Comparative Outcomes in Bacterial Vaginosis Treatment: Resistance Insights from a Case- Control Study

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ABSTRACT

Bacterial Vaginosis (BV) stills one of the more prevalent vaginal infections, which characterize by a dysbiosis of the vaginal microbacteria. Despite the availability of effective antimicrobial treatments, therapeutic resistance and recurrence are significant challenges, affecting patient outcomes and increasing healthcare burdens. This study provides a comparative analysis of treatment outcomes in patients with BV, concentrating on resistance mechanisms, recurrent infection rates, and potential contributing factors. A systemic evaluation of metronidazole, clindamycin, and other therapeutic options was conducted on 126 ladies with BV and assess the efficacy, microbial resistant patterns, and clinical recurrence. The study found no significant correlation between patient age and BV resistance (P= 0.86). However, non- hormonal contraception use showed a significant correlation (P =0.02). Probiotics use, vaginal wash and smoking were all significantly associated with BV resistant (P=0.047). This study identifies gaps in current therapeutics regimens, emphasizing the need for personalized approaches and additional treatments targeting microbial biofilms and enhancing healthy vaginal microbiota restoration. Incorporating molecular diagnostic tools and innovative therapies could improve outcomes and mitigate treatment resistance.

Keywords: Bacterial Vaginosis, Treatment Resistance, Recurrence, Biofilm, Microbiota, Metronidazole, Clindamycin.

INTRODUCTION

Bacterial vaginosis (BV) is considering the most common cause of vaginal infection in the women of reproductive age group globally[1]. As it's affecting about from 23 to 29% of the women worldwide[2]. The most common affected age group was from 16 to 45 years old, and the patients usually present with copious vaginal discharge and also foul smell odour[3]. BV was previously named Gardenella vaginitis as the main cause of the condition was by Gardenella species of anaerobic bacteria which were consider the normal flora of the vagina, and that is why the name vaginosis use as the infection was not from outside of the vagina it is from vagina ecosystem[4]. BV was caused by the overgrowth of the anaerobic bacteria which include (*Gardnerella vaginalis, Atopobium vaginae, Megasphaera spp., Prevotella spp. and Sneathia spp.*) as they make the vaginal environment less acidic so become more susceptible to infection[5]. As typically known that the BV was results from decrease of hydrogen- peroxide production from Lactobacilli in the vagina and the overproduction of those previously mention anaerobic bacterial species, but why this condition occurs is still unknown. As BV was consider is not a sexually transmitted condition but it was found that the sexual intercourse create a condition of imbalance between those normal anaerobic vaginal flora and make the Gardenella species more aggressive and eventually prone to the triggering BV condition[6]. BV was linked with increased incidence of acquiring sexually transmitted infection like herpes simplex virus, human immune deficiency virus, chlamydia, gonorrhea, in addition to other pelvic inflammatory disease, miscarriage, preterm labour in pregnant ladies, posthystrectomy and post-partum infection[7].

Diagnosis of bacterial vaginosis:

The characteristic symptoms associated with BV are abnormal vaginal discharge, typically greyish to white and with fishy odour especially after intercourse, in addition to discomfort and irritation during micturation, although some women are asymptomatic which is consider challenging in diagnosis[8]. But still the diagnostic criteria for BV is was by using Amsel criteria, which include presence three out of four criteria must be present to diagnose BV. Amsel criteria indicators that collectively aid in the specific assessment of the condition and it include:

- Thin, homogenous greyish white vaginal discharge coating the vaginal wall.
- Detection of the Clue cell in wet mounts (anaerobic pathological bacteria resolve the wall of the vaginal epithelial cell) as shown in figure (1).
- PH of vagina > 4.5.
- Positive Whiff test (offensive fishy odour after addition of potassium hydroxide to the vaginal discharge).

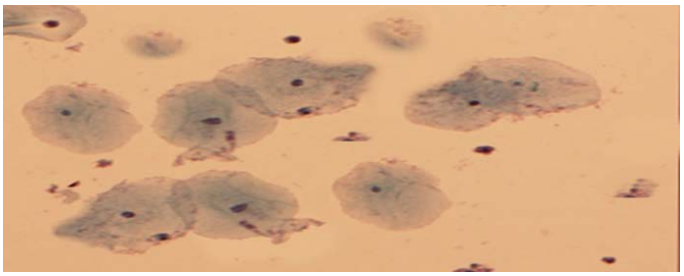

Figure 1. Clue cells

Amsel's criteria have a sensitivity of 95.5- 96.7% and a specificity of 85.8-95%[9].

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Treatment:
Approximately 30% of BV resolves spontaneously without treatment[10]. Treatment was not needed for management asymptomatic patient with BV[11]. However insufficient study supports that management asymptomatic patient may improve the patient outcome. The recommended treatment for BV according to the 2015 Centers for Disease Control and Prevention Sexually Transmitted Disease guidelines, are[12]:

- Metronidazole 500mg orally twice time daily for 7 days.
- Metronidazole 0,75% gel, 2g intravaginally at bedtime for 5 days.
- Clindamycin cream 2% , 5g intravaginally at bedtimes for 7 days.
- Clindamycin gel 2%, 5g intravaginally once only.

Alternative treatment regimens include:

- Tinidazole 2g daily for 2 days, or 1g daily for 5 days.
- Secnidazole granules: 2 g of oral granules all at once.

Those different regimens of treatment of BV are very effective as the cure rate within 1 months range from 80 to 90%[13]. Recurrence of BV may be occurring in about 80% of the condition within 9 months of the initial treatment[14]. While about from 10 to 15% of the condition resolve the condition of BV and need no further management, although there was many Cochrane review study done in 2009 reveal that there was some patient may need additional coarse of antibiotics for those case with recurrent BV and no rule of probiotics or other remedies to resolve the condition[15]. As BV is consider as non-sexually transmitted disease, so there was no need to management of the partner, and also there was no evidence of the recurrent of the condition after resume of intercourse of non-treated partner.

Many studies showed that the treatment of the partner not improve the treated women outcome or prevention of the recurrence of the condition[16]. In 2017, Secnidazole was approved by U.S. Food and Drug Administration (FDA) for single dose oral treatment of BV[17]. Secnidazole, which was a next generation of 5- nitroimidazole, was considering the best treatment option for treating parasitic and bacterial infection[18]. In 2021 U.S. FDA approved that use of single dose of Clindamycin vaginal gel was consider the most convenience and the best compliance for the patient with BV from 12 years and older, because of good compliance[19].

There are many factors could be linked with the development of resistant BV. Probiotics which consider as a live microorganism, it could be giving in diet or through vaginal rout. Probiotics contain lactobacilli, which could be used for management of BV, also probiotics studied as a way for treatment and prevention of recurrence of BV infection[20]. Vaginal washing (douching) as one of the ways used by patients to relive of BV symptoms, it was no significant correlation as relieving and prevent of resistant BV[21].

On the other hand smoking as one of the adverse effect on any infection in body as BV, so consider one of the risk factors that should be modified in lifestyle to be consider in management[22]. Regarding contraception use as their effect on BV either hormonal and non-hormonal, a cross sectional study conducted on 16,314 patient it found that BV more common on patients using non-hormonal contraception like Intrauterine contraceptive device (IUCD) 14,8% , while women with hormonal contraception like oral pills (COCP) 9,7%, and those not using contraception 11.1%[23].

This study aimed to identify predisposing factors for BV resistance and evaluate treatment outcomes, focusing on lifestyle habits, contraception methods, and clinical history.

PATIENT AND METHODS

A prospective study was conducted on 126 women with BV, referred to a private clinic in Mosul city in a period from August 2022 to October 2023. A full history taking from all participants, and if they use any herbal or therapy before referral. Body mass index (BMI) was calculated to all participants.

Inclusion criteria: Women in their reproductive age from 18 -45 years, married, and use contraceptive.

Exclusion criteria: Pregnancy, diabetes mellitus, drugs allergy and refusal to participate. Participants received oral metronidazole (500 mg twice daily for 7 days) and vaginal suppositories containing metronidazole, tinidazole, or clindamycin.

Statistical analysis: Were performed using SAS9 software version 9 (SAS, Inc., Cary, NC, USA). The data were epitomized as the mean with standard deviation and reviewed by using Chi-square test and Fisher test. A P value considered as statistically significant if it is less than 0.05.

RESULTS

A case control descriptive study include 126 ladies complaint from BV, follow up them as 60 (47.6%) women develop resistant to treatment and not cure, while 66 (52.4%) achieve resolution.
Our study enrolled ladies at reproductive age and we concentrated in ladies from 18 to 45 years old, the majority of our patients involved were more than 35 years in their age as shown in the figure (2).

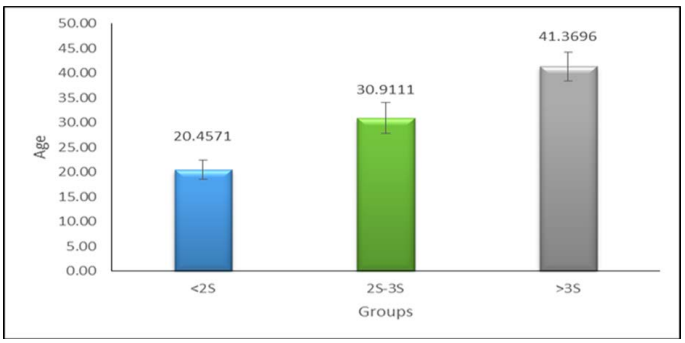

Figure 2. Different Incidence of age groups involve in the study.

Although the majority of them as more than 35 years but this not appear as a risk factors for development of resistant to BV management, as the P value 0.86 which was statistically non-significant as shown by table (1).

Table 1. The Effect of patient age on resistant BV.

Age (years)	cured	Resistant	Total	Chi² value
<25	19(28.8%)	16(267%)	35(27.8%)	1.13
25-35	23(34.8%)	22(36.7%)	45(35.7%)	(0.86)
>35	24(36.4%)	22(36.7%)	46(36.5%)	
Total	66(524	60(476	126(100%)	

Oral probiotics, in addition to vaginal washing (douching), and smoking show there was strong correlation between those habits and resistant BV, as their incidence in our study (22.2%, 8,7% and 7,1%) respectively, and according to chi² test the relation was significant as the P value 0.047 as shown in table (2).

Table 2. Effects of habits on resistant BV infection.

Habits	cure	Resistant	Total	Chi² value
Probiotics	25(19.8%)	28(22.2%)	53(42.1%)	4.912*
Smoking	14(11.1%)	9(7.1%)	23(18.3%)	(0.047)
Vaginal wash	6(4.8%)	11(8.7%)	17(13.5%)	
Nothing	21(16.7%)	12(9.5%)	33(26.2%)	
Total	66(52.4%)	60(47.6%)	126(100%)	

Regarding the effect of contraceptive using by patients enrolled in study, as condom consider as protective for BV, but still non-hormonal contraception like IUD consider as one of risks of resistant in addition to oral hormonal methods OCCP, the correlation was significant as the P value 0.02, as shown in table (3).

Table 3. Effect of contraception on resistance.

contraception	Cure	Resistant	Total	Chi² value
Condom	1(0.8%)	6(4.8%)	7(5.6%)	4.32*
Loop	8(6.3%)	13(10.3%)	21(16.7%)	(0.02)
OCCP	21(16.7%)	14(11.1%)	35(27.8%)	
Not	21(16.7%)	17(13.5%)	38(30.2%)	
Total	66(52.4%)	60(47.6%)	126(100%)	

In regarding to patients education regarding the development of BV and its resistance, our study show there was significant correlation between lower educations and BV resistant as the P value 0.045 by Fisher's test in table (4).

Table 4. Effect of education on BV occurring and resistant.

Education	Cure	Resistant	Total	Fisher value
Primary	61(48.4%)	57(45.2%)	118(93.7%)	3.12*
Secondary	4(3.2%)	1(8%)	5(4.0%)	(0.045)
Illiterate	1(8%)	2(1.6%)	3(2.3%)	
Total	66(52.4%)	60(47.6%)	126(100%)	

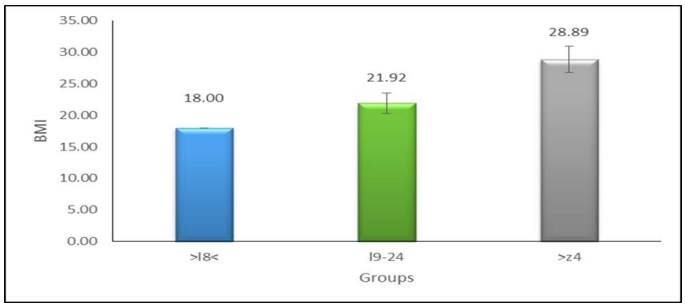

Figure 3. BMI in the studied population with resistance BV.

Regarding to BMI correlation with occurrence of the BV resistant, our study show there was no significant correlation between BMI and BV, as the P value equal 0.05, which showed in figure (3).

DISCUSSION

This study highlights significant associations between lifestyle factors, contraception, and BV resistance. Reproductive age group of women were enrolled in the study, as this age group most commonly complaint from BV in different times during years.

A study done on 212 non pregnant women in reproductive age, where 85 women of them diagnosed to had BV, giving the prevalence 40.1%, and it was commonly at women from 25 to 34 years age range (50; 58.8%)[24]. While our study showed the most age group develop of resistant BV infection were more than 35 years age, but the result was not significant.

Different habits were the referral patients have, like probiotics, smoking and vaginal wash (douching) use, which could be the causes of development of the resistant BV infection. Probiotics which consider as lactobacilli (normal vaginal flora) and had very important rule to resume the vaginal PH and also it consider as therapeutic and also methods for prevention of recurrence or resistant strain of BV bacterial species[25]. Probiotics can be giving as an oral or vaginal way, and many studies showed the strains use of lactobacilli was of gut origin not vaginal[26].

Randomized control trail conducted on 544 ladies with BV and using oral probiotics experience a return of the lactobacilli rich vaginal flora in six weeks period in comparing placebo (61.5%vs 26.9%), some trails show that the probiotics had no evidence to be comparable or enhance the effects of antibiotics use, and they reported no beneficial effects to use probiotics in combine with antibiotics for treating BV[27]. Some studies showed that practicing of vaginal douching by the patients had no rule in BV, while other show it as a risk for development of BV depending in the content of the douching and the frequency of using it[24]. As we know that the smoking had many risks in different body part and could be the cause of infection, as a cohort study done in 956 patient showed that the smoking consider as significant risk for BV as odd ration 0.3, may be due to its effect in lactobacilli concentration and elevated vaginal PH[25]. All those habits show in our study significant correlation.

Regarding contraception use, various studies had examined the use of condom with prevalence and incidence of BV. Meta-analysis and systemic review show that the condom as a protective against BV with the estimated relative risk 0.8, while other research's show that copper IUD increase BV prevalence, while hormonal and condom decrease the risk of BV[20]. Our study also shows a significant correlation between non- hormonal contraception and BV.

Ness et al and Ashraf-Ganjoei et al both studies link significantly between low education and BV. It could be due to low education and low social class associated with high risk sexual behavior, which may increase the acquisition of reproductive tract infection as BV[24].

A study show that during follow up a patients with BV that 41% were under weight, 37.5% normal weight and 35.2% were overweight. In unadjusted analysis show that women with overweight had less incident to develop BV, compare with a women with normal BMI (RR 0.84, 95%CI0.37-0.96)[28].

CONCLUSION

BV is a common yet challenging condition to manage due to frequent resistance and recurrence. While antibiotics remain the primary treatment, alternative approaches such as probiotics, biofilm targeting agents, and lifestyle modifications show promise in improving outcomes. Future research should focus on integrating these strategies to optimize treatment and reduce recurrence. As considering science lack answer about the best management options to prevent the recurrence of BV, the doctors and the patient trying to find the solution by its own.

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and revising it critically for important intellectual content; and (3) final approval of the manuscript version to be published. Yes.

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Competing Interest: None

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