Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2023**; 50(8): 176
https://doi.org/10.31083/j.ceog5008176

Original Research

Pathogenic Factors of Bacterial Vaginitis and Construction of Nomogram Prediction Model

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Academic Editor: Andrea Tinelli
Submitted: 11 March 2023 Revised: 11 April 2023 Accepted: 13 April 2023 Published: 17 August 2023

Abstract

Background: This study aims to explore the risk factors inducing bacterial vaginosis (BV) and establish a nomogram prediction model. **Methods**: Single-factor analysis and multivariate logistic regression were used to analyze the risk factors affecting the onset of BV. The selected risk factors were incorporated into the R software to establish a nomogram prediction model. The effectiveness of the proposed model was evaluated. **Results**: The cleanliness of vaginal secretions above grade III accounted for 90.86% (169/186) of the cases. Multivariate logistic regression analysis showed that the use of nursing pads during non-menstrual periods, history of miscarriage $\geq$1 time, self-vaginal douche, and frequency of sexual activity $\geq$5 time per week were identified as risk factors for the incidence of BV ($p <$ 0.05). Using condoms as a method of contraception was identified as a protective factor for the incidence of BV ($p < 0.05$); A nomogram prediction model was established based on the aforementioned risk factors, and the area under the receiver operating characteristic (ROC) curve was 0.789 (95% confidence interval (CI): 0.751–0.827), indicating that the nomogram had a good degree of discrimination. The slope of the calibration curve was close to 1. Decision curve analysis (DCA) shows that it has good clinical value. **Conclusions**: The nomogram prediction model established based on BV risk factors has good discrimination and high degree of consistency.

Keywords: bacterial vaginosis; prediction model; risk factors

1. Introduction

Bacterial vaginosis (BV) is a common gynecological inflammation, which is associated with the decrease of the number of lactobacilli in vagina and the imbalance of flora caused by significant growth of Gardnerella vaginalis [1]. Previous reports have pointed out that about 60%–64% of BV patients are complicated with cervical erosion [2,3]. The pathological features of BV are mucosal edema and inflammation, and the symptoms include abnormal leucorrhea, sexual pain and vaginal itching, which seriously affect the life of patients. Recent studies have found that BV is closely related to infertility, premature birth and abortion [4]. Women's reproductive health is affected by multiple factors, such as biology, personal behavior, society, etc., which is difficult to be predicted clinically. Individualized prediction of BV risk and preventive intervention are helpful to reduce BV incidence and improve women's living quality. However, there are few reports on individual prediction of BV. The nomogram, also known as Monograph, shows that [5], the nomogram prediction model has good discrimination and high degree of consistency in predicting adverse events. In this study, the clinical data of female patients undergoing physical examination in outpatient department were analyzed, the related risk factors affecting BV were discussed, and a nomogram model was established to predict the risk of BV individually.

2. Research Object and Method

2.1 Research Object

In the experiment, a total of 883 women aged 26–62 years, with an average age of (39.87 $\pm$ 8.49) years, who had undergone physical examination from June 2021 to July 2021 in Meizhou people's Hospital, were chosen as research objects. None of the included women were in menstruation or pregnancy, and all of them had no history of vaginal medication or antibacterial medication in the past 1 week, and had no sexual life in the past 3 days.

2.2 Examination Method

All participants in this study underwent vaginal examination by the same gynecologist. All included subjects had no history of vaginal irrigation within 24 hours, and underwent vaginal examination. Three cotton swabs were used to take the secretion of 1/3 section of vaginal wall for pH value detection, microscopic examination and amine test. Among them, one smear was added with normal saline to detect trichomonas, and one was sent to the laboratory for BV examination. BVBlue rapid detection method and Amsel gold standard method were used to detect polyamine. The other smear was heated, and then observed under a fixed mirror for clue cells.

2.3 Diagnostic Criteria

According to the relevant standards of *Obstetrics and Gynecology* (9th Edition) [6]: ① increased vaginal secre-

Table 1. Single factor analysis of BV occurrence.

Clinical data		Total	Infected group (n = 186)	Non-infected group (n = 697)	χ^2	p
Age (year)	<35	284	61 (32.80)	223 (31.99)	4.443	0.108
	35–50	424	98 (52.69)	326 (46.77)		
	>50	175	27 (14.52)	148 (21.23)		
Education degree	Junior high school and below	346	86 (46.24)	260 (37.30)	5.139	0.077
	High school/technical secondary school	305	59 (31.72)	246 (35.29)		
	Junior college and above	232	41 (22.04)	191 (27.40)		
Monthly income (¥[a])	<¥1000 (US $138.66)	138	39 (20.97)	99 (14.20)	5.936	0.051
	¥1000–3000 (US $138.66–415.99)	309	66 (35.48)	243 (34.86)		
	>¥3000 (US $415.99)	436	81 (43.55)	355 (50.93)		
Marital status	Unmarried	93	12 (6.45)	81 (11.62)	4.536	0.104
	Married	618	139 (74.73)	479 (68.72)		
	Divorced	172	35 (18.82)	137 (19.66)		
Occupation	Farmer	158	29 (15.59)	129 (18.51)	1.247	0.742
	Worker	273	57 (30.65)	216 (30.99)		
	Company employee	280	64 (34.41)	216 (30.99)		
	Other	172	36 (19.35)	136 (19.51)		
Habit of wearing tights	None	424	82 (44.09)	342 (49.07)	1.460	0.227
	Yes	459	104 (55.91)	355 (50.93)		
Use of nursing pad during non-menstrual period	None	651	110 (59.14)	541 (77.62)	25.881	0.000
	Yes	232	76 (40.86)	156 (22.38)		
Abortion history (time)	0	287	35 (18.82)	252 (36.15)	23.107	0.000
	1	380	88 (47.31)	292 (41.89)		
	≥2	216	63 (33.87)	153 (21.95)		
Oral sex	None	778	154 (82.80)	624 (89.53)	6.349	0.012
	Yes	105	32 (17.20)	73 (10.47)		
Sexual partner (each)	0	82	11 (5.91)	71 (10.19)	5.625	0.060
	1	692	145 (77.96)	547 (78.48)		
	≥2	109	30 (16.13)	79 (11.33)		
Self-vaginal irrigation	None	618	111 (59.68)	507 (72.74)	11.928	0.001
	Yes	265	75 (40.32)	190 (27.26)		
Frequency of sexual activity per week (times)	0–2	221	21 (11.29)	200 (28.69)	39.266	0.000
	3–4	483	102 (54.84)	381 (54.66)		
	≥5	179	63 (33.87)	116 (16.64)		
Contraceptive methods	Condom	392	38 (20.43)	354 (50.79)	67.814	0.000
	Contraceptive	164	42 (22.58)	122 (17.50)		
	Intrauterine device	233	65 (34.95)	168 (24.10)		
	No contraception	94	41 (22.04)	53 (7.60)		
History of vaginitis	None	425	78 (41.94)	347 (49.78)	3.623	0.057
	Yes	458	108 (58.06)	350 (50.22)		

BV, Bacterial vaginosis. [a] $1 = ¥6 to 8.

tion with thin character and fishy smell; ② positive amine test; ③ pH value of vaginal secretion above 4.5; ④ positive clue cells (prerequisite). BV was diagnosed when 3 of the above 4 items were positive.

2.4 Research Method

A self-made questionnaire was used to investigate the information of patients, including age, education level, monthly income, abortion history, oral sex, sexual partner, whether to wash the vagina independently, sanitary pads used during menstruation, nursing pads used during non-menstruation, times of sexual activities per week, contraceptive methods, history of vaginitis, etc. All the patients agreed to participate voluntarily in the questionnaire survey. A total of 967 questionnaires were distributed, 883 of which were effectively recovered, with an effective recovery rate of 91.31%. The acquired data were checked and entered by two persons to ensure accuracy.

2.5 Statistical Treatment

Data were processed by SPSS 22.0 software (IBM Corp., Armonk, NY, USA). Continuous variables conform-

Table 2. Multivariate logistic regression variable assignment.

Variable	Assignment
Use of nursing pad during non-menstrual period	None = 0, Yes = 1
Abortion history	0 = 0, 1 = 1, ≥2 = 2
Oral sex	None = 0, Yes = 1
Self-vaginal irrigation	None = 0, Yes = 1
Frequency of sexual activity per week	0–2 = 0, 3–4 = 1, ≥5 = 2
Contraceptive methods	Condom = 0, contraceptive = 1, IUD = 2, no contraception = 3

IUD, Intrauterine device.

ing to normal distribution are expressed in the form of mean ± standard deviation ($\bar{x} \pm S$); classification variables are expressed by case number and rate (%), and χ^2 test was carried out. Taking the occurrence of BV as the dependent variable and the clinical data with statistical significance in univariate analysis as the independent variable, the risk factors affecting BV were screened by multivariate Logistic regression analysis with $\alpha = 0.05$ as the test standard. Independent risk factors were introduced into R software (R3.6.3, R Foundation for Statistical Computing, Vienna, Austria), and rms package was applied to build a nomogram prediction model of BV risk. The Bootstrap method was used for internal verification by repeated sampling for 100 times. Receiver operating characteristic (ROC) curve and goodness-of-fit test were used to evaluate the discrimination and accuracy of the model.

3. Results

3.1 Incidence of BV and Its General Demographic Characteristics

There were 186 cases of BV among 883 women undergoing gynecological examination, and the incidence of BV was 21.06% (186/883). Among them, 17 cases were of grade I–II, accounting for 9.14%; 169 cases were above grade III, accounting for 90.86%; 156 cases were positive in amine test, accounting for 83.87%. There were 284 cases (32.16%) under 35 years old, 424 cases (48.02%) between 35 and 50 years old, and 175 cases (19.82%) over 50 years old. There were 346 cases with educational background of junior high school and below (39.18%), 305 cases (34.54%) with educational background of high school/technical secondary school, and 232 cases (26.27%) with educational background of junior college or above. There were 138 cases (15.63%) with monthly income less than ¥1000 (US $138.66), 309 cases (34.99%) with monthly income between ¥1000 (US $138.66) and ¥3000 (US $415.99), and 436 cases (49.38%) with monthly income more than ¥3000 (US $415.99). There were 93 cases unmarried (10.53%), 618 cases married (69.99%), and 172 cases with history of divorce (19.48%). There were 158 farmers (17.89%), 273 workers (30.92), 280 employees (31.71%) and 172 others (19.48%). There were 424 cases (48.02%) with the habit of wearing tights, and 232 cases (26.27%) who use nursing pads during non-menstrual period. There were 287 cases (32.50%) without abortion history, 380 cases (43.04%) with one abortion, and 216 cases (24.46%) with more than two abortions. There were 105 cases of oral sex (11.89%), 82 cases (9.29%) having no sexual partners, 692 cases (78.37%) having 1 partner, and 109 cases (12.34%) having 2 partners or more; there were 265 cases of self-vaginal irrigation (30.01%). There were 221 cases (25.03%) having sex 0–2 times per week, 483 cases (54.70%) having sex 3–4 times per week and 179 cases (20.27%) having sex more than 5 times per week. There were 392 cases (44.39%) of condom contraception, 164 cases (18.57%) of contraceptive contraception, 233 cases (26.39%) of intrauterine device (IUD) contraception and 94 cases (10.65%) of no contraception. There were 458 cases (51.87%) with history of vaginitis.

3.2 Single-Factor Analysis of BV Occurrence

According to the occurrence of BV, 883 patients were divided into infected group (n = 186) and uninfected group (n = 697). Univariate analysis results showed that use of nursing pads during non-menstrual period, abortion history, oral sex, self-vaginal irrigation, frequency of sexual activity per week and contraceptive methods were the main factors affecting the occurrence of BV ($p < 0.05$) as shown in Table 1.

3.3 Variable Assignment

Values were assigned to meaningful variables in single factor analysis, as shown in Table 2.

3.4 Logistic Regression Analysis of Multiple Factors Affecting BV Occurrence

The significant variables of univariate analysis, including use of nursing pad during non-menstrual period, abortion history, oral sex, self-vaginal irrigation, frequency of sexual activity per week, contraceptive method, were taken as independent variables (see Table 2), and the index of BV occurrence was taken as a dependent variable. They were included in logistics regression equation for multivariate analysis. The results showed that use of nursing pad during non-menstrual period, abortion history ≥1 time, self-vaginal irrigation and frequency of sexual activity ≥5 times per week were the risk factors for BV occurrence ($p < 0.05$) (see Table 3).

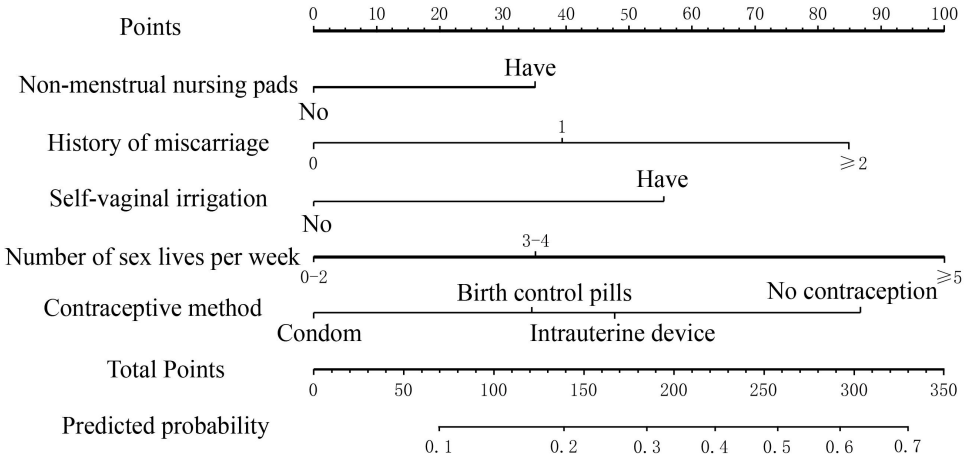

Fig. 1. Nomogram model of bacterial vaginosis (BV) incidence.

Table 3. Multivariate logistic regression analysis of BV occurrence.

Variable	β	*SE*	*Wald* (χ^2)	*p*	OR	95% CI	
						Lower limit	Upper limit
Use of nursing pad during non-menstrual period (1)	0.435	0.190	5.250	0.022	1.545	1.065	2.241
Abortion history			18.624	0.000			
Abortion history (1)	0.459	0.219	4.407	0.036	1.583	1.031	2.431
Abortion history (2)	0.996	0.233	18.314	0.000	2.708	1.716	4.273
Oral sex (1)	0.417	0.255	2.683	0.101	1.517	0.921	2.499
Self-vaginal irrigation (1)	0.659	0.181	13.285	0.000	1.933	1.356	2.755
frequency of sexual activity per week			22.576	0.000			
frequency of sexual activity per week (1)	0.417	0.235	3.156	0.076	1.518	0.958	2.405
frequency of sexual activity per week (2)	1.166	0.261	20.009	0.000	3.210	1.926	5.351
Contraceptive method			15.016	0.002			
Contraceptive method (1)	0.408	0.242	2.854	0.091	1.504	0.937	2.415
Contraceptive method (2)	0.566	0.217	6.779	0.009	1.762	1.150	2.698
Contraceptive method (3)	0.982	0.272	12.996	0.000	2.670	1.565	4.553
Constant	–3.076	0.301	104.464	0.000	0.046		

BV, Bacterial vaginosis; OR, Odds ratio; CI, Confidence interval; SE, standard error; (1), Contraceptive; (2), Intrauterine device; (3), No contraception.

3.5 Construction of Nomogram Model

Based on the main influencing factors of BV obtained by multivariate logistic regression model, a nomogram model was established by using R software (Fig. 1), and the prediction probability associated with the sum of the index scores represents the predictive value for BV occurrence risk. To be specific, 35 points were assigned to the use of nursing pad during non-menstrual period, 39 points to abortion history once, 85 points to sexual activity frequency $\geq$2 times per week, 55 points to self-vaginal irrigation, 35 points to sex frequency of 3–4 times per week, 100 points to sex frequency $\geq$5 times per week, 34 points to contraceptive contraception, 47.5 points to intrauterine device contraception and 86 points to no contraception. If a patient uses nursing pad during non-menstrual period (35 points), has abortion history $\geq$2 times (100 points), does vaginal irrigation by himself/herself (55 points), has sexual activity frequency $\geq$5 times per week (100 points) and takes condom contraception (0 points), the total score would be 290 points, and the prediction probability is about 60%, and eventually this patient is evaluated as a high-risk patient.

3.6 Verification of Nomogram Model

According to the prediction model formula, the risk prediction value of BV was calculated. The area under the ROC curve was used to evaluate the nomogram. The area under the curve was calculated to be 0.789 (95% confidence interval (CI): 0.751–0.827, Fig. 2A) in this work, indicating that the nomogram had good discrimination. The calibration curve of nomogram was plotted, and the slope of calibration curve was close to 1 (Fig. 2B). Hosmer-Lemeshow goodness-of-fit test showed = 6.408 and $p = 0.602$, indicating that the nomogram model had high degree of consistency in predicting BV infection risk. The decision curve

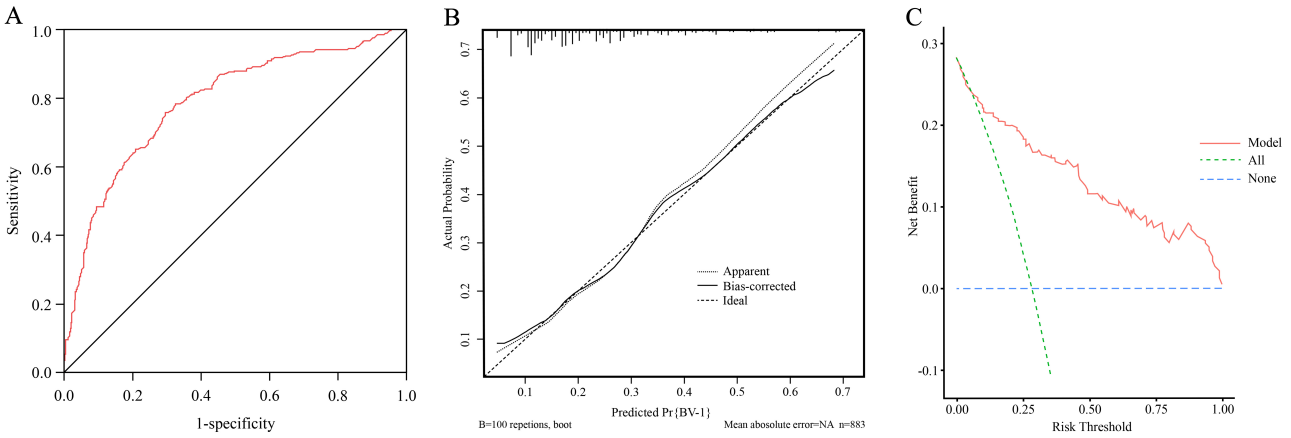

Fig. 2. Verification of nomogram model. (A) ROC curve analysis of nomogram model for predicting BV risk. (B) Calibration curve of nomogram model. (C) DCA curve of BV infection risk nomogram prediction model. ROC, receiver operating characteristic; BV, bacterial vaginosis; DCA, decision curve analysis

analysis (DCA) curve shows that the nomogram model can make valuable judgments and has good clinical applicability (Fig. 2C).

4. Discussion

Vaginitis mostly occurs in women at childbearing age, with bacteria, trichomonas and candida as the main pathogens. Previous reports have pointed out that the incidence of BV is between 10% and 40%, and most women do not see a doctor because their symptoms are not obvious or there are no significant impact on their lives [7,8]. In this study, the present situation of BV was investigated. The incidence of BV was 21.06% in 883 women who had physical examination in gynecological outpatient department of our hospital, which was higher than the value of 5.3% reported by Li M *et al.* [9], which may be related to the difference in sample size. The vaginal flora of healthy women is mainly Lactobacillus, and the lactic acid secreted by it can effectively maintain the acidic environment of vagina. The normal flora in vagina are mutually restricted and dependent, thus maintaining the microecological balance in vagina. Studies have shown that the occurrence of BV is related to the destruction of microecological balance in vagina [10]. 30–40 years old is the age with high incidence of vaginitis. BV can cause cervicitis and pelvic inflammatory disease. If the patient is pregnant, adverse perinatal outcomes may be resulted [11,12]. In addition, recur easily recur and interfere with women's daily life, so attention should be paid in clinical practices. At present, clinical scholars have attached great importance to women's BV, and have conducted research on nursing and cross-sectional investigation [13]. However, how to realize individual prediction of BV is a clinical problem to be solved.

In this study, a nomogram prediction model was established based on the influencing factors of BV, such as use of nursing pad during non-menstrual periods, abortion history, frequency of sexual activity per week and contraceptive methods. The nomogram prediction model visually illustrates the contribution of the aforementioned factors to BV through a scoring system. Based on the sum of scores from these factors, each woman can be associated with a corresponding prediction probability. The nomogram showed that using nursing pad during non-menstrual period could increase the influence weight by 35 points, and self-vaginal irrigation could increase the influence weight by 55 points. At present, it is generally believed that personal hygiene habits and living habits are important factors affecting the occurrence of BV [14]. Vagina itself has self-cleaning and defensive functions, and the number of lactic acid bacteria is stable under acid-base equilibrium. Some women may experience increased vaginal discharge as a result of sexual activity, vaginitis, or other factors. To maintain hygiene, they may often use nursing pads. However, the use of nursing pads and self-vaginal irrigation during non-menstrual period can destroy the natural defense mechanism of vagina, change the restrictive relationship between microorganisms in vagina, lead to pathogen invasion, and affect the microecological balance in vagina, thus causing BV. It is suggested to strengthen public health education, improve women's awareness of health care, correctly carry out vaginal cleaning, and use pads reasonably.

The nomogram proposed in this study shows that higher frequency of sexual activity per week can cause greater influence weight on BV. Previous studies have shown that the stability of vaginal lactobacilli is affected by sexual activity [15]. The reason may be that sexual activity can destroy the acidic environment in vagina, increase the pH value in vagina, and reduce the number of lactobacillus settlement. Scholars at home and abroad believe that contraceptive methods have an important impact on BV, and condoms are the protective factors of BV infection [16]. According to the nomogram of this study, the

scores of influence weight of contraceptive pill, IUD and non-contraception were higher than those of condom contraception. It is suggested that condom contraception can block the pathogenic bacteria and reduce the risk of BV, which is consistent with previous reports [17]. Therefore, we should pay more attention to women's sexual habits, especially the use of condoms, which not only helps to prevent BV, but also facilates the prevention of the spread of other sexually transmitted diseases. Abortion can damage endometrium, induce chronic inflammation, and destroy the normal defense mechanism of vagina. At the same time, abortion can also reduce immunity. This study shown that the risk of BV in women with more than 2 times of abortions was significantly increased. However, studies have also pointed out that BV has nothing to do with pregnancy outcomes such as premature delivery and miscarriage [18]. The relationship between induced abortion and BV needs to be further analyzed by a large-sample multi-center study.

5. Conclusions

To sum up, the proposed nomogram prediction model based on BV risk factors has good discrimination and high degree of consistency, which is helpful for medical staff to screen out the high-risk population of BV according to relevant data of physical examination women.

Availability of Data and Materials

The datasets used during the present study are available from the corresponding author upon reasonable request.

Author Contributions

XC—Manuscript writing, Project development, Data Collection; NL—Revised the paper, Data analysis, Data collection; HL and JL—Data collection. All authors contributed to editorial changes in the manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

This retrospective study involving human participants was in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by our institution's ethics review board (approval number: 2021-C-113). All subjects gave their informed consent for inclusion before they participated in the study.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

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