Recurrent Vulvovaginal Candidiasis Causing Cytological Change: A Study of 1000 Cases to Detect Association with Malignancy

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Vulvovaginal candidiasis (VVC) and Recurrent Vulvovaginal Candidiasis (RVVC) are common fungal disease manifested by foul smelling vaginal discharge of the woman in child bearing age. In this retrospective cross sectional study series it accounted 71.2% which is a bit higher than the incidence rate of other developed countries, possibly due to bad personal hygiene, compromised host immunological status, indiscriminant use of antibiotics and reduce content of cervico-vaginal epithelium in altered state. Among the 1000 cases of cervico-vaginal (Paps) smear 712 cases were positive for candida of which 580 (58%) was RVVC and 132(13.2%) was VVC. Surprisingly 113 cases (11.3%) RVVC and VVC cases associated with dysplastic change and 23 (2.3%) was invasive squamous cell carcinoma. Till now the accepted reason for cytological change is both high and low risk groups of Human Papilloma virus (HPV). But candidial association for dysplastic change or squamous cell carcinoma is quite irrelevant. The aim of this study was to detect the link between VVC and cytological change. Though not directly; chronic infection, inflammation, retardation of immune response or alteration of cellular content may indirectly causes the change.

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Introduction

Vulvovaginal Candidiasis (VVC) is a common infection that affects approximately 75% of woman of child bearing age.[1] Factors that predispose woman to vaginal candidiasis include hormone fluctuation during pregnancy, luteal phase of menstruation, use of broad spectrum antibiotic and use of oral contraceptives.[2] Another 5%-10% of seemingly healthy woman suffer from recurrent vaginal candidiasis without any predisposing factors.[3] It is much more common in pregnant woman than healthy woman. Moreover, a large number of woman chronic recurrent candidiasis first present with infection in pregnancy.[3]

In pregnant woman, vaginal candidiasis is also related to emotional stress and suppression of immune system which set up the risk of candida species overgrowth and become pathogenic.[4] Other factors are associated with the eating habits of pregnant woman of sugar rich food which increases the growth of yeast. Hormonal modification and altered vaginal context also play an important role for growth of candida species.[5] The most common candida species causing valvo vaginal candidiasis is Candida albicans followed by Candida glabrata, Candida tropicalis and Candida parapsilosis.[3]

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VVC is an acute inflammatory disease and a frequent reason for gynocological consultation as it can affect up to 75% woman of child bearing age.[6] Clinical signs and symptoms include intense pruritus, foul smelling vaginal discharge, and erythromatous vulva and dyspareunia. Recent epidermological investigations have suggested that the prevalence of recurrent vulvovaginal candidiasis (RVVC) may be higher than previously estimated and can be as high as 7-8% woman who experiences a first episode.[7]

The discomfort associated with RVVC is intense. It markedly diminishes the quality of life in young woman with a strong negative impact on both work and social life. Moreover, affected woman frequently are attracted by advertisements to purchase over the counter formulating, prebiotics and probiotics which, besides being ineffective, can aggravate their symptoms.[8]

In the recent years, the number of serious opportunistic yeast infections particularly in immuno compromised patients, has dramatically increased.[9] In developing countries, there is scanty data on vulvovaginal candidiasis and the distribution of the vulvovaginal candida species.[10]

The present study therefore intends to determine the prevalence of vulvovaginal candidiasis among the woman of childe bearing age, to identity the causative vaginal candida species, determination of cytological nature of inflammation and more over the change of cervico-vaginal lining epithelium associated with VVC & RVVC.

Methods

The present study is a retrospective cross sectional study among woman of childe bearing age having clinical sign and symptoms of suspected vulvovaginal candidiasis and was performed in a private laboratory at Rajshahi city from January 2014 to January 2016. The age ranges was 15-56 yrs with mean of 35.5 yrs. A total of 1100 cases were primary selected on the basis of clinical history, sign and symptoms and vaginal inspection of cervix, vagina and vulva by Gynecology specialist. The slides of the patient's were primarily examined and 100 cases were discarded due to inadequately of material, ill prepared and badly stained slides. The inclusion criteria was complete clinical history suspected to VVC, adequacy of material and well prepared slides. The slides were stained with Geimsa, Gram and Hematoxyline & Eosin stain methodically by expert technologist.

Results

On careful microscopic examination of 1000 cases of Vulvovaginal (Paps) smears, 712 (71.2%) was positive for candida and 288 (28.8%) were negative. Among the candida positive cases 580 (58%) was RVVC and 132 (13.2%) was VVC. Cytological examinations of the smears revealed mild, moderate and marked dysplasia in 5%, 4.8% and 1.5% respectively (Table I).

Table I: Cytological changes found in candida positive Pap's smears

Cytological change	Number	%
Mild dysplasia	50	5.0
Moderate dysplasia	48	4.8
Marked dysplasia	15	1.5
Squamous cell carcinoma	23	2.3

Discussion

In the present study prevalence of vulvovaginal candidiasis in woman attending in private chamber/clinic of Gynecologist in Rajshahi city was 81.2%. The higher incidence was probably due to suppression of

immune system due to use of oral contraceptives, misuse of antibiotics and antifungal agents, leads to destruction of normal flora (Lactobacilli) resulting to reduction of cervico-vaginal immunity could have also contributed to the increase of prevalence of the infection.[11]

A higher frequency of vaginal candidiasis within different age ranges of the pregnant woman was observed within the age ranges 26-35 yrs (60%) likely to use drugs indiscriminately and use contraceptives to prevent pregnancy.[12] Sehgal at al reported a 54% incidence rate within age 20-30 yrs in Northern Nigeria.[12] Fifty five percent (55%) incidence rate was reported within age group 26-35 yrs in Benia city, in Nigeria.[12] These reports documented that this age group is vulnerable probably due to sexual promiscuity, drug abuse and use of contraceptives. Increased VVC and RVC prevalence also correlate with personal hygiene habit, sexual behavior and use of dirty under clothing.

Candida albican is a eukaryotic micro organism with an extraordinary capacity to adapt to different environmental and host niches. These unique properties allow for the dual life style of C. albicans as both a commensal and an opportunistic pathogen for human and other mammals. This dual transition property is of utmost relevance for C. albicans pathogencity. It remain to be determine whether the presence of commensal C. albicans conveys a benefit to the host in terms of balanced microbiota composition and maintenance of local immune homeostasis. The hyphae form a robust to biofilm layer that strongly adheres to and then invades the outmost layer of the cervico-vaginal epithelium.[13,14,15] Similar to others body sites exposed to potential pathogens. The cervico-vaginal environment must be prepared to activate the innate immunity and mount adaptive immune responses to control, if not eliminate, the pathogens. Consequently the vagina is well equipped with many cellular and humoral factors, including dendritic cells (DC) as well as T-helper, regulatory and cytotoxic lymphocytes, *B*- lymphocytes and natural killer cells producing protective cytokines and chemokines that help to recruit additional defensive factors from distant body sites.[16,17,18] Vaginal epithelial cells not only constitute a mechanical and trapping barrier with their mucin and keratin- like surface material, but are also able to sense the danger constituted by the pathogen and to respond by cell activation and secretion of immune mediators driving inflammation and immune responses.[10] Recruitment of polymorphonuclear cells to vagina and cervix. Cytokine production.[18] and activation of the lymphocytes subsets T- helper 1 and T- helper 17 have been attributed a rule in anti-candida protection.[18,19]

The vagina is also a special telerogenic site as it must accept both contrast (vaginal and cervical microbiota) and occasional (semen and fetal) non-specific material. Hence a delicate balance is maintained that must take into account two equally essential needs for health of the cervico-vaginal epithelial immune defense and immune tolerance.[20]

The cytological infiltration in these case was variable which includes lymphocytes, plasma cells, macrophages and most of the cases plenty of neutrophils. Infiltration of neutrophils may due to acute necrosis due to fungal infection or secondary bacterial involvement. Also a large number of cases show mild to moderate dysplastic change of the cervico-vaginal squamous cells. The changes were marked in RVVC. The reason for dysplastic change was not clear. The suspected pathogenesis of cervico-vaginal epithelial change may due to chronic irritation, change of cellular content,

coexistence of Human papiloma virus (HPV) or super infection with some virus.

Conclusion

VVC and RVVC are trouble some disease that can affect the sexual partner and can transmit through sexual activity. Yet not any evidence is available to make conclusion that VVC and RVVC is related to malignancy. Cervicovaginal malignancy is a sequential process caused by HPV. Must begins with mild dysplasia and proceed to moderate dysplasia, marked dysplasia (CIN iii, carcinoma in site) and ultimately invasive squamous cell carcinoma. In this study VVC and RVVC association with dysplastic change is a major question to be solved with appropriate investigation.

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