# Research Article

# Diabetes in Pregnancy: High Risk for Vulvovaginal Candidiasis

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## Abstract

**Background:** Vulvo-vaginal candidiasis [VVC] is the most common cause of vaginitis and the incidence of candidiasis almost doubles in pregnant women, particularly in the third trimester. Pregnancy can be affected by VVC in a very negative manner as it can lead to candida chorioamnionitis and subsequent preterm delivery. Premature neonates are severely endangered by generalized fungal infections, therefore prevention of fungal infections is of utmost importance.

**Objectives:** The objective of our study was estimation of the incidence of candidal vulvovaginitis in pregnant females, both with and without diabetes.

Study design: Cross-sectional study conducted in Out-patient obstetrics clinic at Fatima Memorial Hospital (FMH), Lahore.

**Materials and Method:** Sampling technique was Non-probability purposive sampling. 150 female subjects (non-diabetic = 75 and Diabetic = 75) of 18-45 years of age were included in the study. Their history was recorded and sterile speculum examination was carried out to collect vaginal swabs. Swabs were cultured on blood agar to find the organism. Glycemic control was measured by estimating HbA1c.

**Results:** There was no significant difference in the age of both groups. Among the diabetics, 45% of the cases developed VVC as compared to the non diabetic group in which only 27% were having the condition (p <0.05). No difference in terms of symptoms was witnessed between both of the study groups (P >0.05). Vaginal culture came out to be positive in 36% of the study subjects. Glycemic control according to HbA1c levels in majority was average (55%). Candidal vulvovaginitis was more common in cases with average blood sugar control as compared to those with good glycemic control. The likelihood ratio was found to be 25.35 by chi square test (p < 0.0001).

**Conclusion:** VVC is more frequent among diabetic pregnant patients and is directly correlated with blood sugar level.

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#### Introduction

Candida or yeast normally resides in the vagina and their unchecked growth is restricted by lactobacillus. Vaginitis is largely and commonly caused by Vulvo-vaginal candidiasis in Europe. In an internet panel survey conducted in European countries and United States, it was found that 29 to 49% of the participating women had been diagnosed by VVC at least once in their lifetime. Among diabetic pregnant females, poor glycemic control in the presence of immunosuppressive effect can lead to VVC and the

symptoms worsen by severe hyperglycemia.<sup>2</sup> Candida organisms probably access the vagina via migration across the perianal area from the rectum.<sup>3</sup> Candida Glabrata and Tropicalis are more common in diabetics and may not be responsive to usual therapy resulting because of intrinsic azole resistance.<sup>4</sup> Nearly 10% of the women in their reproductive age have this condition as a recurrent infection and it translates to about 140 million women being affected worldwide.<sup>5</sup>

Vulvo-vaginal candidiasis can adversely affect the pregnancy outcome by causing candida chorioamnionitis and subsequent preterm delivery. Premature neonates are severely endangered by generalized fungal infection and in case of breast feeding can cause nipple candidiasis as well. Vulvovaginal candidiasis is very rarely a sexually transmitted disease and more than 85% of the times the organism is endogenous, whereas only 10% (or less) of the cases are probably due to sexual transmission.3 Candidal vulvovaginitis is rare in premenarchal and postmenopausal women. Intermittent attacks of Candidal vulvovaginitis usually occur without any precipitating factor. Nonetheless, many factors like diabetes mellitus, antibiotics, increased estrogen levels, immunosuppressive conditions, contraceptive devices and poor hygiene may contribute to development of symptomatic infection. Increased glycogen content of the vaginal secretions in pregnancy and high temperature of tropical areas are the commonest predisposing features among women developing VVC.3

A recent study conducted by Siddique et al in Pakistan revealed that diabetic pregnant females have greater tendency to develop Vulvovaginal candidiasis as compared to non-diabetic pregnant females. Moreover, cases with high blood sugar level had VVC. We designed this study to determine the frequency of Candidal vulvovaginitis using HbA1c as a predictor of developing the infection.

## **Methods**

This was a cross sectional study carried out in Obstetrics and Gynecology Department at Fatima Memorial Hospital (FMH), Lahore. Out patients who attended Obstetrics Clinic of FMH were included in the study. The calculated sample size was 75 diabetic and 75 non diabetic pregnant female. Sampling technique was Non-probability purposive sampling.

Adult pregnant females (with Singleton pregnancy on Ultrasonography) ranging from 18 to 45 years of age in their second or third trimester were included in this study. Confidentiality was confirmed to all participants and informed consent was taken. The participants were equally divided into 2 groups i.e. "Group A" (consisting of pregnant females with diabetes) and "Group B" (consisting of non diabetic pregnant females). Diabetic females, non-diabetics and pregnant females with Gestational Diabetes Mellitus (all as per operational definition) all were enrolled in the study. Our inclusion criteria did not discriminate between patients who were already known diabetics and women with gestational diabetes mellitus. We included both types in our study. Females with gestational diabetes taking insulin for less than 4 weeks, vaginal infection previously in the current pregnancy, kidney disease, patients taking antibiotics, recurrent vaginal thrush and cases with compromised immunity were excluded from the study. A total of 170 patients were studied. History was taken from each patient which included demographic information and vaginal discharge (colour of discharge). Sterile speculum examination was performed and vaginal specimens were collected with sterile cotton tipped swabs. We took high vaginal swabs and samples were sent for culture on blood agar. Patients were investigated for glycemic control (measured by HbA1c). HbA1c can be used as a monitoring tool to predict the outcomes of women with pregnancy combined with DM (already diagnosed patients of DM who become pregnant) and gestational DM. HbA1C is not used for diagnosis in pregnancy (oral Glucose tolerance test being the gold standard) but for monitoring of treatment this is as good as in non-pregnant patients.<sup>20</sup> The patient's information was added in a pre-designed proforma attached in Annex I. SPSS version 20.0 was used for data analysis. Data was analyzed using mean, standard deviation and percentages.

#### **Results**

We interviewed 170 pregnant females and 20 proformas were rejected because of incomplete information. The remaining 150 pregnant females were divided equally in two groups. There was no significant difference in the age of both groups. Majority of the cases belonged to the 28-35 year age group (Table 1)

**Table 1:** Age Distribution of Patient in Both Groups (n=150)

Age in years	Group A (Diabetic patients) (n=75)		Group B (Non-diabetic patients) (n=75)				
	No. of Patients	Percentage	No. of Patients	Percentage			
20-27	02	03.0	10	13.0			
28-35	59	79.0	58	77.0			
36-45	14	18.0	07	10.0			
Total	75	100.0	75	100.0			
Mean+SD $32.57 \pm 2.77$ $30.89\pm3.45$ (SD = Standard deviation)							

There was no significant difference found in the parity of both groups (p>0.05) (Table 2). During the study period, 57% of the cases in Group B were in their second trimester of pregnancy and 56% of the cases in Group A were in their third trimester.

Vaginal culture came out to be positive in 36% of the

**Table 2:** Frequency of Parity in Both Groups (n=150)

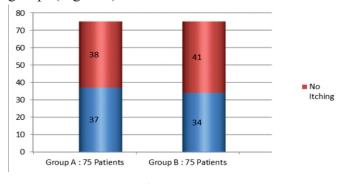
Parity	Group A (Diabetic patients) (n=75)		Group B (Non-diabetic patients) (n= 75)	
		%age	No. of Patients	%age
1	13	17.0	11	15.0
2	24	32.0	26	34.0
3	21	29.0	24	32.0
4	13	17.0	11	15.0
5	4	5.0	3	4.0
Mean+	SD 2.61±1.12	2.59	0±1.04	

study subjects more commonly among the diabetics (Table 3)

**Table 3:** Comparison of Candida in Both Groups (n=150)

Candida	Group A (n=75)	Group B (n=75)	Chis-square	P value
Present	34 (45.0%)	20 (27.0%)	11.76	0.001
Absent	41 (55.0%)	55 (73.0%)		

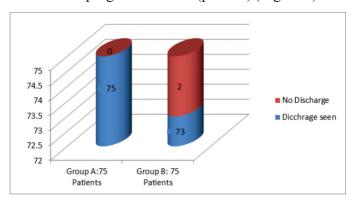
Itching was the main complaint among the two groups (Figure 1)



**Fig1:** Comparison of Itching in Both Groups (n =

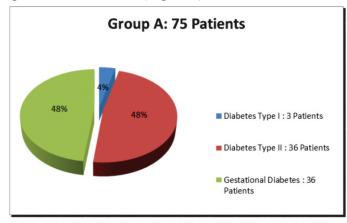
*150*)

Vaginal discharge was more commonly seen among the diabetic pregnant females (p<0.05) (Figure 2)



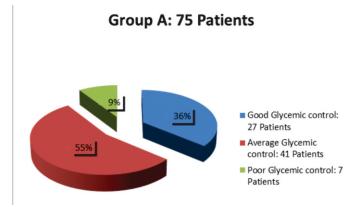
**Fig. 2** Comparison of Vaginal Discharge Seen in Both Groups (n = 150)

Forty eight percent of diabetics had a diagnosis of gestational diabetes. (Figure 3)



**Figure: 3** Frequency of Type of Diabetes in Groups A

Glycemic control according to HbA1c levels was in majority average (55%).(Figure 4)



**Figure: 4** Frequency of Gylcemic Control (according to Hb1c) in Group A

Among the diabetics, 45% of the cases developed

VVC as compared to the non diabetic group in which only 27% were having the condition (p <0.05). Patients having average glycemic control had a higher risk to develop candidal vaginal thrush as compared cases with ideal control. The likelihood ratio was found to be 25.35 by chi square test (p < 0.0001).

### **Discussion**

It is clear from the current study that pregnant females with poor blood sugar control tend to be affected more with VVC as compared to non-diabetic pregnant females. Diabetes is coming forth as an increasing epidemic problem in Pakistan with a prevalence of 9.8% with males having higher prevalence as compared to females.<sup>7</sup>

Diabetes leads to dysfunctional immunity and results in increased rate of vaginal colonization and infection by Candida species. The ability of Candida Albicans to switch between yeast and hyphae morphologies plays a central role in its virulence and is mainly controlled by environmental and transcriptional factors.

Diabetes has been found to be commonly related with systemic infections. In a study involving pregnant females it was found that prevalence of urinary tract infection was higher in diabetic pregnant females as compared to non diabetics. Some other infections which can be seen in patients with diabetes are mucocutaneous candidiasis, vulvovaginitis (due to altered vaginal defense mechanism) and dermal candidal infections.

In a recent study it was found that candida albicans is not able to use the carbohydrate moiety of mucin as carbon source.<sup>12</sup> In another study it was stated that development by candidiasis depends upon nutritional condition of the patient, immune system and adaptability of the patient.<sup>13</sup>

The risk of VVC is increased in late pregnancy and immunosuppressed patients. Factors like local defense mechanisms, genetic mutations, allergies, glucose levels, stress and estrogen levels play a role in developing risk for candida vulvovaginitis. <sup>14</sup> Yeast agents like candida albicans, candida glabrata and tropicalis have a documented role in recurrent VVC. <sup>15</sup>

In a study conducted in Italy it was found that candida

species colonization was more prominent in pregnant females (31%) as compared to non-pregnant (19%). Another study conducted on healthy pregnant females revealed that 28% of the study subjects were positive for candida species. The authors concluded that maternal VVC is a major risk factor for candida infection in neonates as 22% of the neonates were found positive for candida. In a Brazilian study it was found that diabetic pregnant females had more prevalence of VVC and recurrent VVC as compared to non-diabetic controls. The authors concluded that type 2 DM was associated with VVC and vaginal yeast infections.

The common presenting complaints of vaginal thrush are abnormal vaginal discharge, vaginal itch, painful micturition and dyspareunia. In our study, discharge was a prominent feature in patients with VVC. Fungal cultures were performed in all pregnant females to confirm the presence of candida. The distinguishing features of our study are documentation of the frequency of VVC among diabetic pregnant females; revealing an association of glycemic control and VVC; documenting lack of appropriate blood sugar control among randomly selected diabetic pregnant females included in our study.

VVC is an emerging problem for gynecologists, physicians as well as patients. Although safe and specific treatment is available but proper therapy requires accurate diagnosis at first point. Some of the limitations of our study are lack of sub classification of candida among the study population and lack of culture and sensitivity of antifungal agents. The authors suggest more detailed studies in the future with a larger study population to find out the influence of VVC on neonatal outcomes.

### Conclusion

Vulvovaginal candidiasis is more frequent among Pakistani diabetic pregnant females and is directly correlated with glycemic control.

Ethical Approval: Given

Conflict of Interest: The authors declare no conflict

of interest

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#### References

- 1. Foxman B, Muraglia R, Dietz JP, Sobel JD, Wagner J. Prevalence of recurrent vulvovaginal candidiasis in 5 European countries and the United States: results from an internet panel survey. Journal of lower genital tract disease. 2013;17(3):340-5.
- 2. Rodrigues C, Rodrigues M, Henriques M. Candida sp. Infections in Patients with Diabetes Mellitus. Journal of Clinical Medicine. 2019;8(1):76.
- 3. Beigi R. Sexually transmitted diseases. 1st ed. Chichester: John Wiley & Sons. Ltd; 2012.
- 4. Makanjuola O, Bongomin F, Fayemiwo S. An Update on the Roles of Non-albicans Candida Species in Vulvovaginitis. Journal of Fungi. 2018;4(4):121.
- 5. Powell A.M., Nyirjesy P. Recurrent vulvovaginitis. Best Pract. Res. Clin. Obstet. Gynaecol. 2014; 28(2): 967–976.
- 6. Siddique U, Latif H, Hameed A, Rathore R, Farooq Butt N, Iqbal A. Prevalence of Vulvo-Vaginal Candidiasis in Diabetic and Non-diabetic Pregnant Females. PJMHS. 2018;12(2):742-745.
- 7. [Internet]. Who.int. 2016 [cited 13 June 2018]. Available from: http://www.who.int/diabetes/country-profiles/pak\_en.pdf.
- 8. Deorukhkar S.C, Saini S, Mathew S. Non-albicans Candida Infection: An Emerging Threat. Interdiscip. Perspect. Infect. Dis. 2014.
- 9. Peters B.M, Palmer G.E, Nash A.K, Lilly E.A, Fidel P.L, Noverr M.C, et al. Fungal morphogenetic pathways are required for the hallmark inflammatory response during Candida albicans vaginitis. Infect. Immun. 2014;82(4):532–543.
- 10. Onoh R, Umeora O, Egwuatu V, Ezeonu P, Onoh T. Antibiotic sensitivity pattern of uropathogens from pregnant women with urinary tract infection in Abakaliki, Nigeria. Infect Drug Resist. 2013;6(2): 225–33.
- 11. Achkar J, Fries B. Candida Infections of the Genitourinary Tract. Clinical Microbiology Reviews. 2010; 23(2): 253-273.
- 12. Valentijn-Benz M, Nazmi K, Brand H, van't Hof W, Veerman E. Growth of Candida albicansin human

- saliva is supported by low-molecular-mass compounds. FEMS Yeast Research. 2015;15(8):88.
- 13. Serrano-Fujarte I, López-Romero E, Reyna-López G, Martínez-Gámez M, Vega-González A, Cuéllar-Cruz M. Influence of Culture Media on Biofilm Formation byCandidaSpecies and Response of Sessile Cells to Antifungals and Oxidative Stress. BioMed Research International. 2015;2015:1-15.
- 14. Mendling W, Brasch J. Guideline vulvovaginal candidosis (2010) of the german society for gynecology and obstetrics, the working group for infections and infectimmunology in gynecology and obstetrics, the german society of dermatology, the board of german dermatologists and the. Mycoses. 2012; 55(3): 1-13.
- 15. Diba K, Namaki A, Ayatolahi H, Hanifian H. Rapid identification of drug resistant Candida species causing recurrent vulvovaginal candidiasis. Med Mycol J. 2012; 53(1):193.
- 16. Leli C, Mencacci A, Meucci M, Bietolini C, Vitali M, Farinelli S, et al. Association of pregnancy and Candida vaginal colonization in women with or without symptoms of vulvovaginitis. Minerva ginecologica. 2013;1;65(3):303-9.
- 17. Zisova LG, Chokoeva AA, Amaliev GI, Petleshkova PV, Miteva-Katrandzhieva TM, Krasteva MB, et al. Vulvovaginal Candidiasis in pregnant women and its importance for Candida colonization of newborns. Folia medica. 2016;58(2):108-14.
- 18. Gunther LS, Martins HP, Gimenes F, Abreu AL, Consolaro ME, Svidzinski TI. Prevalence of Candida albicans and non-albicans isolates from vaginal secretions: comparative evaluation of colonization, vaginal candidiasis and recurrent vaginal candidiasis in diabetic and non-diabetic women. São paulo medical journal. 2014;132(2):116-20.
- 19. Donders GG, Sobel JD. Candida vulvovaginitis: a store with a buttery and a show window. Mycoses. 2017;60(2):70-2.
- 20. Yu H, Qi X, Wang X. Application of glycated hemoglobin in the perinatal period. Int J Clin Exp Med 2014; 7(12): 4653–4659.