

The influence of bacterial vaginosis and cervical length on preterm delivery in pregnant women in the second trimester

Hacı Öztürk Şahin^{1*}, Ahmet Güllük²

Abstract

Objective: Preterm birth is one of the major cause of perinatal morbidity and mortality. Clinical studies have pointed out the association between preterm birth and bacterial vaginosis (BV) infection. Our aim is to discover the incidence of BV and search for the mean cervical length and parameters for the prediction of preterm delivery.

Materials and Methods: 130 pregnant woman between the 16th and 24th gestational week were included in our study. A detailed medical history was obtained from all of the women, and patients with a history of preterm delivery and the Vaginal Ph values and cervical length measurement were evaluated. Vaginal samples were analyzed, gram staining was performed, and a bacterial vaginosis diagnosis was made with Nugent's criteria.

Results: Of 130 woman that we included in our study, only 19 had bacterial vaginosis (14.6 %), and the mean cervical length was measured as 41.79 mm. Preterm birth occurred in nine of the pregnant women (6.9%), and no statistically significant difference was found between BV and shortened cervical length or preterm labor. When we excluded the known preterm birth risk factors from our study, we could not find a significant difference between preterm labor and BV.

Conclusion: We concluded that BV by itself is not a preterm risk factor. The frequency of BV in the pregnant women in our study group according to the preterm delivery rate and the mean cervical length were similar to those in international studies in which the relationship between cervical length and preterm delivery has been established. We did not come to a significant conclusion in our research; nevertheless, we can relate this result to the preterm delivery rate that is found to be lower than expected.

Key words: Second Trimester Pregnancy, Bacterial Vaginosis, Cervical Length, Preterm Delivery

Introduction

Preterm delivery (termination of pregnancy before 37th week of gestational) is among the important causes of perinatal mortality and morbidity (1,2). There is no previous history of preterm delivery in 70% of preterm deliveries (1,3).

While etiology of preterm delivery is multi-factorial including major risk factors like smoking, ethnicity, the relationship with bacterial vaginosis (BV) was emphasized in many clinical studies (4,5). Bacterial vaginosis is characterized by impairment of vaginal microbiota through the decrease in Lactobacillus species and the increase in anaerobic microorganisms and Mycoplasma species. Diagnosis of BV is made by Amsel criteria (6) or Nugent scoring system based on the decrease in Lactobacillus species and the increase in Gram-stained anaerobic bacteriae (7).

Prevalence of BV was found to be 7,1% in a study conducted with 14.193 pregnant women and used Nugent criteria for diagnosis although it varies among countries (8). Patho-physiologic mechanism of BV could not be fully explained, data are available reporting that BV significantly increases the risk for preterm delivery during the first two trimesters of pregnancy besides the literature data proposing the opposite (9).

Measurement of cervical length between 20-24th week of gestation showed high accuracy for prediction of preterm delivery and different cut-off values were given (10,11,12).

The aim of the present study is to detect the incidence of bacterial vaginosis (BV) and mean cervical length, and also the value of these parameters for prediction of preterm delivery in pregnant women in our population.



Material and Method

Pregnant women in the second trimester (between 16-24th weeks of gestation) who were admitted to obstetrics outpatient clinic for routine control and who had the complaint of vaginal discharge were included in the study. All participants were informed about the procedures and 136 pregnant women who agreed for participation were included.

A detailed anamnesis was obtained from all participants and data about gestational age, number of pregnancies and parities, complaint of vaginal odor and medical history were recorded.

Exclusion criteria included the following;

- *Ages younger than 18 years or older than 40 years,
- * History of smoking and medication use,
- * Multiple pregnancies,
- * History of preterm labor or premature rupture of the membranes,
- * Uterine malformations,
- * History or diagnosis of cervical insufficiency,
- * Presence of medical problems like maternal hypertension, type 1 or type 2 diabetes or thyroid dysfunction,
- * Unexplained vaginal bleeding,
- * Pregnant women who did not know the date of the last menstruation or whose gestational week cannot be estimated due to the absence of a previous ultrasonography,
- * History of in-utero still fetus or congenital anomalies.

The participants were taken to the lithotomy position after a detailed second trimester ultrasonography examination including detection of gestational week, presence of congenital malformations or uterine anomalies had been performed, smear was obtained from the lateral wall of the vagina with a sterile swab by using disposable plastic Graves type speculum and by paying care for not touching cervical mucus plug. Fixation was done in open air after the specimen was spread on the lam. At the second step, vaginal pH was measured with a universal pH stick.

Afterwards, the speculum was removed, the same ultrasonography device was prepared with a lubricant condom, trans-cervical length was measured with vaginal probe at 5 MHz. Care was paid for the urinary bladder's being empty, each measurement was performed in 3 min due to the potential cervical spasms. Vaginal smear was evaluated for Nugent criteria with Gram staining.

Telephone numbers and addresses were obtained from all participants for obtaining delivery data and the required ones were called for control again.

The study was conducted in accordance with the principles of human experiments and informed consent was obtained from the participants prior to the study. Ethics committee approval was obtained from the local ethics committee (date: 9.09.2004/ number:54).

Statistical Analysis

Data were analyzed by using SPSS (Statistical Package for the Social Sciences) ver. 20.0. Number, percent, mean, standard deviation, minimum, maximum values were used. Chi-square test was used for analysis of categorical variables. Significance test of the difference between two averages was used as parametric test according to the results of normality distribution. A p level of <0,05 was accepted as statistically significant.

Results

Of 136 pregnant women, 2 were excluded due to severe preeclampsia beginning at the advanced stage of pregnancy, one was excluded due to intra-uterine still birth and 3 were excluded as they were lost to follow up.

Mean time of admission was 21 weeks and 3 days. Cervical length varied between 28 mm and 52 mm (mean 41.79 mm). Time of delivery varied between 31 weeks and 3 days, and 41 weeks and 6 days (mean 38 weeks and 6 days). Birth weight varied between 1290 gr and 4500 gr (mean 3249 gr) (Table 1).

Of the participants, 79 (60.8%) were multiparous and 51 (39.2%) were nulliparous. Seventy three out of all women (56.2%) also had the complaint of vaginal odor. While bacterial vaginosis was detected in 19 out of 130 women (14.6%), preterm delivery occurred in 9 (6.9%) (Table 2).

No difference was found between the pregnant women who had or who did not have preterm labor ($p>0.05$). As expected, birth week and birth weight of the cases with preterm labor were found to be significantly lower ($p<0.001$) (Table 3).

No significant difference was found in the pregnant women who had preterm labor with regard to nulliparity and presence of BV ($p>0.05$) (Table 4).

No significant difference was found between the pregnant women with and without BV with regard to mean cervical length, birth week and birth weight ($p>0.05$) (Table 5).

Table 1. Distribution of pregnant women and findings

	Minimum	Maximum	Mean	SD
Week of admission	16	24	21,63	2,1
Cervical length(mm)	28	52	41,79	5,25
Vaginal pH	4,0	6,0	4,28	0,43
Gestastional week	31,43	41,86	38,9	1,55
Weight (gram)	1290	4500	3249,23	496,77

(mm:milimeter) SD: standard deviation

Table 2. Results of patient statistics

		n	%
Nulliparity	No	79	60,8
	Yes	51	39,2
Odor	No	57	43,8
	Yes	73	56,2
Bacterial vaginosis	No	111	85,4
	Yes	19	14,6
Preterm labor	No	121	93,1
	Yes	9	6,9

Table 3. Comparison of the women who had preterm delivery or normal vaginal delivery

Preterm Labor	Mean	No SD	Mean	Yes SD	p
Week of admission	21,6	2,10	22,00	2,18	,523
Cervical length	41,95	5,14	39,67	6,44	,323
Vaginal pH	4,28	0,43	4,31	0,451	,778
Weight	3324,88	401,45	2232,22	558,30	< 0,001
Gestational week	39,1783	1,0740	35,3016	2,4583	< 0,001

SD;Standard deviation,p: Significance test of the difference between two averages

Table 4. Characteristics of the pregnant women who had preterm labor

Preterm labor	No	Yes	p
	n	n	
Nulliparity	No 75	4	0,313
	Yes 46	5	
Odor	No 52	5	0,504
	Yes 69	4	
Bv	No 104	7	0,619
	Yes 17	2	

Table 5. Comparison of pregnant women who had or who did not have bacterial vaginosis

Bacterial Vaginosis	No	Yes	p
	Mean	Mean	
Week of admission	21,70	21,21	,347
Cervical length	41,70	42,32	,640
Vaginal pH	4,141	5,111	< 0,001
Weight	3263,92	3163,42	,417
Gestational week	38,94	38,69	,525

SD;Standard deviation,p: Significance test of the difference between two averages

Discussion

The significance of prediction of preterm delivery and informing the risky pregnant women about the potential symptoms would be understood better considering the burden of intensive care of premature babies, loss of labor of the health staff and the potential sequels.

Preterm delivery is usually multi-factorial and many parameters that could be a risk factor for preterm delivery were accepted through an ample of studies.

However no consensus is available about the mechanism of these risk factors, effectiveness of these risk factors alone or in combination.

An ample amount of international studies are available investigating the relationship between BV and cervical length measurement and preterm delivery.

In the study of Surbek et al., bacterial vaginosis was detected in 36 out of 112 preterm deliveries (32%) and cervical length of these cases were found to be significantly shorter than that of the women with normal vaginal flora (13) (p=0.001). A statistically significant difference was not detected in cervical length of 235 primigravid pregnant women who were diagnosed with vaginitis/cervicitis compared to the women who did not have vaginitis/cervicitis. Incidence of BV was found to be 15.7% in pregnancy (14).

Diagnosis of BV was made based on Nugent criteria in the study of Joesoef M. et al. investigating the incidence of BV in pregnancy and the relationship with preterm labor in 490 pregnant women with gestational age of 16-20 weeks. We also used Nugent criteria. Incidence of BV was found to be 17%, while ratio of preterm delivery was 20.2% in these cases, this ratio was found to be 11.8% in BV negative pregnant women (Odds ratio:1,8). It was concluded that there was a significant relationship between BV and preterm delivery. Differently from our study, the pregnant women with the history of preterm delivery were not excluded from the study (15).

In the study of Michael G. et al. which did not include the subjects with the history of preterm delivery, as in our study, while prevalence of BV was found to be 19% in 534 pregnant women, this ratio was significantly higher in women with the history of preterm delivery (16) ($p < 0.01$). In multi-center, double-blinded, randomized PREMEVA study, a significant difference could not be found between groups with regard to late abortion and spontaneous preterm delivery in the Clindamycin or placebo arms in 2869 pregnant women who were diagnosed with BV at 12nd week of gestation (17).

When two meta-analyses were evaluated, while one showed that Clindamycin use reduced preterm delivery risk 40% in pregnant women who had abnormal vaginal flora before 22nd week of gestation (18), another did not report a significant difference (19).

Studies made on asymptomatic pregnancies have gained importance when pregnant women have symptomatic infection and medical treatment in many studies in literature. . Krauss-silva reported that the frequency of asymptomatic BV in pregnancy was high in the early gestational weeks and 40% spontaneously became negative within 8 weeks(20). Cervical length measurement according to Mancusto study was found to be significantly short in BV positive asymptomatic pregnant women with at least 1 spontaneous abortion history but when the covariate adjustment was considered, the result was null(21).

Cervical length measured at 20-24th weeks of gestation was shown to be an important factor for prediction of preterm labor in another data investigating the relationship between cervical length and preterm delivery which is another arm of our study (10,11,12). Different cut-off values were investigated for cervical length, 30 mm length was detected to increase the risk 3.79 fold and shorter than 26 mm length was detected to increase the risk 6.19 fold in the study of D.Iams et al. conducted with 2915 pregnant women (22).

Conclusion

In conclusion, the data of prevalence of BV in pregnant women, ratio of preterm delivery and mean cervical length were similar with those of found in international studies. We could not find a significant difference between cervical length and preterm labor, and concluded that it was not a risk factor for preterm delivery alone. We may explain not finding a significant difference between cervical length and

preterm delivery with the small number of preterm deliveries.

Conflict of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Author's Contributions: The correspondent author conceived the idea, carried out the design, and supervised the findings of this work. The correspondent author and co-authors verified the analytical methods and wrote the manuscript. All authors discussed the results and contributed to the final manuscript.

References

1. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet* 2008; 371: 75–84.
2. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. *Lancet* 2008; 371: 261–69.
3. Esplin MS, O'Brien E, Fraser A, et al. Estimating recurrence of spontaneous preterm delivery. *Obstet Gynecol* 2008; 112: 516–23.
4. Hay PE, Lamont RF, Taylor-Robinson D, Morgan DJ, Ison C, Pearson J. Abnormal bacterial colonisation of the genital tract and subsequent preterm delivery and late miscarriage. *BMJ* 1994;308: 295–98.
5. Kurki T, Sivonen A, Renkonen OV, Savia E, Ylikorkala O. Bacterial vaginosis in early pregnancy and pregnancy outcome. *Obstet Gynecol* 1992; 80: 173–77.
6. Amsel R, Totten PA, Spiegel CA, Chen KC, Eschenbach D, Holmes KK. Nonspecific vaginitis. Diagnostic criteria and microbial and epidemiologic associations. *Am J Med* 1983; 74: 14–22.
7. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. *J Clin Microbiol* 1991; 29: 297–301.
8. Desseauve D, Chantrel J, Fruchart A, et al. Prevalence and risk factors of bacterial vaginosis during the first trimester of pregnancy in a large French population-based study. *Eur J Obstet Gynecol Reprod Biol* 2012;163: 30–34.
9. Leitich H, Bodner-Adler B, Brunbauer M, Kaider A, Egarter C, Husslein P. Bacterial vaginosis as a risk factor for preterm delivery: a meta-analysis. *Am J Obstet Gynecol* 2003; 189: 139–47.
10. Ozdemir I, Demirci F, Yucel O, Erkorkmaz U. Ultrasonographic cervical length measurement at 10-14 and 20-24 weeks gestation and the risk of preterm delivery. *Eur J Obstet Gynecol Reprod Biol*. 2007 Feb;130(2):176-9.
11. Thangaraj JS1, Habeebullah S, Samal SK, Amal SS. Mid-Pregnancy Ultrasonographic Cervical Length Measurement (A Predictor of Mode and Timing of Delivery): An Observational Study. *J Family Reprod Health*. 2018 Mar;12(1):23-26.
12. Mishra S, Bagga R, Kalra J, Jain V, Dutta S. Routine second trimester cervical length screening in low risk women identified women at risk of a 'very' preterm birth but did not reduce the preterm birth rate: a randomised study from India. *J Obstet Gynaecol*. 2018 Aug;38(6):789-795.
13. Surbek DV, Hoesli IM, Holzgreve W. Morphology assessed by transvaginal ultrasonography differs in patients in preterm labor with vs. without bacterial vaginosis. *Ultrasound Obstet Gynecol*. 2000 Mar;15(3):242-5.

14. Jantien J, Boomgaard MD, Karin S, Dekker MD, Elsabet Van Rensburg: *Am J Obstet Gynecol* 1999; 181:964-7.
15. Joesoef M, Riduan JM, Hillier SL, Utomo B, Wiknjosastro G, Linnan M, Kandun N. Bacterial vaginosis and prematurity in Indonesia: association in early and late pregnancy. *Am J Obstet Gynecol*. 1993 Jul; 169(1):175-8.
16. Michael G, Gravett MG, Nelson HP, DeRouen T, Critchlow C, Eschenbach DA, Holmes KK. Independent associations of bacterial vaginosis and Chlamydia trachomatis infection with adverse pregnancy outcome. *JAMA*. 1986 Oct 10; 256(14):1899-903.
17. Subtil D, Brabant G, Tilloy E et al. Early clindamycin for bacterial vaginosis in pregnancy (PREMEVA): a multicentre, double-blind, randomised controlled trial. *Lancet*. 2018 Nov 17; 392(10160):2171-2179.
18. Lamont RF, Nhan-Chang C-L, Sobel JD, Workowski K, Conde-Agudelo A, Romero R. Treatment of abnormal vaginal flora in early pregnancy with clindamycin for the prevention of spontaneous preterm birth: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2011; 205: 177-90.
19. Brocklehurst P, Gordon A, Heatley E, Milan SJ. Antibiotics for treating bacterial vaginosis in pregnancy. *Cochrane Database Syst Rev* 2013; 1: CD000262.
20. Krauss-Silva L, Almada-Horta A, Alves MB, Camacho KG, Moreira ME, Braga A. Basic vaginal pH, bacterial vaginosis and aerobic vaginitis: prevalence in early pregnancy and risk of spontaneous preterm delivery, a prospective study in a low socioeconomic and multiethnic South American population. *BMC Pregnancy Childbirth*. 2014 Mar 19; 14:107. doi: 10.1186/1471-2393-14-107.
21. Mancuso MS, Figueroa D, Szychowski JM, Paden MM, Owen J. Midtrimester bacterial vaginosis and cervical length in women at risk for preterm birth. *Am J Obstet Gynecol*. 2011 Apr; 204(4):342.e1-5. doi: 10.1016/j.ajog.2010.11.003.
22. Iams JD1, Goldenberg RL, Meis PJ, Mercer BM, Moawad A, Das A, Thom E, McNellis D, Copper RL, Johnson F, Roberts JM. The length of the cervix and the risk of spontaneous premature delivery. National Institute of Child Health and Human Development Maternal Fetal Medicine Unit Network. *N Engl J Med*. 1996 Feb 29; 334(9):567-72.