Original article

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The Significance of Bacterial Vaginosis and Periodontal Infection as Predictors of Preterm Labour

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Abstract

Context: original. *Aims and Objectives:* To study the relationship between bacterial vaginosis in third trimester and preterm labor. To study the relationship between periodontal infection in third trimester and preterm labor. To find out the incidence of bacterial vaginosis and periodontal infection in antenatal patients at PGIMSR, New Delhi. *Settings and Design:* The prospective case control study. *Methods and Material:* A total of 500 patients were enrolled for the study. The incidence of Bacterial vaginosis and periodontal infection was calculated for the hospital. Out of these 500 patients, 200 patients were randomly selected and divided into 4 groups. Group 1(n = 50): Patients with no evidence of bacterial vaginosis and periodontal infection. Group 2(n = 50): Patients positive for periodontal infection. Group 3 (n = 50): Patients positive for bacterial vaginosis Group 4(n = 50): Patients positive for periodontal infection and bacterial vaginosis. Group 1 was the control group with sample size of 50 patients. Groups 2, 3, 4 were compared with the control group and correlated to the preterm birth and perinatal outcomes. *Results:* 14(29.2%) patients in group 1 had PROM, 29(59.2%) patients in group 2 had PROM, 15(31.3%) patients in group 3 had PROM and 19(40.4%) patients in group 4 had PROM. The difference in all the groups was statistically significant ($p<0.05$) (Table 6, Figure 6). *Conclusion:* Significant correlation is seen between periodontal infection and preterm labor & preterm premature rupture of membranes. Bacterial vaginosis is not found to be associated with preterm labor. Both of them have no significant correlation with perinatal outcomes.

Keywords: Bacterial Vaginosis; Periodontal Infection and Preterm Labour.

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Introduction

Preterm birth (PTB) is defined as that occurring before 37 weeks of gestation [1]. It occurs in 11% of all pregnancies and is responsible for the majority of the neonatal deaths and nearly one half of all cases of congenital neurological disability, including cerebral palsy [2,3]. Although all births before 37 weeks of gestation are considered premature, births before 32 weeks of gestation (2% of all births) account for most neonatal deaths and disorders. Important risk factors for spontaneous preterm birth include multiple gestation, black race, low socioeconomic status, low maternal body mass index. Urogenital infections (e.g. chorioamnionitis, asymptomatic bacteriuria and bacterial vaginosis) and infection at other sites (e.g. appendicitis, pneumonia and periodontal disease) have all been associated with preterm birth [3-5]. Bacterial vaginosis (BV) is a most common polymicrobial lower genital tract infection characterized by an overgrowth of several anaerobic or facultative bacteria and with a reduction or absence of lactobacillus colonization. It is a complex alteration of vaginal ecosystem where physiological lactobacilli dominant flora is replaced by an over growth of mixed flora

with high concentration of anaerobic bacteria [6]. The prevalence of bacterial vaginosis ranges from 4 to 64%, depending on the racial, geographic and clinical characteristics of the study population. In asymptomatic women, the prevalence varies from 12 to 25%, and similar percentages are observed in pregnant women. The most common symptoms are a thin, homogenous, vaginal discharge and a malodorous fishy smell. Colour and amount varies from patient to patient [7]. Periodontal disease has been identified as a risk factor for heart disease, rheumatoid and other medical condition perhaps through pathways of increased systemic inflammation [8]. Periodontal disease is characterized by low grade infection of gums and tooth support structure by gram negative predominantly anaerobic bacteria. This result in a built up of endotoxins and cytokines which results in tooth loss and bone destruction [9]. The study aims at analyzing the correlation between the bacterial vaginosis and periodontal infection in 3rd trimester of pregnancy with preterm labour and to estimate the incidence of both in the antenatal patient population reporting to PGIMSR. The delivery and the perinatal outcomes in cases will be compared with the controls and also between the patients who will complete the treatment after diagnosis with those who will not be adequately treated because of the onset of preterm labour.

Subjects and Methods

A total of 500 patients were enrolled for the study. The incidence of Bacterial vaginosis and periodontal infection was calculated for the hospital. Out of these 500 patients, 200 patients were randomly selected and divided into 4 groups. Group 1(n = 50): Patients with no evidence of bacterial vaginosis and periodontal infection. Group 2(n = 50): Patients positive for periodontal infection. Group 3(n = 50): Patients positive for bacterial vaginosis Group 4 (n = 50): Patients positive for periodontal infection and bacterial vaginosis. Group 1 was the control group with sample size of 50 patients. Groups 2, 3, 4 were compared with the control group and correlated to the preterm birth and perinatal outcomes. This was a prospective case control study. All the antenatal patients presenting to the out patient Department of Obstetrics and Gynecology fulfilling following criteria's were antenatal patients after 28 weeks of period of gestation and singleton pregnancy. Exclusion criteria's were twin gestation, previously diagnosed uterine anomalies and any medical disorder like heart disease, chronic renal disease, diabetes, auto immune diseases like SLE etc. Examination of the patient for bacterial vaginosis was carried out in Antenatal clinic by the Gynecologist who recorded the findings on the basis of Amsel's criteria 31: 1) Character of discharge- Vaginal discharge if present was characterized by color and character of the discharge. 2) Vaginal pH- Swabs were taken from vaginal side walls and tested for pH >4.5 using pH indicator strips. 3) Detection of clue cells- A wet mount was prepared and 2 drops of saline applied to the wet mount. Slides were then examined under high power microscopy for clue cells. 4) Whiff test- 10% KOH was added to the vaginal secretions and production of fishy odor noticed.

A minimum of 2 Amsels criteria's out of 4 if present were considered diagnostic for bacterial vaginosis. The periodontal examination was carried out in Dental OPD by the Dentist who recorded the periodontal status by using the CPITN Index (Community Periodontal Index of Treatment Needs) with help of a CPITN probe. Ten teeth are recorded in this Index. The ten specified Index teeth were 17 – Maxillary Right Second Molar, 16 - Maxillary Right First Molar, 11 - Maxillary Right Central Incisor, 26 – Maxillary Left First Molar, 27 - Maxillary Left Second Molar, 37 - Mandibular Left Second Molar, 36 - Mandibular Left First Molar, 31 - Mandibular Left Central Incisor, 46 - Mandibular Right First Molar and 47 - Mandibular Right Second Molar [10].

CPITN considers the periodontal treatment need with respect to-

I. Score 0 – healthy.

II. Score 1 – bleeding gingivae on gentle probing.

III. Score 2 – presence of calculus.

IV. Score 3 – presence of 4 or 5 mm pockets.

V. Score 4 – presence of more than or equal to 6 mm pockets.

Patients with a score of 3 or 4 were considered positive for periodontal infection. The results were not reported to the clinician who was taking care of women during pregnancy, child birth or puerperium and treatment was offered only to patients who were symptomatic for the disease.

Epidemiological data of all the patients including their age, registration number, residential address and socioeconomic status were recorded on a preset proforma specially designed for the study. Gestational age was calculated from the first day of last menstrual period. Expected date of delivery was calculated by using Naegele's rule that is by adding seven to the first day of last menstrual period and counting back three months. B.M.I was calculated from the height and weight of the patient. Parity of the patient was

also recoded. A sample size of 50 patients in each group was calculated to conduct study with a power greater than 80% at a significance level of 5%. Data was analyzed using SPSS version 15.0 for Windows. Bacterial vaginosis and periodontal infection were separately correlated to the preterm birth and perinatal outcome. For ordinal data, groups were compared using Mann Whitney U-test, for continuous data groups were tested for normal distribution using the Kolmogorov-Smirnov test and for categorical data groups were compared using the chi-square test. $p<0.05$ was considered statistically significant.

Result

Bacterial vaginosis: Amsel's criteria's: Group 1: Clue cells were positive in 17(34%) patients and negative in 33(66%) patients. Vaginal pH was >4.5 in 4(8%) patients and <4.5 in 46(92%). Whiff test was positive in 3(6%) patients and negative in 47(94%) patients. Vaginal discharge was suggestive of bacterial vaginosis in 4(8%) patients, mixed in 27 (54%) patients and normal in 19(38%) patients. None of the patients had two parameters positive so they were grouped in bacterial vaginosis negative (Table 1).

Group 2: Clue cells were positive in 21(42%) patients and negative in 29(58%) patients. Vaginal pH was >4.5 in 3(6%) patients and <4.5 in 47(94%). Whiff test was positive in 5(10%) patients and negative in 45(90%) patients. Vaginal discharge was suggestive of bacterial vaginosis in 4(8%) patients, mixed in 27(54%) patients and normal in 19 (38%) patients. None of the patients had two parameters positive so they were grouped in bacterial vaginosis negative (Table 1).

Group 3: Clue cells were positive in 39(78%) patients and negative in 11(22%) patients. Vaginal pH was >4.5 in 20 (40%) patients and <4.5 in 30(60%). Whiff test was positive in 8(16%) patients and negative in 42(84%) patients. Vaginal discharge was suggestive of bacterial vaginosis in 41(82%) patients, mixed in 6(12%) patients and normal in 3(6%) patients. 42(84%) patients had 2 parameters positive: Clue cells and vaginal pH >4.5 were seen in 5(10%) patients, clue cells and positive whiff test were seen in 2(4%) patients, clue cells and discharge suggestive of bacterial vaginosis seen in 25(50%) patients, vaginal pH >4.5 and discharge suggestive of bacterial vaginosis seen in 8 (16%) patients and positive whiff test and discharge suggestive of bacterial vaginosis seen in 2(4%) patients. 8(16%) patients had 3 parameters positive: Clue cells, vaginal pH >4.5 and positive whiff test were seen in 2(4%) patients; Clue cells, vaginal pH >4.5 and discharge suggestive of bacterial vaginosis seen in 4 (8%) patients; Clue cells, positive whiff test and discharge suggestive of bacterial vaginosis were seen in 1(2%) patient and vaginal pH >4.5, positive whiff test and discharge suggestive of bacterial vaginosis were seen in 1(2%) patient. These 50 patients were grouped in bacterial vaginosis positive (Table 1).

Group 4: Clue cells were positive in 38(76%) patients and negative in 12(24%) patients. Vaginal pH was >4.5 in 21 (42%) patients and <4.5 in 29 (58%). Whiff test was positive in 16(32%) patients and negative in 34(68%) patients. Vaginal discharge was suggestive of bacterial vaginosis in 39(78%) patients, mixed in 3(6%) patients and normal in 8(16%) patients. 38(86%) patients had 2 parameters positive: Clue cells and vaginal pH >4.5 were seen in 2(4%) patients, clue cells and positive whiff test were seen in 5(10%) patients, clue cells and discharge suggestive of bacterial vaginosis seen in 21(42%) patients, vaginal pH >4.5 and positive whiff test were seen in 1(2%) patient, vaginal pH >4.5 and discharge suggestive of bacterial vaginosis seen in 5(10%) patients and positive whiff test and discharge suggestive of bacterial vaginosis seen in 4(8%) patients. 10(20%) patients had 3 parameters positive: Clue cells, vaginal pH >4.5 and positive whiff test were seen in 3 (6%) patients; Clue cells, vaginal pH >4.5 and discharge suggestive of bacterial vaginosis seen in 6(12%) patients and vaginal pH >4.5, positive whiff test and discharge suggestive of bacterial vaginosis were seen in 1(2%) patient. 2(4%) patients had all 4 parameters positive. These 50 patients were grouped in bacterial vaginosis positive (Table 1). Treatment: Group 1 and 2 were negative for bacterial vaginosis. 4 patients in group 1 and 6 patients in group 2 were treated as they were symptomatic for the discharge which was suggestive of bacterial vaginosis. Group 3 and 4 were positive for bacterial vaginosis. 20 patients were treated in group 3 and 4.

Periodontal infection: Group 1: 25(50%) patients had category 0 periodontal infection, 20(40%) had category 1 periodontal infection and 5(10%) had category 2 periodontal infection. These patients belonged to periodontitis negative group (Table 2). Group 2: 24(48%) patients had category 3 periodontal infection and 26(52%) had category 4 periodontal infection. These patients belonged to periodontitis positive group (Table 2, Figure 2b). Group 3: 25(50%) patients had category 0 periodontal infection, 20(40%) had category 1 periodontal infection and 5(10%) had category 2 periodontal infection. These patients belonged to periodontitis negative group (Table 2). Group 4: 25(50%) patients had category 3 periodontal infection and 25(50%) had category 4 periodontal

infection. These patients belonged to periodontitis positive group (Table 2). Treatment: 9, 2 and 9 patients were treated for periodontal infection in groups 2, 3 and 4 respectively. Further analysis about the antenatal complications, delivery details, postpartum complications and details of the baby will be calculated for 48 patients of group 1, 49 patients of group 2, 48 patients of group 3 and 47 patients of group 4 excluding the patients who were lost to follow up.

Delivery details: Gestational age at delivery: 7(14.6%) patients had delivery at <37 weeks and 41 (85.4%) had delivery at >37 weeks in group 1. 16 (32.7%) patients had delivery at <37 weeks and 33 (67.3%) had delivery at >37 weeks in group 2. The difference was statistically significant (p=.036) when compared with group 1. 5(10.4%) patients had delivery at <37 weeks and 43(89.6%) had delivery at >37 weeks in group 3. The difference was statistically insignificant (p=.537) when compared with group 1. 15(31.9%) patients had delivery at <37 weeks and 32(68.1%) had delivery at >37 weeks in group 4. The difference was statistically significant (p=.045) when compared with group 1 (Table 3, Figure 1) (Table 4), (Table 5).

PROM: 14(29.2%) patients in group 1 had PROM, 29(59.2%) patients in group 2 had PROM, 15(31.3%) patients in group 3 had PROM and 19(40.4%) patients in group 4 had PROM. The difference in all the groups was statistically significant (p<0.05) (Table 6).

Indications of induction of labor: 13 patients were induced in group 1 (5 for PD pregnancy, 1 for PROM and 7 for TROM). 11 patients were induced in group 2 (1 for GH, 1 for IUGR, 1 for PD pregnancy, 3 for PROM and 5 for TROM). 14 patients were induced in group 3 (2 for IUGR, 5 for PD pregnancy, 1 for PROM and 6 for TROM). 15 patients were induced in group 4 (3 for IUGR, 2 for PD pregnancy, 1 for PE, 2 for PROM and 7 for TROM). The difference in all the groups was statistically insignificant (p>0.05).

Table 1: Amsel's criteria's

			GROUPS			
			Group 1	**Group 2**	**Group 3**	**Group 4**
Amsel's Criterias	Clue cells	+	17	21	39	38
			34%	42%	88%	76%
		-	33	29	11	12
			66%	58%	22%	24%
		>4.5	4	3	20	21
			8%	6%	40%	42%
	Vaginal pH	<4.5	46	47	30	29
			92%	94%	60%	58%
		+	3	5	8	16
			6%	10%	16%	32%
	Whiff test	-	47	45	42	34
			94%	90%	84%	64%
	Discharge	B	4	4	41	39
			8%	8%	82%	78%
		M	27	27	6	3
			54%	54%	12%	6%
		N	19	19	3	8
			38%	38%	6%	16%

Table 2: Periodontal infection

		GROUPS			
		Group 1	**Group 2**	**Group 3**	**Group 4**
CPITN INDEX	0	25	0	25	0
	% within group	50%	0%	50%	0%
	1	20	0	20	0
	% within group	40%	0%	40%	0%
	2	5	0	5	0
	% within group	10%	0%	10%	0%
	3	0	24	0	25
	% within group	0%	48%	0%	50%
	4	0	26	0	25
	% within group	0%	52%	0%	50%

Table 3: Gestational age at delivery: comparison between group 1 and group 2

			GROUPS		Total
			Group 1	Group 2	
G-DEL	<37	Count	7	16	23
		% within group	14.6%	32.7%	23.7%
	>=37	Count	41	33	74
		% within group	85.4%	67.3%	76.3%
Total		Count	48	49	97

p value = 0.036

Table 4: Gestational age at delivery: Comparison between group 1 and group 3

			GROUPS		Total
			Group 1	Group 3	
G-DEL	<37	Count	7	5	12
		% within group	14.6%	10.4%	12.5%
	>=37	Count	41	43	84
		% within group	85.4%	89.6%	87.5%
Total		Count	48	48	96

p value = 0.537

Table 5: Gestational age at delivery: Comparison between group 1 and group 4

			GROUPS		Total
			Group 1	Group 4	
G-DEL	<37	Count	7	15	22
		% within group	14.6%	31.9%	23.2%
	>=37	Count	41	32	73
		% within group	85.4%	68.1%	76.8%
Total		Count	48	47	95

p value = 0.045

Table 6: Comparison of prom between the groups

			GROUPS				Total
			Group 1	Group 2	Group 3	Group 4	
PROM	-	Count	34	20	33	28	115
		% within group	70.8%	40.8%	68.8%	59.6%	59.9%
	+	Count	14	29	15	19	77
		% within group	29.2%	59.2%	31.3%	40.4%	40.1%
Total		Count	48	49	48	47	192

p value = 0.010

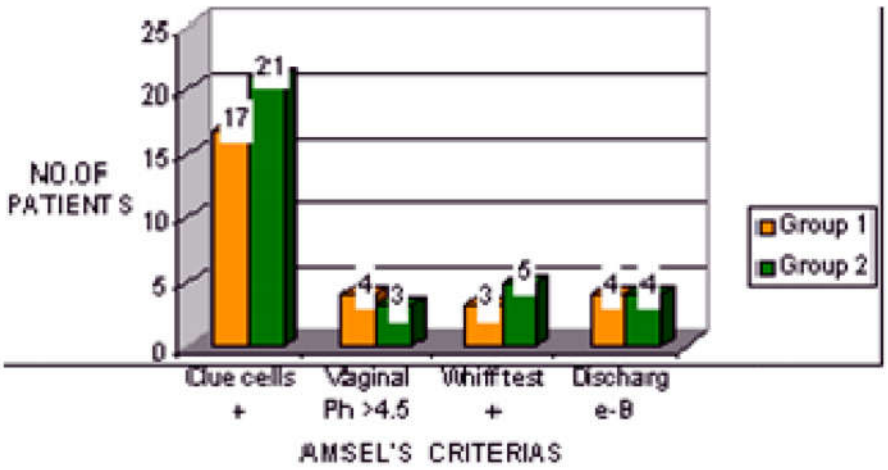

Fig. 1: Comparison between group 1 and group 2

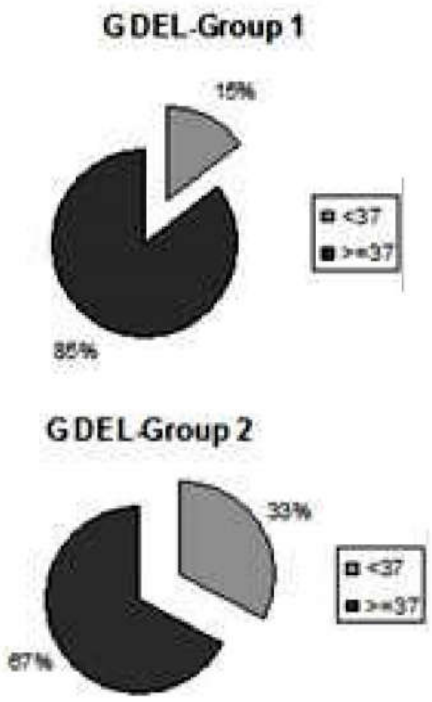

Fig. 2: Gestational age at delivery: Comparison between group 1 and group 2

Discussion

Preterm delivery (birth before 37 completed weeks of gestation) is one of the leading causes of neonatal morbidity and mortality. Despite improved neonatal care, 70-80% of all perinatal deaths occur among neonates without congenital malformations who are born prematurely. However the causes of preterm labour are poorly understood.

Intrauterine infection has been found to play a major role in preterm birth and is thought to be responsible for preterm birth in up to 40% of cases [5]. The etiology is multifactorial but there is overwhelming evidence to implicate infection. This infective link has focused on association between abnormal genital tract flora in pregnancy as in bacterial vaginosis and preterm birth. Recently infections at other places like periodontal disease have been linked to preterm birth. The mechanism has been an initiation of systemic immune response as a result of infection whether local or distant leading to secretion of pro inflammatory mediators at the chorio-amnion junction which further causes changes progressing to preterm labor. Pretorius et al [11] studied an inter relationship between periodontal infection, bacterial vaginosis and preterm labor and found microbiological similarities between the oral cavity and the female genital tract giving rise to a possible common pathophysiology.

This result signifies that discharge suggestive of bacterial vaginosis is the single parameter having high sensitivity, high specificity, high positive predictive value and high negative predictive value.

Currently the clinical criteria's for diagnosing bacterial vaginosis requires the presence of three out of four Amsel's criteria's. In this study presence of only two criteria's was taken diagnostic as supported by various studies [12,13]. In study done by Desire Lee [12], the prevalence of bacterial vaginosis was 38.7%. Vaginal pH was the most sensitive criterion with a sensitivity of 89% & a positive amine odor was most specific criterion with a specificity of 93%. In a study by Dr. Guttman and colleagues [13] the most sensitive indicator was vaginal pH more than 4.5 with a sensitivity of 84% and most specific being the amine odor with a specificity of 97%. In comparison, in this study positive clue cells and vaginal discharge were the more sensitive criterions with a sensitivity of 77% and 80% respectively and positive amine odor and vaginal discharge were more specific criterions with a specificity of 92% each.

Similar observations were given by Gene et al [14], Boggess [15], Jeffcoat et al [16] and BK Yeo et al [17]. A study by K Jarjoura et al showed higher prevalence of periodontitis in patients with preterm labor (p=0.027). In this study 83 were cases and 120 were controls and periodontal examination was done after delivery within 48 hrs [18].

A Bosanjak et al [19] carried out a study in 81 primiparous Croatian mothers aged 18-39 years. The cases had significantly worse periodontal status than controls (p = 0.008). Multivariate logistic regression model, after controlling for other risk factors, demonstrated that periodontal disease is a significant independent risk factor for preterm birth, with an adjusted odds ratio of 8.13 (95% confidence interval 2.73-45.9).

Nejad et al [20] conducted a study similar to this study that is analyzing 160 patients in third trimester for bacterial vaginosis and found 25% preterm deliveries in study group compared to 11.3% in control group (p=0.039). JA Svare et al [21] found only marginal association of preterm delivery with bacterial vaginosis. This may be because patients in this study were examined in third trimester as compared to other studies carried out in early gestation and acquiring bacterial vaginosis in late gestation might not be associated with increased incidence of preterm labor. This is supported by a study carried out by J Shoeman et al [22] the study showed that women who were diagnosed with bacterial vaginosis before 20 weeks' gestation were at higher risk

of delivering pre-term than those who developed bacterial vaginosis after 20 weeks.

This can be explained as the subjects were selected in the third trimester in this study. They were symptomatic for the disease at that time only and were offered treatment then. The infection might have been present since the early gestation and patients had already mounted a systemic immune response which was refractory to treatment later. Thus treating a patient after the infection has established itself does not alter the course. A study by Morency et al [23] on administration of antibiotics in second trimester shows that Metronidazole does not prevent preterm labor but Macrolides do have a role in decreasing the preterm birth.

Association was found by Marakoglu et al [24]. The study results indicated that periodontitis (OR: 3.6 95% CI: 1.06-12.18) together with bacterial vaginosis (OR: 11.57 95% CI: 1.26-105.7) were independent risk factors of a preterm low birth weight. Further analysis was done to study any association of periodontal infection and bacterial vainosis with perinatal outcomes. Majority of the newborns had an apgar of 9 at 1 minute (97.4%). Only 2.6% neonates presented with apgar of 7 at 1 minute. 4 of these neonates belonged to group 2 that is with periodontal infection positive (p=0.035) which is significant for the study. 191 neonates had an apgar of 9 at 5 minutes (99.5%). 12 (6.3%) neonates had respiratory distress at birth which recovered within few minutes. These neonates were equally distributed in all the groups and no significant association could be put forward (p=0.882). Out of these 12, 8 had distress due to prematurity itself, 3 had transient tachypnea of newborn and 1 had birth asphyxia.

Similar observations were made in various studies. H Leitich et al [25] carried out a study which showed association of bacterial vaginosis with preterm labor but not with any adverse perinatal outcomes.

Present study concludes that periodontal infection is individually correlated with preterm labor, it might have some different mechanism of initiation of the process of preterm labor than other infections like bacterial vaginosis. Both of them have no significant correlation with perinatal outcomes. Since the present study was conducted on a limited number of patients, it is suggested that large scale randomized control trials may be conducted in future in patients with varied demographic profile to further elucidate the etiology of preterm labor.

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