

# Association between Folic Acid and Zinc Concentration with Incidence of Bacterial Vaginosis in The First Trimester of Pregnancy

Noroyono Wibowo, Rima Irwinda, Jimmy S. N. Berguna, Mohammad Azmi

Department of Obstetrics and Gynecology,  
FM Universitas Indonesia-dr. Cipto Mangunkusumo Hospital

Correspondence: wibowonoroyono@yahoo.com

## Abstract

Bacterial vaginosis (BV) in pregnancy is associated with the increase of adverse pregnancy outcomes such as premature rupture of membranes and preterm labor. One of the multifactorial causes of BV is the change in vaginal immunity. Malnutrition, including micronutrient deficiency, increases the vulnerability to infections. This study aim to investigate the association between folic acid and zinc concentration with the incidence of bacterial vaginosis in the first trimester of pregnancy. This descriptive cross sectional study involved 139 mothers with first trimester pregnancy, aged between 17-39 years old. The study was conducted at dr. Cipto Mangunkusumo Hospital from September 2013 until August 2014. Vaginal secretions was sampled to diagnose BV under nugen criteria. Folic acid and zinc in the serum were measured. From 139 subject, 18.7% (n=26) were found to be BV positive (nugen score  $\geq 7$ ). No deficiency of folic acid ( $<7$  ng/mL) and 40.3% (n=56) of zinc deficiency ( $<60$   $\mu\text{g/dL}$ ) were found. Bivariate analysis used Kruskal-Wallis test between folic acid and zinc concentration with BV incidence gives p value of 0.668 and 0.478 respectively. Prevalence of BV in this study was 18.7%. The relation between the maternal statuses of folic acid with BV in the first trimester of pregnancy was not found.

**Keywords:** bacterial vaginosis, folic acid, zinc, pregnancy.

## Hubungan antara Kadar Asam Folat dan Seng terhadap Kejadian Vaginosis Bakteri pada Trimester Pertama Kehamilan

### Abstrak

Bakterial vaginosis (BV) pada kehamilan dihubungkan dengan meningkatnya luaran maternal yang buruk seperti ketuban pecah dini dan persalinan prematur. Penyebab BV multifaktor salah satunya adalah perubahan imunitas di vagina. Malnutrisi termasuk defisiensi mikronutrien meningkatkan kerentanan terhadap infeksi. Studi ini dilakukan untuk mengetahui hubungan antara kadar asam folat dan seng terhadap kejadian vaginosis bakteri pada trimester pertama kehamilan. Penelitian ini merupakan studi deskriptif potong lintang yang mengikutsertakan 139 ibu hamil trimester pertama berusia 17–39 tahun. Penelitian dilakukan di Rumah Sakit Cipto Mangunkusumo pada bulan September 2013–Agustus 2014. Sekret vagina diambil untuk mendiagnosis BV berdasarkan kriteria nugen. Dilakukan pengukuran kadar asam folat dan seng dalam serum. Dari 139 subjek, didapatkan 18,7% (n=26) positif BV (skor nugen  $\geq 7$ ). Tidak terdapat defisiensi asam folat ( $<7$  ng/mL) dan 40,3% (n=56) defisiensi seng ( $<60$   $\mu\text{g/dL}$ ). Analisis bivariat menggunakan uji kruskal-wallis antara kadar asam folat dan seng dengan BV memberikan nilai p masing-masing 0,668 dan 0,478. Disimpulkan prevalensi BV pada penelitian ini adalah 18,7%. Tidak ditemukan hubungan antara status asam folat dan seng maternal trimester pertama dengan BV.

**Kata kunci:** bakterial vaginosis, asam folat, seng, kehamilan

## Introduction

Bacterial vaginosis (BV) is the most frequent reproductive tract infection occurred in productive female.<sup>1</sup> BV is a clinical syndrome caused by polymicrobial imbalance causing vaginal normal flora, *Lactobacillus sp.* to be replaced with high concentration of facultative anaerobic bacteria especially *Gardenerella vaginalis*, *Prevotella sp.*, *Bacteroides sp.*, *Mobiluncus sp.*, gram positive cocci, and genital mycoplasma (*Mycoplasma hominis* and *Ureaplasma urealyticum*).<sup>2</sup> BV is reported as a risk factor of adverse pregnancy outcomes such as recurrent abortus, postabortal sepsis, premature rupture of fetal membranes, and preterm labor.<sup>3,4</sup> Prevalence of BV in pregnancy varied between population. It accounts between 16% in low risk (23-26 week gestational age) until 42% in high risk population (22-24 week gestational age) in America, 26.5% population (16-26 week gestational age) in Australia, 51% (gestational age not stated) in Africa, 13.6% (gestational age not stated) in Japan, and 18% (14-26 week gestational age) in Indonesia.<sup>5,6</sup>

Previous study reported that blacks, smoking, sexual intercourse, anal before vaginal intercourse, sexual intercourse with uncircumcised man, and herpes simplex-2 antibody are independent risk factors toward BV.<sup>7</sup> One of multifactorial BV causes the change in vaginal immunity. A theory stated that malnutrition, including micronutrient deficiency, increases the vulnerability to infections.<sup>8-9</sup> In the previous study, deficiency of vitamin D, iron, and folic acid are reported to be strongly associated with BV incidence.<sup>10-14</sup>

Many studies investigate the association between nutrition and BV; however, there is no study in Indonesia investigates the association between micronutrient level and the incidence of bacterial vaginosis in pregnant or non-pregnant woman. The objective of this study is to investigate the association between folic acid and zinc toward BV incidence in pregnant woman.

## Methods

This cross-sectional study was conducted at Dr. Cipto Mangunkusumo Hospital from September

2013 until August 2014. The subjects were 139 pregnant women in their first trimester. Subjects that came to the antenatal care (ANC) checkups were interviewed. The interview covered subjects' demographic characteristic the age, parity, education, and job. Vaginal swab was performed in all subjects in order to collect samples for gram staining. Nugent criteria was used to diagnose BV from gram staining results. BV is considered positive in pregnant woman if Nugent score is  $\geq 7$ , intermediate BV if Nugent score is 4-6, and negative BV if Nugent score is  $\leq 3$ . Serum sample was also collected to measure folic acid and zinc concentration.

The data were analyzed using IBM SPSS statistics 20. Kruskal-wallis and kolmogorov-smirnov test were used for bivariate analysis to investigate the differences of BV incidence in each variable.

## Results and Discussion

The subject for this research were 139 pregnant women. The demographic characteristics of subjects with BV can be seen in table 1. The average age of the subjects were 29.17 years old, which consist of  $\leq 19$  years old (1.4%), 20–25 years old (19.4%), 26–30 years old (43.9%), and  $> 30$  years old (35.3%). Most of the subjects education background were from university graduates (51.1%). The majority of the subjects were housewives (43.2%) and 18.7% of them were diagnosed with BV (Nugent score  $\geq 7$ ).

There was no subject found to have folic acid deficiency ( $< 7$  ng/mL), 14 of them (10.1%) had enough folic acid concentration (7–14 ng/mL), and 125 of them (89.9%) had excess folic acid concentration ( $> 14.9$  ng/mL). Zinc deficiency ( $< 60$   $\mu$ g/L) was found in 56 subjects (40.3%), however, 83 subjects (59.7%) had normal zinc concentration. Furthermore, there were no subjects with excess zinc concentration ( $> 130$   $\mu$ g/L). Based on Nugent criteria, positive results (Nugent score  $\geq 7$ ) were found in 26 subjects (18.7%), intermediate results (Nugent score 4-6) in 31 subjects, and negative results (Nugent  $\leq 3$ ) were found in 82 subjects (59%).

Table 1. Demographic Characteristic and Incidence of BV

Demographic Characteristic	n (%)	BV n (%)	p value
<b>Age (years)</b>			
≤ 19	2 (1.4)	1 (3.8)	Ref
20–25	27 (19.4)	7 (26.9)	0.530
26–30	61 (43.9)	12 (46.2)	0.474
> 30	49 (35.3)	6 (23.1)	0.531
<b>Education</b>			
Elementary school	3 (2.2)	1 (3.8)	NS
Junior high school	9 (6.5)	4 (15.4)	0.515
High school	56 (40.3)	10 (38.5)	NS
University	71 (51.1)	11 (42.3)	Ref
<b>Job</b>			
Housewife	60 (43.2)	14 (53.8)	NS
Government employee	3 (2.1)	0 (0)	NS
Private employee	56 (40.3)	9 (34.6)	0.416
Others	20 (14.4)	3 (11.6)	Ref

Ref: reference

NS: not significant

Table 2. Folic Acid and Zinc Adequacy

Concentration	n (%)
<b>Folic Acid</b>	
<7	0 (0)
7–14.9	14 (10.1)
>14.9	125 (89.9)
<b>Zinc</b>	
<60	56 (40.3)
60–130	83 (59.7)
>130	0 (0)

Table 3 shows that there is no association between folic acid and zinc with the incidence of

BV. From kruskal-wallis test, the p values for both micronutrients are 0.668 and 0.478.

Table 3. Folic Acid and Zinc Concentration with Positive, Intermediate, and Negative BV

BV	n	Median (minimum-maximum)	p value
<b>Folic Acid</b>			
Positive	26	19.46 (10.69 – 34.94)	0.668
Intermediate	31	18.87 (13.19–31.52)	
Negative	82	19.34 (11.67–34.16)	
<b>Zinc</b>			
Positive	26	68 (42-101)	0.478
Intermediate	31	61 (39-88)	
Negative	82	61 (30-102)	

The result of this research is different compared with the previous research, which stated that folic acid deficiency has strong association with the incidence of BV during pregnancy.<sup>13</sup> Other research also stated that low concentration of zinc has a association with the incidence of BV.<sup>9</sup> In theory, suboptimal nutrition can influence body's immune system which results in increased susceptibility to infection.<sup>10</sup> The difference between this research with the previous ones might be due to the presence of other micronutrients such as vitamin A, vitamin C, vitamin D, vitamin E, iron, and calcium in maintaining body's immune function. There are some interactions between nutrients inside the body and imbalance of nutrients appear for several nutrients simultaneously. Thus, there is a need for further research in several nutrients simultaneously.

BV is caused by a change in normal acid environment of the vagina. There are a lot of factors that may change the normal acid environment in vagina into base condition and promote the overgrowth of many facultative anaerobic bacteria. Those risk factors include vaginal douching, frequency of sexual intercourse in the first trimester, history of usage of hormonal contraception, smoking, and uncircumcised sexual couple.<sup>15-17</sup>

Difference in the result of this research with the previous ones could also be caused by the small number of subjects. Aside from that, risk factors are also not included in the variable whereas it can be a confounding factor.

## Conclusion

Prevalence of BV in this research is 18.7%. Any association between folic acid and zinc status in the first trimester of pregnancy with BV is not found.

## References

- Pirotta M, Fethers KA, Bradshaw CS. Bacterial vaginosis: more questions than answers. *Aust Fam Physician*. 2009;38:394–7.
- Krauss-Silva L, Almada-Horta A, Alves MB, Camacho KG, Moreira, MEL, 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 and Childbirth*. 2014;14:107.
- Donders GG. Definition and classification of abnormal vaginal flora. *Best Pract Res Clin Obstet Gynaecol*. 2007;21:355–73.
- Lamont RF, Sobel JD, Akins RA, Hassan SS, Chaiworapongsa T, et al. The vaginal microbiome: new information about genital tract flora using molecular based techniques. *BJOG*. 2011;118:533–49.
- Menon R, Dunlop AL, Kramer MR, Fortunato SJ, Hogue CJ. An overview of racial disparities in preterm birth rates: caused by infection or inflammatory response? *Acta Obstet Gynecol Scand*. 2011;90:1325–31.
- Ocviyanti D, Rosana Y, Wibowo N. Profil flora vagina dan tingkat keasaman vagina perempuan Indonesia. *Maj Obstet Ginekol Indones*. 2009;3(2):124–31.
- Koumans EH, Markowitz LE, Hogan V. Indications for therapy and treatment recommendations for bacterial vaginosis in nonpregnant and pregnant women: a synthesis of data. *Clin Res Infect Dis*. 2002;35(Suppl 2):S152–72.
- Cherpes TL, Hillier SL, Meyn LA, Busch JL, Krohn MA. A delicate balance: risk factors for acquisition of bacterial vaginosis include sexual activity, absence of hydrogen peroxide-producing lactobacilli, black race, and positive herpes simplex virus type 2 serology. *J Sex Transm Dis*. 2007;35(1):78–83.
- Hemalatha R, Ramalaxmi BA, Swetha GK, Rao DM, Charyulu S, Kumar D. Nutritional status, bacterial vaginosis, and cervical colonization in women living in an urban slum in India. *Int J Nutr and Metab*. 2012;4(5):77–82. Ahluwalia N, Grandjean H. Nutrition, an under-recognized factor in bacterial vaginosis. *J Nutr*. 2007;137(9):2128–33.
- Verstraelen H, Delanghe J, Roelens K, Blot S, Claeys G, Temmerman M. Subclinical iron deficiency is a strong predictor of bacterial vaginosis in early pregnancy. *BMC Infectious Diseases*. 2005;5(1):55..
- Bodnar LM, Krohn MA, Simhan HN. Maternal vitamin D deficiency is associated with bacterial vaginosis in the first trimester of pregnancy. *J Nutr*. 2009;139(6):1157–61.
- Dunlop AL, Taylor RN, Tangpricha V, Fortunato S, Menon R. Maternal vitamin D, folate, and polyunsaturated fatty acid status and bacterial vaginosis during pregnancy. *Infect Dis Obstet Gynecol*. 2011.
- Negggers YH, Nansel TR, Andrews WW, Schwebke JR, Yu KF, Goldenberg RL, Klebanoff MA. Dietary intake of selected nutrients affects bacterial vaginosis in women. *J. Nutr*. 2007;137:2128–33.
- Ocviyanti D, Rosana Y, Olivia S, Darmawan F. Risk factors for bacterial vaginosis among Indonesian women. *Med J Indones*. 2010;19:130–5.
- Smart S, Singal A, Mindel A. Social and sexual risk factors for bacterial vaginosis. *Sex Transm Infect*. 2004;80:58–62.
- Risk factors for bacterial vaginosis during pregnancy among African-American women. *Am J Obstet Gynecol*. 2007;197(5):e1–477. e8.