



## BACTERIAL VAGINOSIS; COMPARISON OF VAGINAL METRONIDAZOLE WITH VAGINAL CLINDAMYCIN IN THE TREATMENT OF BACTERIAL VAGINOSIS

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**ABSTRACT...** Bacterial vaginosis is the most common vulvovaginal infection and represents the 35% of all the infections occurring in women in the reproductive age. Serious forms of can induce several complications such as spontaneous preterm labour and preterm birth, late miscarriage and postpartum endometritis, PID, infertility, vaginal cuff infection and postabortal sepsis. **Objective:** To compare the efficacy of vaginal metronidazole and vaginal clindamycin in the treatment of bacterial vaginosis. **Study Design:** Interventional: Quasi experimental study. **Setting:** Obstetrics outpatient department, Ghurki Trust Teaching Hospital, Lahore. **Duration of study:** Six months i.e. from 01-01-2009 to 30-06-2009. **Results:** Mean age of patients was found to be 24.33 years. In the 100 patients enrolled, no statistically significant difference was found between Clindamycin 2% vaginal cream compared with metronidazole 0.75% vaginal gel using Amsell's criteria. Metronidazole has a failure rate of 13% while failure rate was 6% in the clindamycin group. **Conclusion:** A 3 day regimen of clindamycin 2% vaginal cream was as effective as 5 day regimen of metronidazole 0.75% vaginal gel in the treatment of bacterial vaginosis.

**Key words:** Bacterial vaginosis, clindamycin, metronidazole.

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## INTRODUCTION

Bacterial vaginosis is a polymicrobial condition characterized by replacement of normal vaginal flora by pathogens i.e. Gardnerella vaginalis and mixed vaginal anaerobes, mycoplasma hominis and mobiluncus species.<sup>1</sup> This replacement causes lack of hydrogen peroxide producing lactobacillus<sup>2</sup> responsible for maintaining pH which is an essential ingredient in defense and control of vaginal environment.<sup>3</sup>

Bacterial vaginosis is among the most common lower genital tract infections in women of reproductive age.<sup>4</sup> Although it is more common in sexually active women, IUCD and other non-barrier contraceptive users. It is also found in virgins and lesbians. Incidence rate of bacterial vaginosis is 2.33/ person- year.<sup>5</sup> It affects 19% of pregnant females.<sup>6</sup>

Bacterial vaginosis leads to obstetrical and gynaecological complications<sup>3, 4</sup> like premature rupture of membranes, amniotic fluid infection,

pre-term labour<sup>7</sup>, pre-term delivery, post partum endometritis, surgical infection and post abortion pelvic inflammatory diseases.

Half of women with bacterial vaginosis are asymptomatic and symptomatic patients generally complain of `musty` or fishy odor with an increased thin grey-white to yellow discharge. The discharge may cause mild vulval irritation, commonly in approximately 1/5<sup>th</sup> of cases.<sup>8</sup> Diagnosis of bacterial vaginosis is based on Amsel's criteria by finding 3 out of 4 of the following<sup>9, 10</sup>;

1. Homogenous white vaginal discharge
2. pH > 4.5
3. Whiff test- Fishy smell of volatile amines after adding drop of potassium hydroxide.
4. Clue cells on wet mount test- Epithelial cells coated by bacteria visible on microscopy.

The use of laboratory tests in conjugation with clinical findings is necessary for diagnosis of

bacterial vaginosis. The composite clinical criteria for diagnosis of bacterial vaginosis are rapid, reliable and inexpensive method.<sup>11</sup>

Bacterial vaginosis is treated with anti bacterial drugs, metronidazole or clindamycin, which can reduce the complications of bacterial vaginosis. As these drugs have many systemic side effects when given orally, so this study is designed to compare effectiveness of local treatment of bacterial vaginosis with metronidazole and clindamycin phosphate vaginal cream to find out the efficacy of local use of these drugs for this most common infection in females of reproductive age.

### OBJECTIVES

- To compare the efficacy of vaginal metronidazole and vaginal clindamycin in the treatment of bacterial vaginosis.

### OPERATIONAL DEFINITION

**Efficacy:** The ability of a drug to cure the disease according to Amsels criteria.

**Whiff Test:** Mixing vaginal discharge with 10% KOH liberates amines detected by fishy odour. (+ve whiff test)

**Wet Mount Test:** After adding one drop of saline to vaginal discharge microscopic examination reveals clue cells which are epithelial cells studded with numerous bacteria.

### HYPOTHESIS

There is no difference between 0.75% vaginal metronidazole once daily for 5 days and 2% vaginal clindamycin cream once daily for 3 days in treatment of bacterial vaginosis

### MATERIALS AND METHODS

It was a Intervantional: Quasi\_ experimental study with non-probability: purposive sampling technique done in the out patient department of Obstetrics and Gynaecology, Ghurki Trust Teaching Hospital, Lahore over a period of six months from 15-08-2009 to 14-02-2010. The calculated sample size was 100 cases i.e. two groups of 50 patients each. Pregnant women

having bacterial vaginosis confirmed on Amsells criteria were included in the study. However, pregnant ladies in first trimester were excluded from the study. One hundred women according to inclusion criteria were asked to volunteer for study. Purpose of study and their involvement was explained and informed consent taken. After taking history regarding color and odor of discharge, and itching, vagina visualized with a vaginal speculum and adherent discharge from lateral vaginal walls was sampled using three swabs. Care was taken to avoid the sampling from cervical os, mucus and posterior vaginal fornix.

The first swab was used to find the pH. The pH determination was made following the application of the vaginal discharge specimen on pH paper with a ph range of 3.0 to 5.5. The resulting colormetric reaction was compared with the corresponding pH reference scale to determine the vaginal pH.

The saline wet mount was prepared by rolling second swab on a slide and then vaginal discharge mixed with one drop of normal saline and covering it with a cover slip, and examining it by light microscope for the presence of clue cells, i.e. vaginal epithelial cells studded with bacteria.

Whiff test was performed by combining a small specimen from third swab with 10% KOH on a glass slide. The fluid was immediately evaluated for the presence of fishy odor indicative of a positive Whiff test.

Subjects were randomly assigned to one of treatment groups of 50 patients each. One group was labeled as group A and other was labeled as group B. Group A was treated with metronidazole 0.75% vaginal gel once daily for five days and group B was treated with clindamycin phosphate 2% vaginal cream once daily for three days. Subjects were encouraged abstain from coitus, douching and using other intravaginal products until after the follow up visit.

The effects of both treatments were determined by follow up of both groups. Subjects were asked

to return after 7 days after initiation of treatment for questioning, re-examinations and vaginal specimen testing. Persistent vaginal symptoms, complications, side effects noted. A brief vaginal examination performed and vaginal specimens were obtained for test of cure. Efficacy of treatment was measured in terms of Amsel's criteria. Clinical treatment failure was defined as the persistence of three out of four features of Amsel's criteria i.e. homogenous white discharge, pH greater than 4.5, clue cells and a positive Whiff test. Information were collected on proforma. Data was analyzed by SPSS (VERSION 10.0).  $P \leq 0.05$  will be considered as significant.

**RESULTS**

Table-I shows that 66% patients presenting with bacterial vaginosis were between 14 and 26 years of age whereas patients were 34% patients were between 27 to 40 years of age. Mean age of patients was found to be  $24.3 \pm 6.8$  (SD).

Age in Years	No. of Patients	Percentage
14-26	66	66%
27-40	34	34%
<b>Mean <math>\pm</math> SD</b>	<b><math>24.3 \pm 6.8</math></b>	

**Table-I. Cases distribution by age (n=100)**

Table-II, III and IV show effect of each treatment on bacterial vaginosis symptoms i.e., itching, odor and clinical discharge respectively. 32% patients presented with itching, 19% presented with bad odor and 62% patients presented with vaginal discharge. Symptoms of itching and discharge improved following treatment in both cohorts as on follow up visit 19% patients had itching, 11% patients had odor and 28% patients had vaginal discharge. So no marked difference was observed while comparing both treatments in context of itching and odor but clindamycin found superior in relief of abnormal discharge.

Table-V shows the percentage of patients with discharge evident on speculum examination and effect of each treatment on vaginal discharge (sign). 91% patients had vaginal discharge at the time of presentation. Both treatments are found effective but no significant difference was noted

in efficacy when analyzed in comparison ( $P$  value=0.544).

	Itching		Total	P-Value
	Yes	No		
<b>Initial Visit</b>				
Group A	17	33	50	
Group B	15	35	50	
Total	32	68	100	
<b>Follow up</b>				
Group A	13	37	50	0.125
Group B	06	44	50	
Total	19	81	100	

**Table-II. Effect of each treatment on itching**

	Itching		Total	P-Value
	Yes	No		
<b>Initial Visit</b>				
Group A	08	42	50	
Group B	11	39	50	
Total	19	81	100	
<b>Follow up</b>				
Group A	08	42	50	0.200
Group B	03	47	50	
Total	11	89	100	

**Table-III. Effect of each treatment on odor**

	Abnormal Discharge		Total	P-Value
	Yes	No		
<b>Initial Visit</b>				
Group A	26	24	50	
Group B	36	14	50	
Total	62	38	100	
<b>Follow up</b>				
Group A	21	29	50	0.003
Group B	07	43	50	
Total	28	72	100	

**Table-IV. Effects of each treatment on abnormal discharge (Symptom)**

	Abnormal Discharge		Total	P-Value
	Yes	No		
<b>Initial Visit</b>				
Group A	43	07	50	
Group B	48	02	50	
Total	91	09	100	
<b>Follow up</b>				
Group A	31	19	50	0.544
Group B	27	23	50	
Total	58	42	100	

**Table-V. Effects of each treatment on vaginal discharge (Sign)**

Table-VI shows that 93% patients presented with vaginal pH  $>4.5$  and only 7% patients had normal pH but at follow up visit 16% patients had

normal vaginal pH. While considering effects of both treatments on vaginal pH, no statistically significant difference was observed in both groups (P value=0.054).

	Ph>4.5		Total	P-Value
	Yes	No		
<b>Initial Visit</b>				
Group A	45	05	50	
Group B	48	02	50	
Total	93	07	100	
<b>Follow up</b>				
Group A	38	12	50	0.054
Group B	46	04	50	
Total	84	16	100	

Table-VI. Effects of each treatment on vaginal pH

Table-VII shows that clue cells were found in 85% of patients on wet mount test at the time of presentation but on follow up visit clue cells were found only in 23% patients. While comparing both medications no significant difference found in reduction of clue cells with P value 0.342.

	Clue Cells		Total	P-Value
	Yes	No		
<b>Initial Visit</b>				
Group A	41	09	50	
Group B	44	06	50	
Total	85	15	100	
<b>Follow up</b>				
Group A	14	36	50	0.342
Group B	09	41	50	
Total	23	77	100	

Table-VII. Effects of each treatment on clue cells

Table-VIII shows that Whiff test was positive in 47% of patients at time of presentation and on follow up visit only 9% patients had positive whiff test. A significant reduction in amine odor on Whiff test was noted with both the medications but clindamycin 2% vaginal cream was found superior than metronidazole 0.75% vaginal gel in this context with P value 0.031.

	Whiff test		Total	P-Value
	Positive	Negative		
<b>Initial Visit</b>				
Group A	26	24	50	
Group B	21	29	50	
Total	47	53	100	
<b>Follow up</b>				
Group A	08	42	50	0.342
Group B	01	49	50	
Total	09	91	100	

Table-VIII. Effects of each treatment on Whiff test

Table-IX shows that both treatments were found effective but no significant difference was in efficacy when analyzed in comparison (P value=0.074).

Groups	Recovered		Total
	Yes	No	
A	37	13	50
B	44	06	50
Total	81	19	100

Table-IX. Cure rates of both treatments of brachial vaginosis

P value = 0.074

### DISCUSSIONS

Bacterial vaginosis is the most common type of vaginal infection among the young women.<sup>4</sup> The condition represents an alteration of normal Lactobacillus mediated vaginal ecosystem. In addition to the offensive vaginal discharge, bacterial vaginosis has been identified as a risk factor for the spontaneous preterm labour<sup>7</sup> and preterm birth, late miscarriage<sup>12,13,14</sup>, postpartum endometritis<sup>15,16</sup>, postabortal sepsis<sup>17,18</sup>, and post hysterectomy vaginal cuff infection.<sup>19,20</sup>

In our study it was found that mean age of subjects was 24.3 years (standard deviation (SD) = 6.8. This is comparable with a study carried out in Georgia<sup>21</sup> which was carried out in non pregnant women.

Although main bulk of patients in our study (62%) presented with abnormal vaginal discharge, but 38% of patients had no complaint of vaginal discharge. However these subjects had complaints of vaginal itching or bad odor. After

visualization of vagina with vaginal speculum, characteristic white homogenous adherent vaginal discharge found which was diagnosed as bacterial vaginosis according to Amsel's criteria, this showed that every patient with vaginal itching or malodor should be evaluated for bacterial vaginosis as bacterial can occur without symptomatic vaginal discharge.

Marked symptomatic relief was noted in both treatment groups and at the follow up visit only 19% subjects had itching, 28% had abnormal discharge and 11% subjects had odor. Vaginal clindamycin found superior in this context with p value 0.03 for relief of abnormal discharge, however no statistically significant difference was noted in between two study groups while considering itching ( p value 0.125) and odor (p value 0.200). These results are also comparable with the study carried out by Ferris et al (1995).<sup>21</sup>

The results of our study confirms the traditionally held view of the vaginal pH test as the most sensitive test for the diagnosis of bacterial vaginosis. Improper specimen collection may have explained the unexpected persistence of vaginal pH levels greater than 4.5. Sampling of cervical mucus or blood instead of vaginal side walls will yield higher vaginal pH. Researchers have reported a significant return of vaginal pH to normal values following bacterial vaginosis. Alternatively, Cook et al<sup>1</sup> have demonstrated that women with bacterial vaginosis have evidence of a mild persistent elevation of vaginal pH and a small number of clue cells following effective treatment. However both treatments were found effective for decreasing clinical discharge, pH and clue cells and no statistically significant difference was noted in between two study groups.

No statistically significant difference found among cure rates for metronidazole 0.75% vaginal gel and clindamycin 2% vaginal cream. In our study cure rate for clindamycin vaginal cream is found to be 88% which is comparable with Stein et al (1993)<sup>22</sup>, who reported cure rate of clindamycin vaginal cream 77%, in another study carried out in Germany<sup>23</sup> in 1993, the cure rate of clindamycin

vaginal cream was reported 83%, which is also consistent with our results. Another study carried out in USA<sup>21</sup> in 1995 reported 86% cure rate of clindamycin vaginal cream which is comparable with our results. Hillier et al (1990)<sup>24</sup> reported 94% cures of clindamycin vaginal cream which is slightly higher but still comparable with our results.

In our study cure rate reported for metronidazole vaginal gel is 74% which is comparable with study done by Ferris et al (1995).<sup>21</sup> Another study carried out by Livengood et al in 1994<sup>25</sup> who reported 78% cure rates for metronidazole vaginal gel, which is consistent with our study. In another study carried out by McGregor et al in 1995<sup>25</sup> reported 84% cure rate for metronidazole vaginal gel. Hillier et al in 1993<sup>26</sup> reported 87% cure rates for metronidazole vaginal gel, this cure rate is slightly higher but still comparable with our results.

So our hypothesis proved true that there is no difference between 0.75% vaginal metronidazole once daily for 5 days and 2% vaginal clindamycin cream once daily for three days in treatment of bacterial vaginosis.

The failure rate of metronidazole 0.75% vaginal gel is noted as 26% while the failure rate of clindamycin 2% vaginal gel is noted as 12% comparable with the study done by Ferris et al.<sup>21</sup>

Limitations to this study are that it did not consider long term cure rates reported by other authors.<sup>1, 24, 26, 27</sup> It would generally be expected that longer duration of follow up testing would correspond with increase in failure rates. Long term failure rates have been reported previously for both medications.<sup>1, 24, 26, 27</sup>

## CONCLUSION

Treatment of bacterial vaginosis in pregnancy is important issue. Keeping in view the complications of bacterial vaginosis in pregnancy its treatment is necessary but because of problems associated with oral medication, the local treatment of bacterial vaginosis is now preferred because of its low systemic absorption, once daily dosage



and highest concentration at target site.

In this study the two currently recommended local treatment options vaginal metronidazole gel and clindamycin cream are evaluated and both achieved nearly equivalent cure rates for the treatment of bacterial vaginosis with statistically insignificant difference (p value 0.074).

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“Always do your best.  
What you plant now,  
you will harvest later.”

Og Mandino



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