

Risk factors for candida infection of the genital tract in the tropics

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Abstract

Objective: To investigate the risk factors associated with candida infection of the genital tract in the tropics.

Methods: We performed questionnaire survey and experiments at the Hainan branch of General Hospital of People's Liberation Army, Hainan General Hospital and Sanya Maternity and Child Health Care Hospital in 2013. Controls were without Candida infection of genital tract, and cases had from Candida infection.

Results: We recruited 689 cases and 652 controls. The average age of cases with Candida infection of the genital tract was higher than that of controls. In the multivariate modeling, marriage (adjusted odds ratio: 2.49, 95% confidential interval: 1.09-5.67) and vaginal lavage (adjusted odds ratio: 4.41, 95% confidential interval: 1.13-5.14) were significantly associated with Candida infection of genital tract in tropics.

Conclusion: Candida infection was related with age. Marriage and Vaginal lavage were significant risk factors. Attention should be paid to health education for the prevention of these infections.

Key word: Candida infection, risk factors, genital tract.

DOI: <http://dx.doi.org/10.4314/ahs.v14i4.10>

Introduction

Candidal vaginitis represents one of the most common gynecological disorders¹. Common risk factors for Candida infection are recent antibiotic use, pregnancy, diabetes mellitus, oral-contraceptives and inadequate therapy².

Isolation of Candida (species) spp. from samples of vaginal exudates is a very frequent thing.

Candida albicans accounts for the majority of cases with Candida infection³⁻⁴. Almost 75% women will have a candidal vulvovaginitis during their life span, and nearly half of them will suffer from a second event⁵. It is widely perceived that the incidence of Candida infection is rising. This motivated the study to search for potential risk factors and to potentially prevent Candida infection.

Identification of risk factors is a very important way in the prevention of diseases. The objective of this study was to determine the risk factors for Candida infection of genital tract in the tropics and provide a basis for disease infection.

Methods

Study design

This study was a case control study. Information on the cases was collected from the Hainan branch of General Hospital of People's Liberation Army, Hainan General Hospital and Sanya Maternity and Child Health Care Hospital from January in 2013 to October 2013 using a detailed questionnaire survey. Cases were sexually active patients. Vaginal examination was performed in the cases. Vaginal secretion examination, microscopic examination and thin prep cytology test (ICT) were employed to diagnose Candida infection of genital tract. Controls were patients without Candida infection who were randomly selected from patients presenting to the hospitals. This study was approved by the Ethics committee of Chinese People's Liberation Army General Hospital, and informed consent was acquired from the patients.

Data was collected by physicians. Data included patient baseline demographic characteristics, underlying disease, potential risk factors for Candida infection of genital tract. Risk factor information for cases and controls included: age, marriage, household register, length of residence in Hainan, education, procreation of children, abortion, tight pants wearing, use of sanitary towel, vaginal lavage, use of pantyliners, times of sex, cleaning the vulva before sex, sexual partners, type of registered permanent residence, type of current address, type of current domicile, occupation, disease, ways of cleaning knickers, ways of drying knickers, times of swimming,

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menstrual cycle, sexual during menstrual period, frequency of daily shower, ways of shower, contraceptive method, frequency of shower during menstrual period, cleaning the vulva after sex, fabric of knickers, knickers replacement, working environment.

Statistical analysis

Univariate analysis was conducted for each case-control study to identify potential risk factors for Candida infection of Genital tract. The χ^2 square or Fisher's Exact Test was used for categorical variables, and independent t-test was used for continuous variables. Variables with p values ≤ 0.10 by univariate analyses were included in multivariate modeling. Multivariate analysis was performed by conditional multiple logistic regression for the risk factors associated with Candida infection of the genital tract. Adjusted odd ratios (ORs) were calculated. Categorical covariates analysis were used Indicator. Two-sided p values of <0.05 were considered statistically significant. Sta-

tistical analysis was performed using SPSS ver. 13.0.

Results
Cases characteristics

Total 1341 patients participated in the questionnaire. Among them, 689 patients were infected by Candida spp. 382 infected patients and 263 controls responded to a simplified questionnaire survey. Blank and input errors were excluded from the study. In the cases, only 2.6% (n=683) patients had first time infection and 97.3% were infected by more than 2 times. 46.2% (n=671) were unsure of the reason for infection. 33.8% (n=674) infected person were unknown drug treated for disease. In 142 (72.4%, n=196) cases, leucorrhea was abnormal, accompanied with pruritus vulvae.

Risk factors for Candida infection

Table1 shows the results of univariate analyses. Patients with infection were older (p=0.003).

Table 1 Univariate analyses for risk factors associated with Candida infection of genital tract in tropics

Variables ^a	Case	Control Group(%)	P value	Unadjusted
Age,Median(interquartile range)	35(28-41)	32(25-38)	0.003	
Marriage			<0.001	2.0(1.484-2.601)
Yes(n=1075)	585(54.4)	490(45.5)		
No(n=254)	96(37.8)	158(62.2)		
Length of residence in Hainan			0.095	
Short stay(n=72)	35(48.6)	37(51.4)		
2-6 months(n=55)	23(41.8)	32(58.2)		
6-12 months(n=59)	30(50.8)	29(49.2)		
1-3 years(n=145)	62(42.8)	83(57.2)		
Long term(n=988)	526(53.2)	462(46.8)		
Education			0.045	
Primary school (n=99)	50(50.5)	49(49.5)		
Junior school(n=439)	233(53.1)	206(46.9)		
High school(n=198)	101(51.0)	97(49.0)		
Special school(n=141)	71(50.4)	70(49.6)		
College(n=197)	127(64.5)	90(35.5)		
University (n=207)	87(42.0)	120(58.0)		
Graduate and above(n=20)	12(60.0)	8(40.0)		
Procreation of Children			<0.001	
None(n=477)	196(41.1)	281(58.9)		
One(n=464)	261(56.3)	203(43.7)		
Two(n=314)	173(55.1)	141(44.9)		
Three(n=90)	49(54.4)	41(45.6)		
≥Four(n=11)	7(63.6)	4(36.4)		
Abortion			<0.001	
None(n=641)	263(41.0)	378(59.0)		
One(n=335)	180(53.7)	155(46.3)		
Two(n=210)	141(67.1)	69(32.9)		
Three(n=81)	58(71.6)	23(28.4)		
≥Four(n=56)	39(69.6)	17(30.4)		
Tight pants wearing			<0.001	1.5(1.204-1.870)
Yes(n=539)	309(57.3)	230(42.7)		
No(n=798)	377(47.2)	421(52.7)		
Vaginal lavage			<0.001	1.9(1.347-2.760)
Yes(n=198)	138(69.7)	60(30.3)		
No(n=421)	229(54.4)	192(45.6)		
Cleaning the vulva before sex			0.067	
Day-to-day(n=338)	189(55.9)	149(44.1)		
Once in a while(n=133)	87(65.4)	46(34.6)		
No(n=97)	64(66.0)	33(34.0)		
Sexual partner			0.001	
One(n=602)	355(59.0)	247(41.0)		
Two(n=16)	15(93.8)	1(6.2)		
Thrice(n=6)	1(16.7)	5(83.3)		
≥Four(n=4)	3(75)	1(25)		

Ratio a, Only these variables with P values less than or equal to 0.10 are included. The following variable are also tested: household register, use of Pantyliners, use of sanitary towel , times of sex, type of registered permanent residence, type of current address, type of current domicile, occupation, disease, ways of cleaning knickers, ways of drying of knickers, times of swim-

ming, menstrual cycle, sexual life during menstrual period, frequency of daily shower, ways of shower, contraceptive method, frequency of shower during menstrual period, cleaning the vulva after sex, fabric of knickers, knickers replacement, working environment. b, OR are available for 2×2 χ^2 test.

The average age of cases was 35 years, while for controls it was 32 years. Cases tended to be married than uninfected control (unadjusted OR: 2.0, p<0.001). Length of residence in Hainan Province, education and cleaning vulva before sex, to some degree, were not associated with infection, demonstrated by P=0.095, 0.045 and 0.067 respectively. Cases had given birth more times, compared with controls (p<0.001). Abortion was linked to a high chance of Candida infection (p<0.001). Patients always wearing tight pants were more likely to suffer from infection, compared with these who did not wear (unadjusted OR:1.5(1.204-1.870), p<0.001). The probability of infection in patients with vaginal lavage was 1.9 times of control group (unadjusted OR:1.9(1.347-2.760), P<0.001). Cases commonly manifested more sexual partners than control (P=0.001). There were no significantly differences in household

register, use of pantyliners, use of sanitary towels , frequency of sexual intercourse, type of registered permanent residence, type of current address, type of current domicile, occupation, disease, ways of cleaning knickers, ways of drying of knickers, times of swimming, menstrual cycle, sexual intercourse during menstrual periods, frequency of daily shower, ways of shower, contraceptive method, frequency of shower during menstrual period, cleaning the vulva after sex, fabric of knickers, knickers replacement and working environment in either of case-control study. Data are not shown in Table1. Table 2 displays the logistic regression analysis for risk factors. Since length of residence in Hainan Province and education were considered to be potential confounders, they were included in the subsequent analysis.

Table 2 Logistic regression analysis for risk factors associated with Candida infection of genital tract in tropics

Variables	B	S.E.	Wald	P value	Adjusted OR (95% CI)
Marriage	0.910	0.421	4.679	0.031	2.485(1.089-5.667)
Length of residence in Hainan				1.000	
2-6 months	-21.023	11371.907		0.999	
Long term	-20.417	30980.364		0.999	
Education			0.021	1.000	
Junior school	-0.523	30612.812		1.000	0.593(—)
High school	-0.248	50747.745		1.000	0.780(—)
Special school	-20.320	51207.827		1.000	
College	-42.432	52436.590		0.999	
University	-65.822	2576.564		0.999	
Graduate and above	-65.956	52576.564		0.999	
Procreation of Children			17.744	P<0.001	
One	0.072	40879.255		1.000	1.075(—)
Two	0.718	42632.209		1.000	2.050(—)
Three	-0.029	42632.209		1.000	0.132(—)
Abortion			21.554	P<0.001	
One	42.176	10126.212		0.997	2E+018(—)
Two	83.645	11945.469		0.994	2E+036(—)
Three	88.521	11945.469		0.994	2E+038(—)
≥Four	89.759	11945.469		0.994	2E+039(—)
Vaginal lavage	0.880	0.386	5.205	0.023	2.412(1.132-5.128)
Constant	-23.655	30981.954		0.999	0.000

In defining Categorical Variables, Reference Category for Length of residence in Hainan, Education, Procreation of Children and abortion was short term, Primary school, none and none separately. Variables in univariate models were examined one by

one in multivariate modeling. Marriage and vaginal lavage were independent risk factors for Candida infection. High education can protect females against infection. Abortion was a dangerous factor, increased possibility of illness.

Discussion

In our study, age was a factor related to the infection. In univariate analysis, the average ages in cases was generally older than controls (35 years versus 32 years, $p=0.003$), which was consistent with previous study that incidence of Candida infection increased with age⁶. In multivariate analysis, patients who had the marriage (married or divorced status) were more prone to vaginal candidiasis (adjusted OR: 2.5(1.089-5.667)). Therefore, married or divorced females should be concerned about Candida infection.

Particular attention should be paid to vaginal lavage. Women carrying out vaginal lavage were more likely to develop vaginal candidiasis than no-users (adjusted OR: 2.4(1.132-5.128)). Vaginal lavage increased the case rate by 1.4. Females lacked professional knowledge about lavage and used the wrong methods for lavage. On one hand, lavage caused vaginal dysbacteriosis, especially the *laetobacillus*, which competed with Candida spp. for nutrients⁷. On the other hand, lavage destroy epithelial cell. As a result, Candida spp. could easily penetrate and invade vaginal surface cells⁸.

Education was also closely linked to the infection. We discovered that patients with higher education were unlikely to be infected by Candida species. The possible explanation for this outcome maybe that the high educated woman mastered the knowledge of candidal vaginitis and discerned how to protect herself for infection. Along with the data collected in this study that 46.2% ($n=671$) patients were unsure the reason for infection, it is clear that female knowledge about candidal vaginitis and some preventive methods is an essential strategy.

Worldwide, observed predisposing factors for Candida infection include pregnancy, diabetes mellitus, contraception and antibiotics⁹⁻¹⁰. In this study, we did not observe the relationship of diabetes mellitus and infection. The reason maybe the fact that only 7 diabetic patients (0.5%, $n=1317$) responded to the questionnaire survey. Due to the small numbers, this result is not surprising. increased candidal colonization has been shown in several studies in patients using oral contraceptives containing a high estrogen dose¹¹. However we did not find that contraceptive use was a risk factor for infection ($P=0.328$). This discrepancy can be understood when considering sexual behavior of the Chinese and using contraceptive ring. In our survey, only 15.2% patients ($n=639$) were sexually active, which resulted in no difference of contraceptive between cases and controls.

Brabin and colleagues demonstrated reproductive tract infections induced abortion in girls in rural areas¹². Meizoso et al. reported three of the cases had predisposing risk factors, like rupture of membranes or intrauterine contraceptive device, and ended in fetal death¹³. Our results revealed abortive women had a high proportion of infection than women without abortion, providing strong evidence that there is a firm relationship between vaginal infection and abortion.

In the present paper, to some extent, we observed the childbearing was the predisposed factor infection. Pregnancy was associated with an increased vaginal colonization rate and stimulate the adherence of *C.albicans* to vaginal epithelia cells in vitro^{2, 14-15}. The more childbearing, the more times of pregnancy, the higher risk of infection. However, we noticed that when patients bore three times, on the contrary, the case rate declined (shown in Table2). Considering the birth control policy, it is normal to observe this evidence due to limited samples available.

Hainan Province located on the southern coast of China with a tropical monsoon climate. No association between tropical monsoon climate and Candida infection had been investigated. In order to research the relationship, we added the length of residence in Hainan to the questionnaire survey. We found long-term residence had an increased vaginal susceptibility to infection than that of short stay. Muggy and relative humid environment favour the growth of Candida species and the temperature in Hainan is suitable for propagation of pathogena. Finally, more females suffer from this disease under this tropic environment in Hainan.

Recurrent vulvovaginal candidiasis was a problem in gynecological disorders. Widespread use of antibiotics contributes to an increased prevalence of Candida vaginal infection¹⁶. In our study, 44.5% females ($n=683$) were infected at least three times by Candida species. 38.1% infected patients ($n=207$) admitted that they had used antibiotics in recent 6 months. It is necessary to perform further study to investigate the relationship between antibiotics and infection in tropics. This study had several limitations. A relatively small number of cases with diseases, such as diabetes and cancer, were included and we did not analyze the influence of antibiotics on Candida infection between cases and controls in tropics. We need further experiments to research the distribution of Candida spp. isolated from cases and controls in tropics. However, to our knowledge, this is the first report on the risk factors for Candida infection of genital infection in tropics.

Conclusions

We found several risk factors for Candida infection. Candida spp. belongs to the pathogenic fungi, its infectivity is the result of interaction by host, fungi, environment and nosocomial factors¹⁷⁻¹⁹. To understand the mechanism of candidal vulvovaginitis and exploit it for treatment, further studies using new advances in Candida biology as well as high-quality, large-scale data are needed.

Acknowledgement:

This work was supported by a grant from Peoples Liberation Army General Hospita, China, No. 2012FCT-SYS-4025.

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