measuring under 2500 gm.) is classified as PLBW [2].

The causative factors for PLBW can be divided broadly as 1) Maternal factors (systemic illness e.g. hypertension, chronic infection, short cervical length and complications of pregnancy etc.), 2) Fetal factors (multiple pregnancy, etc.), and 3) Placental (placenta previa etc.) [3]. In addition, previous history of PLBW, early/ old age for pregnancy, inter-pregnancy interval, socio-economic status and life style have been accepted as established risk factor [4-10]. Although almost 50% of PLBW are not found to have any established etiologic factor, and this has been an area of interest for the researcher since long.

Role of infection, even remote from the feto-placental unit, in causation of preterm labour, has got increasing concern recently. Chronic microbial infection, in genito-urinary tract or elsewhere in body, exerts its detrimental effect on pregnancy either indirectly by increase in production of inflammatory products, which shorten the gestational age; or directly by the toxic effect of pathogens by ascending route via vagina and endo-cervix; or by hemotogenous route [11, 12]. Any of these creates a pro-inflammatory condition in uterine tissue, resulting myometrial contraction, cervical effacement and premature rupture of membrane (PORM); and that induce preterm labor.

Periodontal disease is basically a chronic inflammatory disease of mixed microbial origin, which results prolong increase in a plethora of cytokines and prostaglandins level locally as well as systemically^[13, 14]. Therefore, according to the hypothesis, periodontal infection can possibly trigger preterm labour indirectly (through inflammatory products) or directly (by bacterial assault on amnion). In addition, periodontal infection is quite prevalent among pregnant women (as high as 30-100%) Relation between periodontal infection and different systemic condition; including cardio-vascular diseases like sub-acute bacterial endocarditis & ischemic heart disease, diabetes mellitus and CVA; has been already accepted^[15, 16]

In 1994, in the landmark animal study, Collins and co-workers reported a 25% reduction of birth weight on challenging pregnant hamster with *P.gingivalis* – a known periodontal pathogen^[17]. 2 years later, following a case-control study on 124 women, Offenbacher (1996) et al reported that mother's periodontal disease could produce 7 times increased risk of preterm low birth weight^[18]. After that, Williams et al (2000) explained the possible mechanism of causal relationship between maternal periodontal infection and preterm low birth weight^[19]. The next year, after a prospective study on 1313 female, Jeffcoat (2001) showed that mothers' periodontal disease had increased the risk for preterm labor; Madiano (2001) reported 2.9 folds higher prevalence of antibodies against some periodontal pathogens in cord-blood among premature newborns compared to term newborns; and Lopez (2001) showed that periodontal care during pregnancy significantly had reduced chance of preterm labour on 870 women^[20, 21, 22]. Although, in 2002, Davenport and co-workers, in a case-control study on a multi-ethnic study population of East London, found no association of mother's periodontal disease and preterm low birth weight^[23]. Various studies by different researcher have been made on the co-occurrence of maternal periodontal infection and preterm low birth weight, yet failed to establish a definite correlation, and the fact whether mothers' periodontal disease has bearing on preterm low birth weight remained controversial.

The present case-control study was designed to introspect the relation between maternal periodontal infection and PLBW of offspring, and it was conducted on post-partum women in Kolkata during 2016-17. The study was undertaken with the objectives to evaluate the periodontal status of mothers having PLBW newborns, and to evaluate the periodontal status of mothers having full term normal weight newborns, and to compare the periodontal status of both group, and to examine whether there has been a correlation (if any) between mothers' periodontal disease and PLBW.

MATERIALS AND METHODS

Study Design

The clinical study was conducted on 60 post-partum women, who gave birth at a private health care facility in Kolkata from July, 2015 to June, 2016. The subjects, within 72 hours of delivery, were randomly selected for the study, from maternity ward, after qualifying inclusion and exclusion criteria. Then they were divided into two groups, called 'case' and 'control'. Mothers, whose infants were weighing below 25000 gm. and born before 37 weeks, were defined as 'case', while mothers, whose infants were weighing 25000 gm. or above and born after 37 weeks were defined as 'control'. Total sample size was 60, which comprised of 30 cases and 30 controls (with 1:1 matched ratio). Each of them signed a written consent, after they had been explained the purpose of study and methods thoroughly.

- The inclusion criteria were as following:

1. Voluntary involvement of subjects
2. Age between 20-35 years

- The exclusion criteria were as following:

1. Who had undergone oral prophylaxis during the course of pregnancy
2. Female with established risk factor for PLBW, like:
 - a. Systemic illness like any inflammatory condition, hypertension, anemia, vitamin deficiency etc.
 - b. Genital tract or other local infection
 - c. Stress and anxiety, smoking and other life style related issues
 - d. Poor socio-economical level (monthly family income of Rs.20,000 was taken as benchmark)
 - e. Fetal developmental defect (as indicated in anomaly scan)
 - f. Short cervical length (as detected by ultra-sonography)
 - g. Placental pathology
 - h. Multiple pregnancy

3. Assisted pregnancy
4. Previous history of PLBW.

Periodontal Examination

Within 72 hours of delivery, the mothers were examined for 1) Simplified Oral Hygiene Index (OHI-S; Greene and Vermillion, 1964), 2) Papillary Bleeding Index (PBI; Muhlemann, 1977), 3) Probing Pocket Depth (PPD), and 4) Community Periodontal Index (CPI; Inamo et al, 1982) with standard tools and protocols, and data were recorded in a spread sheet.

Obstetric Outcomes

Duration of term (as measured in weeks from the first day of Last Menstrual Period to the date of delivery) and newborns' birth weight (as measured in grams within one hour of delivery) were collected from obstetrics' record. History regarding patient's socio-demographical status and life style (stress and anxiety level and tobacco or other habits) was obtained from subject through a questionnaire; and medical and gynecological details were elicited from obstetrician record as provided by hospital authority. Stress was assessed in HARS (Hamilton Anxiety rating scale).

Statistical Analysis

Statistical analyses were done using Stata software (Version 17.0, StataCorp, College Station, TX, USA). Interval metrics (pregnancy term, neonatal birth weight and PPD) were first examined for distributional normality using the Shapiro-Wilk test, and then these variables were subjected to independent two-sample t-tests for significance. Descriptive metrics for these parametric parameters were reported as Mean $\pm$ Standard Deviation (SD) along with minimum and maximum values. For ordinal metrics (OHI-S, PBI, and CPI), differences between the Case and Control cohorts were evaluated by the Wilcoxon rank-sum (Mann-Whitney U) test. Non-parametric datasets were detailed via Medians, Interquartile Ranges (IQR), Means, and ranges.

Bivariate association matrices were generated for determining directional proportionality across the combined sample (N = 60), Pearson product-moment correlation (r) was used to test associations with interval data (PPD), while Spearman's rank correlation coefficient (ρ) was applied to evaluate the ordinal datasets (OHI-S, PBI, CPI) against continuous independent variables, i.e. term of pregnancy and neonatal birth weight. All statistical testing was two-tailed, and statistical significance was established a priori at $p < 0.05$.

RESULTS

Total 60 post-partum women, comprising 30 'cases' and 30 'controls', were included in the study. The independent two-sample t-test revealed, the control group had a significantly longer term of pregnancy over case group (37.67 $\pm$ 0.66 weeks vs. 34.77 $\pm$ 1.55 weeks, $t = 9.44$, $p < 0.001$; Table 1, 7). The control mothers also reported a significantly higher newborns' birth weight than case cohort (2788.33 $\pm$ 207.07 grams vs. 2132.50 $\pm$ 329.78 grams, $t = 9.22$, $p < 0.001$; Table 2, 7), matching the assigned grouping criteria. In addition, newborns' birth weight was found significantly proportional to their terms of pregnancy. The obstetric outcomes of both of groups has been presented in Figure. 1.

The periodontal parameters (PPD, PBI, OHI-S, CPI) were uniformly and significantly worse in case mothers than control mothers. As independent two-sample t-test showed, the mean probing pocket depths were significantly deeper in case group compared to the Control group (3.94 $\pm$ 0.75 mm vs. 3.04 $\pm$ 0.59 mm, $t = -5.14$, $p < 0.001$; Table 3,7) Similarly, the Mann-Whitney U test demonstrated, the case group had significantly higher median Papillary Bleeding Index than control group (2.37, IQR: 0.54 vs. 1.44, IQR: 1.12; $z = -4.85$, $p < 0.001$; Table 4, 7). The median Oral Hygiene Index- simplified score of case group was nearly double of that of control group (3.08, IQR: 0.83 vs. 1.66, IQR: 1.50; $z = -5.23$, $p < 0.001$; Table 5, 7). The case group also reported significantly higher median Community Periodontal Index score relative to control group (3.00, IQR: 0.16 vs. 2.16, IQR: 1.67; $z = -3.84$, $p = 0.001$; Table 6,7). These, all together, indicate that the 'case' mothers had significantly worse periodontal status compared to 'control' mothers; or in other words, periodontal disease was more prevalent, as well as severe, in 'mothers with PLBW delivery' relative to 'mothers with normal-weight, term delivery'. Figure 2 shows graphical presentation of all the periodontal parameters of both of the groups.

Bivariate correlation matrices across the entire sample (N = 60) demonstrated reliable, statistically significant negative correlations between all measured maternal periodontal parameters (PPD, PBI, OHI-S and CPI) and both of

the pregnancy outcomes (term of pregnancy and newborns' birth weight). In addition, all periodontal indices showed proportionality among themselves.

Pearson's correlation test, applied for interval variable like PPD, showed that deeper Probing Pocket Depths were significantly correlated with shorter pregnancy terms ($r = -0.503$, $p < 0.001$) and lesser newborn birth weights ($r = -0.356$, $p < 0.001$; Table 8). Spearman's correlation test, used on the ordinal variables like PBI, OHI-S and CPI, revealed an even stronger inversely proportional relationship (Table 8). The OHI-S exhibited the strongest inverse proportionality with gestational length ($p = -0.637$, $p < 0.001$) and birth weight ($p = -0.540$, $p < 0.001$; Table 8). Significant inverse proportionality was also verified for the gingival bleeding on probing (PBI vs. Term: $p = -0.580$, $p < 0.001$; PBI vs. Newborn Birth Weight: $p = -0.484$, $p < 0.001$) and generalized periodontal status (CPI vs. Term: $p = 0.489$, $p < 0.001$; CPI vs. Newborn Birth Weight: $p = -0.400$, $p < 0.001$; Table 8). Collectively, these confirm that as mothers' periodontal status worsen, their pregnancy outcomes, i.e. newborn birth weight and pregnancy duration reduce proportionally.

Table 1: Comparison of 'Term of pregnancy' (in Weeks) between study groups

Group	Mean	Std. Err.	Std. Dev.	95% Conf. Interval.	
Control (n=30)	37.67	0.12	0.66	37.42	37.91
Case (n=30)	34.77	0.28	1.55	34.19	35.34
Diff.	2.9	0.31		2.29S	3.51

Table 2: Comparison of 'Newborn's birth weight' (in Gm.) between study groups

Group	Mean	Std. Err.	Std. Dev.	95% Conf. Interval.	
Control (n=30)	2788.33	27.80	207.07	2711.01	2865.65
Case (n=30)	2132.50	60.20	329.78	2009.36	2255.64
Diff.	655.83	71.09		513.52	798.14

Table 3: Comparison of 'Probing Pocket Depth (PPD) in mm. between study groups

Group	Mean	Std. Err.	Std. Dev.	95% Conf. Interval.	
Control (n=30)	3.04	0.11	0.59	2.82	3.26
Case (n=30)	3.94	0.14	0.75	3.66	4.22
Diff.	0.90	0.17		1.24	-0.55

Table 4: Comparison of 'Papillary Bleeding Index' (PBI) between study groups

Group	Mean	Median	Inter-quartile range	Min.	Max.
Control (n=30)	1.23	1.44	1.12	0	2.35
Case (n=30)	2.22	2.37	0.54	0.69	3.08
Diff.	0.99	0.97			

Table 5: Comparison of 'Simplified Oral Hygiene Index' (OHI-S) between study groups

Group	Mean	Median	Inter-quartile range	Min.	Max.
Control (n=30)	1.61	1.66	1.5	0.33	2.66
Case (n=30)	3.06	3.08	0.83	0.83	4.5
Diff.	1.45	1.42			

Table 6: Comparison of 'Community Periodontal Index' (CPI) between study groups

Group	Mean	Median	Inter-quartile range	Min.	Max.
Control (n=30)	1.96	2.16	1.67	0	3.16
Case (n=30)	2.88	3	0.16	0.5	3.83
Diff.	0.92	0.84			

Table 7: Comprehensive presentation of all obstetric outcomes and periodontal parameters between study groups

Variables	Case (n=30)	Control (n=30)	Statistical test value	p-value ***
Pregnancy Term (Week) *	34.77 ± 1.55 (30 - 36)	37.67 ± 0.66 (37 - 39)	t = 9.44	<0.001
Weight (Gm.) *	2132.50±329.78 (1150 - 2450)	2788.33±207.07 (2500 - 3500)	t = 9.22	<0.001
PPD (mm.) *	3.94 ± 0.75 (2.21 - 5.01)	3.04 ± 0.59 (2.25 - 3.98)	t = - 5.13	<0.001
PBI**	2.37 (0.54) 2.22 ± 0.62 (0.69 – 3.08)	1.44 (1.12) 1.23 ± 0.67 (0 – 2.35)	z = - 4.85	<0.001
OHI-S**	3.08 (0.83) 3.06 ± 0.96 (0.33 – 4.50)	1.66 (1.50) 1.61 ± 0.76 (0.33 – 2.66)	z = - 5.23	<0.001
CPI**	3.00 (0.16) 2.88 ± 0.82 (0.50 – 3.83)	2.16 (1.67) 1.96 ± 1.02 (0 – 3.160)	z = - 3.84	<0.001

*Interval data, presented as Mean ± SD (Min. – Max.), evaluated via independent two-sample t-test.

** Ordinal data, presented as Median (Inter-quartile range), Mean ± SD (Min. – Max.), evaluated by Mann-Whitney U test

*** Statistically highly significant at $p \leq 0.001$

Table 8: Bivariate correlation matrix mapping maternal periodontal parameters against obstetric outcomes (N=60)

Periodontal variables	Proportionality to Term of Pregnancy	Proportionality to Newborn's Birth Weight
PPD	$r = -0.50, p < 0.001$	$r = -0.36, p < 0.001$
PBI	$\rho = -0.58, p < 0.001$	$\rho = -0.48, p < 0.001$
OHI-S	$\rho = -0.64, p < 0.001$	$\rho = -0.54, p < 0.001$
CPI	$\rho = -0.49, p = 0.001$	$\rho = -0.40, p < 0.001$

r = Pearson product-moment correlation coefficient, ρ = Spearman's rank correlation coefficient, Statistically highly significant at $p < 0.001$

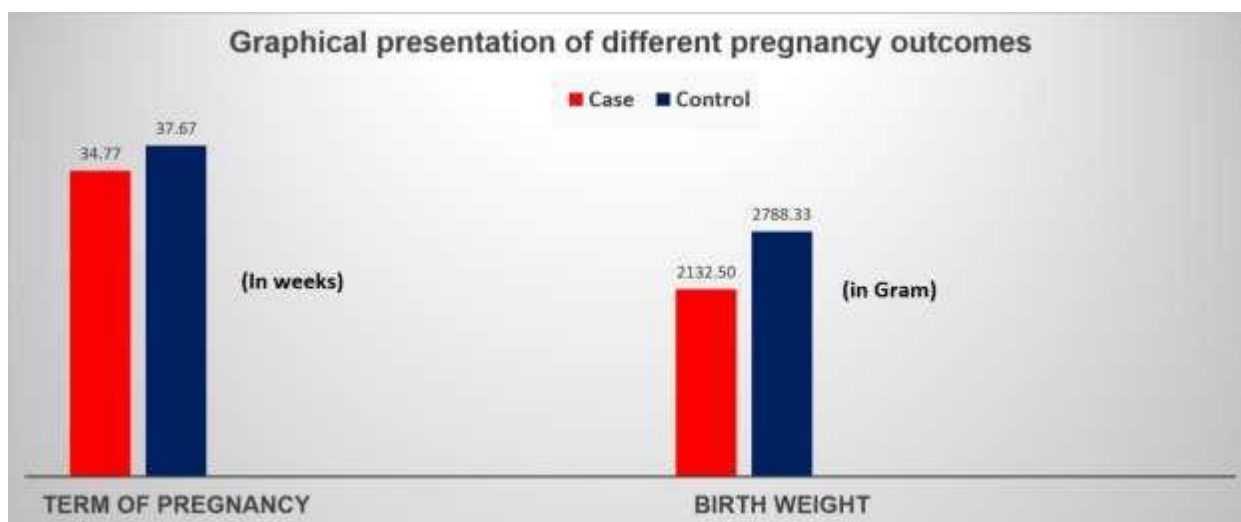


Fig.1: Comparison of obstetric outcomes between two groups.

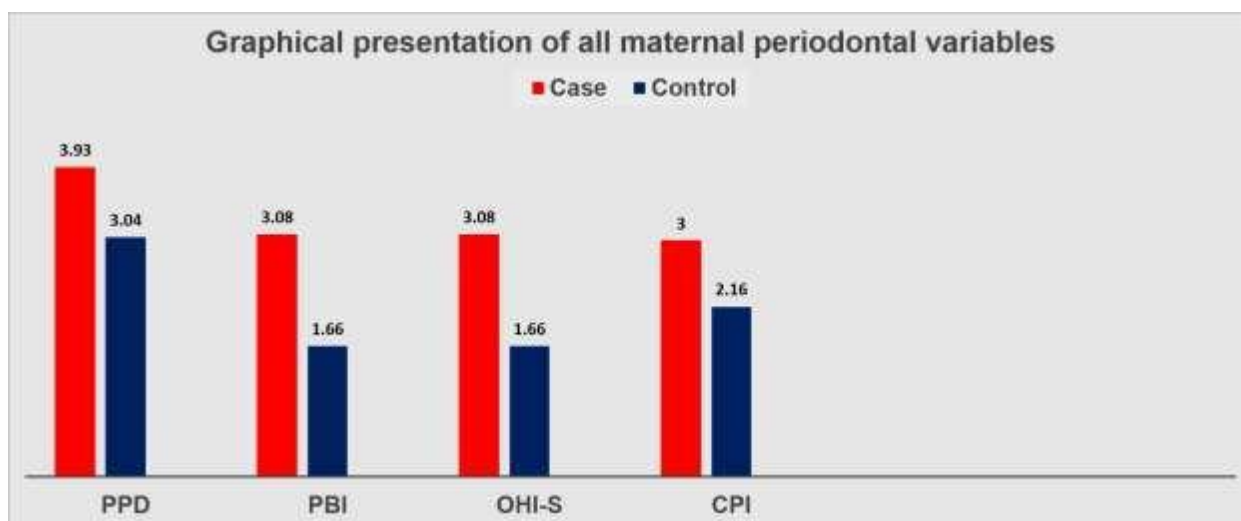


Fig. 2: Comparison of periodontal variables between two groups.

DISCUSSION

The purpose of the study was to examine the relation between maternal periodontal infection and preterm low birth weight of newborn. Hence, within 72 hours of delivery, 60 post-partum women were recruited for the study including 30 cases and 30 controls (1:1; matched ratio). Mothers, who gave birth of preterm low birth weight newborn, were enrolled as 'cases'; while mothers, who had full-term normal weight neonates, were enrolled as 'controls'. Both of the groups were examined for periodontal status, and information on their outcomes of pregnancy were collected from hospital records, and both set of data were subjected to statistical analysis.

Hypothetically, mothers' periodontal infection, being a local chronic inflammatory disease, leads to a systemic pro-inflammatory state, inducing preterm labor and low birth weight. Now, gingival bleeding and pocket depth present reliable estimate of current inflammatory status of gingiva. Again, oral hygiene bears a direct causal relationship with severity and occurrence of periodontal disease, as plaque represent the prime etiologic factor for periodontal infection. In this study, the periodontal status was evaluated by 1) gingival bleeding on probing, and 2) pocket depth; 3) oral hygiene (in terms of plaque and calculus) and 4) periodontal disease burden. PBI was used to assess gingival bleeding on probing; and OHI-S and CPI were used for oral hygiene and periodontal disease respectively for simplicity, acceptability, validity and uniformity.

The results showed, all periodontal indices were significantly higher in case mothers than control mothers. This indicated a more prevalent, as well as severe distribution of periodontal disease in mothers with PLBW infants, relative to mothers with full-term, normal weight infants. It implied that mothers having poor periodontal health are more likely to have premature deliveries; which is in agreement with Offenbecher et al. (1996) and others; while in disagreement with Davenport (2002) and others^[18, 23]. Though all the subjects, irrespective of case-control status, showed an increased tendency of bleeding, which was attributed to altered temporal hormone profile (Tilakaratne et al, 2000)^[24].

Till-date research studies give conflicting review on the relation between maternal periodontal infection and PLBW. Davenport (1998)^[25], in a case-control study on 800 post-partum female, assessing gingival bleeding, reported that mothers' periodontal disease increases the risk of PLBW. In similar study design, Offenbecher (124 women, U.S.A; 1996), Dasanayeke (110 women, Thailand; 1998), Radnai (85 women, Hungary; 2004) found similar results^[18, 26, 27]. Though, in another case-control study, Davenport himself reported no relation between maternal periodontal infection and PLBW^[23]. Lunardelli (215 women, Brazil; 2005), Moore (154 women, UK; 2005), Buduneli (181 women, Turkey; 2005), Noack (101 women, Germany; 2005) also found no significant relation between two entity^[28-31]. These contradictory findings can be attributed to the possible genetic variation or socio-economical disparities among study population; or other unnoticed confounding factors^[32].

As preterm labor is multi-factorial in causation, it was important to control the confounding factors. Maternal systemic illness (like hypertension) and condition (vitamin/ iron deficiency), any infection during pregnancy, cervical incompetency, previous history of PLBW etc. represent established risk factors for PLBW, and could act as confounder for this study^[9-12]. Hence, mothers with such conditions were not included in the study. Multiple pregnancy or assisted pregnancy also contribute to birth prematurity; and hence, such cases also were excluded from the study. In addition, subjects, who underwent any form of periodontal therapy during the course of pregnancy, were not taken into our study; because it could influence of periodontal status on examination. Known case of anxiety or depression or substance abuse, and mothers belonging to poor socio-economical status were removed from the study; because all of those contribute to adverse pregnancy outcomes^[6,7].

This study had some limitation also. Firstly, bacteriological study to examine any common microbial source of the both the pathology (i.e., periodontal infection and chorio-amnionitis) was not performed. Secondly, immunological study on inflammatory markers were also not conducted. Thirdly, mothers were not questioned on oral sexual practice, as bacteria from oral cavity of male partner could transmit to vagina and cervix and fetoplacental unit directly through ascending route by oro-genital contact, bypassing the proposed descending route^[33]. Finally, sample size wasn't ample enough to firmly establish a causal relationship. A prospective, multi-centric, controlled study with larger sample size addressing microbiological and inflammatory factors could produce more conclusive results.

CONCLUSION

Our study lends credence to the hypothesis that mother's periodontal status is linked to outcomes of pregnancy, as it influences term of pregnancy and weight of newborn, and there lies a definite correlation between periodontal disease and preterm low birth weight; but further prospective, multi-centric, controlled study with larger sample size addressing microbiological and inflammatory factors are required to establish the causal relationship firmly. Understanding this relationship is crucial to unveil a possible risk factor for preterm labor, to help in prediction by pre-natal oral screening; and to aid in prevention, thereby reducing the risk for the mortality and morbidity, and health care burden related to premature birth. Though our study was not designed to determine whether periodontal therapy during pregnancy would reduce risk of preterm labor, it is justified to ask the expecting mothers to maintain a standard oral health and hygiene. As an oral health care provider, it becomes a dentist's duty to create awareness among expecting mothers as well as the obstetric care givers, and motivate for maintenance of oral hygiene, and mandatory pre-natal periodontal screening, and also non-surgical periodontal therapy (when needed) to avoid as much as possible such adverse pregnancy outcomes and its consequences.

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