e-ISSN:2320-3528
p-ISSN:2347-2286

RESEARCH AND REVIEWS: JOURNAL OF MICROBIOLOGY AND BIOTECHNOLOGY

Genital Candida in Patients with Sexually Transmitted Infections – An Innocent Bystander or a Pathogenic Culprit?.

Ritika Goyal[1]*, Shukla Das[1], Sambit N Bhattacharya[2], and Ashwani Kumar[1].

[1]Department of Microbiology, University College of Medical Sciences & Guru Teg Bahadur Hospital, Dilshad Garden, Delhi -110095, India.
[2]Department of Dermatology & STD, University College of Medical Sciences & Guru Teg Bahadur Hospital, Dilshad Garden. Delhi -110095, India.

Short Communication

Received: 05/12/2013
Revised: 09/03/2014
Accepted: 10/03/2014

***For Correspondence**

Department of Microbiology, University College of Medical Sciences & Guru Teg Bahadur Hospital, Dilshad Garden, Delhi - 110095, India.

Keywords: *Candida*, sexually transmitted infection, phospholipase, hemolysin.

ABSTRACT

The presence of one STI increases the risk of having concomitant and co-transmission of other STI. An evolving trend of *Candida* infections in STI patients, showing a transition from harmless colonizers to unrelenting pathogens, is a fine line attributable to extensive repertoire of virulence determinants. The present study was carried out to identify the genital *Candida* flora prevalent in patients attending sexually transmitted disease (STD) Clinic and to determine the haemolysin and phospholipase activity amongst these isolates. Further, correlation of species of infecting/ prevalent *Candida* with the co-existing STI was done. A total of 75 consecutive male and female patients, presenting with one or more of the complaints as enunciated by World Health Organization (WHO) in the Syndromic Approach for the diagnosis of STIs, were included in the study. *Candida* was isolated in significantly higher numbers from patients presenting with discharge (47%) followed by balanitis (30%), and genital ulcer (23%). *C. albicans* (73%) was predominant isolate in various STIs. Hemolysin index and phospholipase activity of *C. albicans* was found significantly higher enhancing their pathogenic potential. The study suggests the role of genital inflammation by *Candida* as a significant cofactor in STI acquisition and existence of genital *Candida* as colonizer or pathogen. The study provides a rational basis for empirical therapy in STI patients.

INTRODUCTION

It is well recognized that, the presence of one STI increases the risk of having another, through the same route, as a consequence of mucosal barrier damage and inflammation [1]. Although Candidal vulvo-vaginitis is not always considered a STI, evidence in favor of sexual transmission exists [2]. Whether genital *Candida* is a commensal or a pathogen, capable of causing substantial morbidity, is not fully understood. The ability of *Candida* to transform itself from a harmless commensal to an unrelenting pathogen is attributed to an extensive repertoire of virulence determinants, selectively expressed under suitable predisposing conditions [3]. In this study, we investigated the clinical significance of genital *Candida* isolated, as a co-pathogen amongst STI patients and determined expression of phospholipase and hemolysin activity, as indicator of pathogenicity.

A prospective study, approved by institutional ethical committee, was conducted on 75 consecutive male and female STI patients, attending STD Clinic, between April 2009 to March 2010. Patients with age ≥ 18 yrs diagnosed with a STI Syndrome, as per "WHO Syndromic Approach for the diagnosis of STI" [4], were included. Detailed history followed by physical and genital examination was undertaken. All patients were managed according to NACO guidelines [5]. Relevant samples were collected from each patient based upon the diagnosis varying from urethral discharge, vaginal discharge and exudates, expressed by gentle compression of fresh unhealed genital ulcer. Samples were subjected to direct microscopy and culture (wherever possible), as per standard laboratory

procedures for detecting STI agents [6]. They were further processed for Candidal isolation and identification. HBsAg, HSV-1 & 2 IgM and VDRL tests were performed from serum samples. Patient's HIV status was determined as per NACO guidelines [7]. Determination and quantification of phospholipase [3] and hemolysin [8] activities were assayed for all *Candida* isolates. The reference strain included ATCC *C. albicans* 90028. Twenty healthy non-pregnant women and men, each between ages of 21 and 50, were taken as controls and investigated for genital *Candida.*

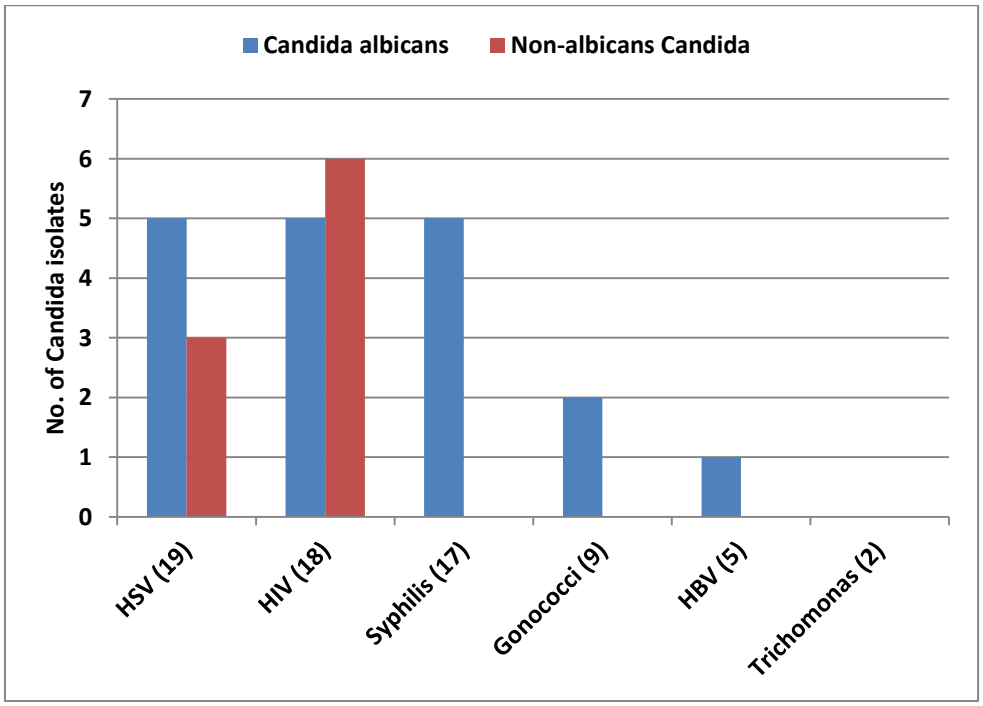
Statistical analysis of continuous quantitative variables, between groups, was tested by unpaired t-test. Associations of presenting complaints with culture positive *Candida* and phospholipase index were analyzed by Pearson's Chi-square test of Fisher's Exact test. Unadjusted odds ratio (OR) and 95% confidence interval (CI) were calculated for STIs with and without concomitant *Candida*. ANOVA followed by Tukey's test was used to compare hemolytic index in different *Candida* species.

Age of the patients ranged from 18 to 62 years, with the maximum in age group of 20-30 years (68%), which represented the maximum sexually active age group.

Distribution of cases according to presenting complaints with candidal culture positivity is given in [Table-1]. Genital ulceration and genital discharge were found to be statistical significant presenting complaint ($p < 0.001$) amongst male and female STD clinic attendees respectively. Out of 32 (61.5%) patients clinically suspected to have herpes progenitalis, 17 (32.7%) were found to have IgM antibodies against HSV-1 / 2. While 13 (25.1%) patients clinically suspected to have chancre, 11(26.8%) were found to be VDRL reactive [Table-2]. Overall prevalence of genital candidiasis amongst the study group was found to be 34.6%.

Species distribution of *Candida* in STIs is shown in Figure 1. Favorable odds ratio of 1.438 (CI .540-3.832) was found in patients diagnosed with herpetic ulcer for having coexisting *Candida* infection. Concomitant *Candida,* if expressing virulence factors, may increase the severity of disease in such patients. Interspecies comparison of phospholipase and hemolysin activity is tabulated in [Table-3]. It is generally believed that phospholipases situated at hyphal tip, contribute to organisms increased hydrophobicity, adherence to epithelial cells and invasiveness. It is worth noting, C. *glabrata* isolated from a HIV seropositive patient was found to produce very high amount of phospholipase indicating its pathogenic potential in this immunologically challenged condition. Hemolysin index of C. *albicans* was significantly higher ($p < 0.001$) followed by C. *glabrata*, a finding similar to a study demonstrated by Luo et al [9], suggesting the importance of hemolysin in making C. *albicans* a more hardy survivor (and subsequently a more common pathogen) on human mucosal surfaces. Candidiasis in association with genital ulcers maybe one such situation, where mucosal damage and inflammation allows Candidal bystander yeast form to undergo a phenotypic change, leading to a prolonged non- healing ulcerative condition.

Figure 1: Species distribution of Candida in STIs



e-ISSN:2320-3528
p-ISSN:2347-2286

Table 1: Association of presenting complaints with culture positive *Candida*

Presenting complaint* (Male : Female : Total)	Culture positive *Candida*			p value
	Male	Female	TotalN (%)	
Discharge (8:62:70)	2	31	33 (47.1%)	0.003
Ulcer (41:11:52)	11	1	12 (23%)	0.004
Balanitis (20:0:20)	6	0	6 (30%)	0.973
Umblicated nodule (2:4:6)	1	0	1 (16.7%)	0.665†
Wart (4:2:6)	0	0	0 (0%)	0.094

*Multiple complaints; † Fisher's exact test

Table 2: Etiological diagnosis of patients with genital ulcer disease

	Herpes		Syphilis		Others	
	Herpes progenitalis	IgM HSV-1/ 2 seropositive	Chancre	VDRL reactive	Chancroid	Non-specific
Male (n=41)	21 (51.2%)	14 (34.1%)	13 (31.7%)	11 (26.8%)	7 (17%)	16 (39%)
Female (n=11)	11 (100%)	3 (27.3%)	-	4 (36.4%)	-	4 (36.4%)
Total (n=52)	32 (61.5%)	17 (32.7%)	13 (25.1%)	15 (28.8%)	7 (13.4%)	20 (38.5%)

Table 3: *Candida* interspecies comparison of Hemolysin & Phospholipase activity

Species	No. of isolates tested	No. of isolates with Hemolysis (Hemolysin index*, mean ± SD)		
		Alpha	Beta	Gamma
C. albicans	38	-	38 (1.9592±0.356)	-
NAC	14	1	10 (1.380±0.066)	3

Species	No. of isolates tested	Phospholipase index(P_Z) †			
		$P_Z = 1$ (null)	$P_Z < 1$ $P_Z \geq 0.64$ to < 1 (high)	$P_Z < 0.64$ (very high)	
C. albicans	38	18	8	12	
NAC	14	10	3	1	

* Hemolysin index: diameter of translucent zone of hemolysis divided by diameter of colony size.
† Phospholipase index (P_Z): diameter of colony divided by diameter of colony plus precipitation zone.
P_Z value < 1: Phospholipase producer.
P_Z value = 1: Null activity.

From the women control group, five were found to harbor *C. albicans* in their genital flora and none demonstrated phospholipase activity; however two isolates showed hemolysin activity. Of male control group, none were found to harbor *Candida.*

Our observation highlights that concomitant Candida may be a potential contributor to recurrences and impaired healing of certain patient population especially with viral ulcerative lesions as documented in HIV-HSV co-infection [10]. This mandates thorough workup for identifying hidden *Candida* co-infection. Given the pathogenic synergy of *Candida* and STI pathogens, therapy with antifungals is crucial in the routine syndromic management. Molecular tools for strain delineation amongst *Candida* species as a part of microbial surveillance may help elucidate factors that predict *Candida* infection preceded by colonization.

e-ISSN:2320-3528
p-ISSN:2347-2286

ACKNOWLEDGEMENT

We are most grateful to the study participants whose cooperation made this study possible.

REFERENCES

1. Schiffer JT, Corey L. New concepts in understanding genital herpes. Curr Infect Dis Rep. 2009;11:457-64.
2. Holmes KK. Sexually transmitted diseases: Overview and clinical approach. In: Fauci AS, Braudwald E, Kasper DL, Hauser SL, Longo DL, Jameon JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine, 18th ed. New York: McGraw Hill Medical Publishing Division; 2008. p. 821-35.
3. Ghannoum MA. Potential role of phospholipases in virulence and fungal pathogenesis. Clin Microbiol Rev. 2000;13:122-43.
4. http://www.who.int/hiv/pub/sti/en/STIGuidelines2003.pdf.
5. Available from: http://www.naco.gov.in/NACO/About_NACO/Policy_Guidelines /Policies_Guidelines1.
6. Forbes BA, Sahm DF, Weissfeld AS. Genital tract infections. In: Forbes BA, Sahm DF, Weissfeld AS, editors. Bailey & Scott's Diagnostic Microbiology, 12th ed. Missouri: Mosby Elsevier; 2007:856.
7. http://www.naco.gov.in/NACO/About_NACO/Policy_Guidelines/Policies_Guidelines1. Accessed on 14th June 2013.
8. Tsang CSP, Chu FCS, Leung WK, Jin LJ, Samaranayake LP, Siu SC. Phospholipase, proteinase and haemolytic activities of Candida albicans isolated from oral cavities of patients with type 2 diabetes mellitus. J Med Microbiol. 2007;56:1393-8.
9. Luo G, Samaranayake LP, Yau JYY. Candida species exhibit differential in vitro hemolytic activities. J Clin Microbiol. 2001;39:2971-4.
10. Sarna J, Sharma A, Naik E, Toney J, Marfactia YS. Protean manifestations of herpes infection in AIDS cases. Indian J Sex Transm Dis. 2008;29:26-8.