

*Evaluation of periodontal disease as a risk factor for preterm birth and low birth weight in pregnant women attending the Gineco-obstetrics service of the Amistad Mexico-Nicaragua Hospital in the municipality of Ticuantepe in the first half of 2016*

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## ABSTRACT

Preterm Birth (PP) and Low Birth Weight (LBW) is a serious problem in developed and developing countries, as it causes 35% of neonatal deaths and is the second cause of death only surpassed by The Pneumonia. In Nicaragua, it is estimated that for the year 1990 to 2010, the preterm birth rate was 9.3% for every 100 live births. This phenomenon has been linked to several infectious processes that could cause an inflammatory response in the amniotic fluid and cause PP and LBW; Of these infections, Periodontal Disease (PD) is not exempt. The objective of this study is to evaluate periodontitis as a risk factor for causing preterm birth and low birth weight. For the study, 29 pregnant women were examined, who were classified into four experimental groups according to type of PD. Two clinical examinations were performed; The first one was prior to dental treatment and the second examination, after treatment and before the 35th gestational week.

The results show that, 89.7% of the patients presented moderate periodontitis and 10.3% had mild periodontitis. 27.6% had PP and 20.7% had LBW. There was no statistically significant relationship between PD and periodontitis on PP ( $p=0.24$ ) or LBW ( $p=0.81$ ). These results indicate that periodontal disease is not a causal or risk factor for PP and LBW in pregnant women attending the Amistad México-Nicaragua hospital.

## INTRODUCTION

Preterm birth and low birth weight are pathologies that occur in most cases simultaneously and cause 35% of neonatal deaths globally, becoming the second cause of death of neonates only surpassed by pneumonia. Preterm birth is defined as the birth of the product before 37 weeks of gestation or 259 days and describes the low birth weight of any child born weighing less than 2500 grams (Beck, et al., 2010).

On the other hand, periodontal disease is one of the most common diseases and the major cause of tooth loss and edentulism in adult patients. It is a pathology with numerous factors involved in its development as microbiological factors, environmental and systemic factors such as pregnancy, which due to the hormonal changes it causes, induces the worsening of the inflammatory response in the periodontium. Beck et al. (2010) affirm that periodontal disease is a possible cause of preterm and low birth weight infants. This association is attributed to the invasion of periodonopathogenic bacteria that travel via hematogen to the amniotic fluid where they provoke an inflammatory response.

With the objective of evaluating periodontal disease as a risk factor for preterm birth and low birth weight, in pregnant women attending the Gineco-obstetrics service of the Amistad Mexico - Nicaragua Hospital in the municipality of Ticuantepe, in the first semester of 2016, the design and execution of a quasi-experimental, observational and analytical study was required.

Four types of treatments and 10 statistical replicates were designed in each of them and the research hypothesis was tested: Periodontal disease could be a risk factor for preterm birth and low birth weight in pregnant women attending to the Gineco-obstetrics service of the Hospital Amistad Mexico-Nicaragua in the first half of 2016.

The results of this study are of great value to the hospital and the National Health System, because it was shown the non-relation of periodontal disease to be a risk factor for preterm birth and low birth weight, so that the System of Health reinforce and prioritize the care and management of the oral health of pregnant women in order to guarantee and improve the periodontal health status of pregnant women. Besides, of being a contribution to the scientific production of the country.

## **MATERIAL AND METHOD**

This prospective, quasi-experimental and analytical study was carried out in the Dental Clinic of the Amistad Mexico-Nicaragua Hospital in the municipality of Ticuantepe, Managua, Nicaragua, in collaboration with the Gineco-obstetrics service, from January to June 2016. A total of 29 pregnant women between the ages of 18 and 35, who did not present any type of drug, alcohol or cigarette addiction, had more than 20 teeth in their mouths and gave their consent to be part of the study were taken into account. They were distributed in 3 different experimental groups, designed from the diagnosis of each patient's periodontal disease. Data were collected through clinical inspection, using a periodontogram taken from Ramseier (2010) and modified to be used in non-digital (printed) format. They were annexed sections that include the socioeconomic data of the patients, periodontal diagnosis and boxes referring to the presence of preterm birth and low birth weight. In addition, Mühlrmann's gingival bleeding index was added.

A general periodontal examination of the oral cavity was performed, and a periodontal probe of William and periodontogram was used, assessing the insertion level, presence of periodontal pocket, gingival margin and bleeding at the catheter. Three measurements (distal, medial and mesial) were made on each face of each piece (buccal and lingual / palatal). First, the probe was introduced into the gingival sulcus of the distal portions of each piece through its vestibular face (until progressing to the mesial area), the value was obtained from the gingival margin to the bottom of the groove, taking into account a measurement Greater than three millimeters, this was considered as a periodontal pocket, then the catheter was removed by making a slight contact

with the tooth until the amelo-cementary union was found and the gingival margin was always taken as reference, the measurement of the margin was scored on the data sheet. (Being negative or positive).

To obtain the measure of clinical insertion loss, the measurement of the gingival margin was subtracted from the probing depth or added when the values were negative. The measurement of bleeding was done after the two procedures described above were made to each tooth. For the measurement of dental mobility, the mirror handle and the index finger of the left hand were used, applying lingual / palatal vestibular forces for each tooth. Once the measurements were obtained, the diagnostic criteria for each case were defined according to the clinical criteria presented by Armitage (1999).

## RESULTS

A total of 29 pregnant women between 18 and 35 years old were registered, with an average of 23.5 years, of which 62% belong to the rural area and 38% to the urban area. 17% have had schooling reaching primary school; 14% of the patients studied have obtained the professional degree and 69% have completed secondary education and obtained the bachelor's degree.

To assess the periodontal health status, contingency tables were drawn, which show that of the 29 cases studied, 89.7% of the patients had moderate periodontitis and 10.3% of the patients had mild periodontitis. Of the total number of patients with moderate periodontal disease, 55.5% came from rural areas. When interpreting the hypothesis test, this was not statistically significant  $P = 0.862$ .

Following the analysis of the data and correlating the variables, marital status and periodontal disease prior to dental treatment, it was determined that 41% of the patients attended belonged to a stable civil union; At the same time, the prevalence of moderate periodontal disease was 41.4%; 24.1% of the patients were married, of whom 10.3% had moderate periodontitis and 13.8% had mild periodontitis. Of the unmarried patients, all presented moderate periodontitis, which represented 34.5% of the global total. These data were statistically significant ( $p=0.5$ ).

With regard to scholarship, no statistically significant correlation was found between the variables under study. Of the total number of women studied, 17.2% reached primary school; of the patients, 3.4% had mild periodontitis and 13.8% had moderate periodontitis. Women achieving high school accounted for 69% of the global total; 62.1% have moderate periodontitis and only 6.9% have mild periodontitis.

Those women who reached a professional career (13.8%) had moderate periodontal disease (13.8%). With regard to periodontal disease and preterm delivery, 50% had preterm birth and the other 50% did not. In the moderate PD classification, 44.4% presented preterm delivery and 55.6% did not present it. Of the healthy patients (14 patients), only 7.1% (corresponding to one patient) presented PP and 92.9% did not present the study phenomenon (see Table 1).

Table 1. Contingency table type of periodontal disease after periodontal treatment \* preterm birth as a dichotomous variable.

			Preterm birth		Total
			Yes	No	
Type of periodontal disease after periodontal treatment	Mild	Re-count	3	3	6
		%	50,0%	50,0%	100,0%
	Moderate	Re-count	4	5	9
		%	44,4%	55,6%	100,0%
	Healthy	Re-count	1	13	14
		%	7,1%	92,9%	100,0%
Total		Re-count	8	21	29
		%	27,6%	72,4%	100,0%

For the weight of the baby at birth, the mean weight in grams was 3171 g. 2.5% of patients with mild periodontal disease had no LBW and 50% did. Those belonging to the diagnosis of moderate periodontitis, 11.1% had LBW and 85.7% did not; 14.3% of the patients diagnosed as healthy did give birth to children with LBW; However, 79.3% did not deliver children with LBW (see Table 2).

Table 2. Contingency chart type of periodontal disease after periodontal treatment \* low birth weight.

			Dichotomous low birth weight		Total
			Yes	No	
Type of periodontal disease after periodontal treatment	Mild	Re-count	3	3	6
		%	50,0%	50,0%	100,0%
	Moderate	Re-count	1	8	9
		%	11,1%	88,9%	100,0%
	Healthy	Re-count	2	12	14
		%	14,3%	85,7%	100,0%
Total		Re-count	6	23	29
		%	20,7%	79,3%	100,0%

Subsequently, we checked the parameters of the variables dependent, PP and weight of the baby at the time of birth. To verify the normality of the data, it was applied the Shapiro-Wilks test, which showed normality of the data, with a  $p=0.36$ , compared with the  $\alpha = 0.05$  is non-significant and the null hypothesis is assumed for both variables (Data are normal). The Diagnosis of Homogeneity of Variance of treatments residues by the Levene Test,  $p=0.99$ , greater than the critical level of comparison  $\alpha = 0.05$ . This analysis gave “non-significant”, demonstrating the homogeneity of residue variance.

The analysis of variance performed between variables, periodontal disease after treatment Vs LBW and PP, determines whether or not there is a cause-effect relationship of periodontal disease

as a cause of low birth weight and preterm delivery.

There is no significant effect of post-treatment periodontal disease on the response variable underweight at birth and preterm delivery, which is evidenced with  $p=0.81$  and  $p=0.24$  respectively (random probability of occurrence), which was found to be higher than the critical level of comparison,  $\alpha = 0.05$ . Therefore, the null hypothesis is accepted. This means that the statistical response is not significant, which shows that there is no cause-effect relationship of periodontal disease on PP and LBW (see Table 3 and 4).

Table 3. Analysis of the Variance of periodontal disease and preterm birth

F.V.	SC	gl	CM	F	p-value
Model	6,43	2	3,22	1,47	0,2474
Periodontal-Desease-PosTreat	6,43	2	3,22	1,47	0,2474 ns
Error	56,73	26	2,18		
<b>Total</b>	<b>63,16</b>	<b>28</b>			

Table 4. Analysis of the variance, the variable periodontal disease and low birth weight

F.V.	SC	gl	CM	F	p-value
Modelo.	157715,66	2	78857,83	0,21	0,8159
Periodontal-Desease-PosTreat	157715,66	2	78857,83	0,21	0,8159 ns
Error	9995569,65	26	384444,99		
<b>Total</b>	<b>10153285,31</b>	<b>28</b>			

To determine the effect of the severity of periodontal disease on the PP and LBW response variables, orthogonal comparisons of the different categories were performed. It was found that for preterm delivery, the contrast periodontal disease “mild Vs moderate” was statistically non-significant, as was the “moderate Vs Healthy” contrast, which further corroborated that preterm delivery does not depend on type or absence of periodontal disease (see Table 5).

Table 5. Table detailing orthogonal contrasts of the categories of periodontal disease and preterm birth.

Periodontal-Desease-PosTreat	Contrast	E.E.	SC	gl	CM	F	p-value
"Mild VS Healthy"	1,08	0,72	4,89	1	4,89	2,24	0,1466 ns
"Moderate VS Healthy"	0,82	0,63	3,71	1	3,71	1,70	0,2036 ns
<b>Total</b>	<b>6,43</b>	<b>2</b>	<b>3,22</b>		<b>1,47</b>	<b>0,2474</b>	

On the other hand, the statistical analysis was also performed through orthogonal contrasts of the variables periodontal disease Vs underweight at birth. After applying the contrasts, a  $p=0.67$  was obtained for the contrast “Mild Vs Moderate” and  $p=0.76$  for “Moderate Vs Healthy”. Similarly, it can be seen that the type and degree of periodontal disease is a factor cause for low birth weight (see Table 6).

Table 6. Contrasts of periodontal disease and low birth weight

Periodontal-Disease-PosTreat	Contrast	E.E.	SC	gl	CM	F	p-value
"Mild VS Healthy"	129,76	302,55	70720,24	1	70720,24	0,18	0,6715 ns
"Moderate VS Healthy"	79,46	264,91	34589,42	1	34589,42	0,09	0,7666 ns
<b>Total</b>			157715,66	2	78857,83	0,21	0,8159

## DISCUSSION

Many studies, such as Offenbacher, Jared, and O'Reilly, (1998), suggest that Gram-negative pathogens from periodontal disease and the association of endotoxins and maternal inflammatory mediators are related and affect fetal development.

The most reasonable theory suggested by this relationship is that maternal infections may create an excessive production of proinflammatory cytokines and prostaglandins, which have been established as biochemical mediators of normal birth (Keelan et al., 1999). Observations of high levels of Prostaglandin E2 and tumor necrosis factor  $\alpha$  (*TNF $\alpha$* ) make these factors constitutive and reproducible of preterm birth and low birth weight, in clinical or subclinical genitourinary infections, as another type of infection of unknown origin. The possibility that periodontal disease could constitute a remote maternal infection could adversely affect the development of preterm birth and low birth weight, since hormonal factors increase the incidence and severity of gingival diseases (Newman, Taikie, Klokkevold and Carranza, 2010).

Although periodontal disease is no different than another type of infection, it is likely that bacteria in the oral cavity could contribute to the development of adverse perinatal alterations, within these pathogens include those who are opportunistic such as *Prevotella*, *Porphyromonus*, *Bacteroides*, and species of *Peptostreptococcus* and which have also been detected in the lower genital tract and in pelvic infections in the form of bacterial vaginosis. This leads to think and extrapolate that oral microbial species could be associated and have a role in the process of childbirth through the activation of inflammatory processes.

Goldenberg, Hauth and Andrews (2000) suggest that the routes of dissemination of infection include the ascending route through the vagina and cervix, hematogenous dissemination, the retrograde route from the peritoneal cavity and accidental inoculations during intrauterine processes such as amniocentesis. The hematogenous route is the most common route in terms of bacterial spread and has been related to preterm birth and low birth weight (Ercan, et al, 2013); March of Dimes; PMNCH; Save the Children; WHO (2012). Using an animal model, Collins, Windley, Arnold, and Offenbacher (1994) inoculated *P. Gingivalis* into the subcutaneous tissue of a hamster, finding that the fetus weight was significantly affected compared to the control group, as well as the Levels of *TNF- $\alpha$*  and PGE2 at the site of inoculation.

The present study was carried out in 29 pregnant females, initially grouped in T1, T2, T3 and T4 treatment, with the objective of applying different periodontal therapies to eliminate periodontal disease, if it existed, and then make comparisons of experimental treatments. However, these groups were modified, since the complete elimination of the disease was not achieved in all the

patients that comprised the repetitions of each treatment, therefore, it was necessary to regroup and accept as an experimental treatment the type of periodontitis (mild, Moderate, severe) or their absence (healthy) obtained from the second clinical examination.

Authors such as Kothiwale and Panwar (2011) have reported a direct cause-effect relationship between the inflammatory status of gingival tissue and preterm and low birth weight infants. The results of this research have a direction opposite to the one proposed by this author, since his study evaluates the inflammatory state of the gingiva, which could vary from a gingivitis to a gingival enlargement, on the contrary, this study evaluates clinically and specifically the type of periodontal disease. It was important to perform this type of measurement since this allowed an approach to the type of periodontitis, as well as to the bacterial agent. Studies such as that of Ercan et al. (2013) reflect a relationship of pathogens such as *P. Gingivali*, *F. Nucleatum*, *T. Forgythia*, as pathogens that frequently invade amniotic fluid and produce an inflammatory response that could lead to PP, at the same time, these pathogens of the oral cavity are related to the development of localized aggressive periodontitis, which is why periodontitis was classified according to its severity in this study.

Zermeño et al. (2011), in their research present similar results. They found no association between periodontitis and preterm birth. It is of interest to mention that in this study periodontal treatment was applied to the patients to make measurements and comparisons, trying to avoid the effect of bacteria on the weight and time of birth of the babies, so, after this procedure between 20 and 28 weeks), no case of severe periodontitis was present. This diagnosis is related to the presence of bacteria, described by Ercan and others (2013), which could cause preterm birth and low birth weight, activating cytokine factors related to the chain of events for preterm delivery proposed by Lookwood and Kuczynsky (1999) and Gutiérrez and Pareja (2010).

Associations of factors such as maternal age, systemic diseases, alcohol consumption or drugs are factors reported as risk factors for preterm delivery and low birth weight. This study included 29 healthy women aged 18 to 32 years, which facilitated the analysis of the disease as a cause of preterm birth and low birth weight, since variables that could cause bias in the research were excluded. The objective of this work was to determine periodontal disease as a cause of LBW and PP, however, it is important to delve, from a microbiological point of view, and to detail the contamination pathways of bacteria that are related to severe periodontitis, and that this condition, through tissue damage and increased vascular permeability, could cause hematogenous dissemination and be the cause of data reported in the studies of Offenbacher, Jared, and O'Reilly (1998), Goldenberg, Hauth, and Andrews (2000), Keelan, et al. (1999).

## CONCLUSIONS

89.7% of patients had moderate periodontitis and 10.3% of patients had mild periodontitis. Of the total number of patients with moderate periodontal disease, 55.5% came from rural areas. The diagnosis that prevailed according to the marital status and academic level was that of moderate periodontitis. These findings were not statistically significant and did not indicate a cause-effect relationship.

A frequency of 20.7% of children with low birth weight and 28% of children born prematurely was reported.

No significant cause-effect relationship was found to determine periodontal disease as a causal factor of preterm birth and low birth weight, with  $p=0.2474$  and  $p=0.8459$ , respectively.

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