Original Article

Role of transforming growth factor beta-1(TGF-β1) in pathogenesis of Trichomonas vaginalis

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Abstract

Trichomoniasis caused by the parasiteTrichomonas vaginalisis the most common non-viral, curable sexually transmitted disease worldwide that annually affects millions of people. It was found that several immunologic and biochemical factors play a role in the pathogenesis of Trichomonas vaginalis. In this study, we aimed to investigate the role of transforming growth factor beta-1(TGF-β1) in the pathogenesis of Trichomonas vaginalis.

In this study, vaginal swabs, urine and blood samples were taken from (350) women, whose ages ranged between (15-65) yearsand were attending the women's obstetrics and gynecology hospital in Karbala province during the period from November 2021 to June 2022. The general urine examination and direct microscopic examination of the vaginal swabs were used to detect the parasite, while the serum (TGF-β1) level was estimated by ELISA technique. A questionnaire form was used to collect information from the participant women including age, residency, marital status, educational level, fertility and using contraceptives.

The results showed that only (100) cases were positive for Trichomonas vaginalis, and the highest incidence of positive cases was within the age group (15-24) years and the lowest incidence was within the age group (55-65) years. The number and percentage of positive women from rural areas was 49 (28.49%), while the number and percentage of positive women from urban areas was 51 (28.65%), with no significant difference (P=0.973). The mean and standard deviation of serum TGF-β1 was (22.06±10.74) in the healthy non-infected women, while the mean and standard deviation of serum TGF-β1 was (97.93±28.6) in the patient infected women, with a highly significant difference (P<0.001).

It can be concluded from the current study that the levels of serum TGF-β1 was highly increased in women infected with Trichomonas vaginalis.

Keywords: Trichomonas vaginalis, Trichomonasiasis, TGF-β1.

INTRODUCTION

Sexually transmitted diseases (STD) are a major global health problem. Each year, an estimated 500 million people acquire one of four sexually transmitted infections: Chlamydia, Gonorrhea, Syphilis and Trichomoniasis. Moreover, more than 530 million people are living with HSV2 and more than 290 million women have an HPV infection [1].

Trichomoniasis is a neglected sexually transmitted infection (STI) caused by Trichomonas vaginalis, a flagellate protozoan responsible for a prevalence of 110.4 million cases and 156.0 million rate of incidence [2, 3]. The last estimative from the World Health Organization (WHO) demonstrated the incidence rate for trichomoniasis across the globe, highlighting the African Region with the highest rates, followed by America, Western Pacific, Eastern Mediterranean, South-East Asia, and last, the European region [3]. Although most cases are asymptomatic, complaints such as pruritus, vaginal discharge, irritation, and odor are still reported. The long-lasting infection of T. vaginalis, which can persist for months to years, may lead to severe complications such as the premature delivery and low weight of newborns, infertility, pelvic inflammatory disease, and a positive association with the onset of cervical and prostate cancer [4,5]. Moreover, a bidirectional relationship with human immunodeficiency virus (HIV) transmission and acquisition has already been described, where patients infected with T. vaginalis are 1.5 times more likely to acquire HIV than those not infected [6].

Trichomonas vaginalis is transmitted from person to person through sexually intercourse. In the life cycle of this parasite, trophozoites attach to mucosal surfaces of urogenital tract and divides by longitudinal binary fission. Successful colonization of the host mucosa by T.vaginalis is the result of multiple pathogenic mechanisms, including adhesion; secretion of cytotoxic molecules and soluble factors; interaction with member of vaginal microbiome; evasion of host immune system and regulation the development of the immune response [7].

The TGF-β family comprises TGFB1, TGFB2, and TGFB3. All three genes are highly conserved across species and humans, in which their products share strong sequence similarity and also display nearly identical three-dimensional structures. They signal through the same ubiquitously expressed transmembrane receptors, generally referred to as TβRI and TβRII, which develop a similar affinity for isoforms TGF-β1 and TGF-β3, whereas only TβRII binds with less intensity to TGF-β2 [8].

TGF- β2 controls the magnitude and type of immune responses against microbes, and has fundamentally important roles in maintaining immune tolerance and homeostasis against self- and benign antigens at steadystate [9]. TGF- β2 was shown to regulate the differentiation and function of different classes of leukocytes, and it modulates immune activities, from conception to autoimmunity and infection [10].

Materials and methods

In this study, vaginal swabs, urine and blood samples were taken from (350) women, whose ages ranged between (15-65) years and were attending the women's obstetrics and gynecology hospital in Karbala province during the period from November 2021 to June 2022. The general urine examination and direct microscopic examination of the vaginal swabs were used to detect the parasite, while the serum (TGF-β1) level was estimated by ELISA technique. A questionnaire form was used to collect information from the participant women including age, residency, marital status, educational level, fertility and using contraceptives.

The venous blood samples were collected in gel tubes free of anticoagulants, and kept for 15 minutes at room temperature to clot, then centrifuged for 10 minutes at 3000 rpm to obtain serum. The enzyme-linked immune sorbent assay (ELISA) technique was used to detectserum TGF-β1 levels. The general urine examination and direct microscopic examination of the vaginal swabs were used to detect the presence ofTrichomonas vaginalis parasite.

Statistical analysis

Data were analyzed using the SPSS version 25 program. The t-test and Chi square were used for variances, and ($P<0.05$) was considered as significant [11, 12].

Results

In this study, 350 women were examined for the presence of ofTrichomonas vaginalis parasite, and only 100 (28.57%) of them were positive, while 250 (71.42%) of them were negative as shown in table (1).

Table (1): No. and percentage of positive cases depending on microscopic examination

Total number of examined samples	**Positive samples**		**Negative samples**	
350	Number	Percentage	Number	Percentage
	100	28.57	250	71.42

Results in table (2) showed that the highest No. and percentage of incidence of positive cases of trichomonasiasis 34 (29.31%) was within the age group (25-34) years, while the lowest No. and percentage of incidence of positive cases of trichomonasiasis 6 (16.21%) was within the age group (55-65) years, with non-significant differences between the age groups (P=0.353).

Table (2): Distribution of positive cases according to age groups

Age group (years)	Total number	Positive cases		P value
		No.	%	
15-24	70	24	34.28	0.353
25-34	116	34	29.31	
35-44	59	18	30.5	
45-54	68	18	26.47	
55-65	37	6	16.21	

The distribution of positive cases according to residency of positive cases demonstrated that 51 (28.65%) were residents of urban areas, while 49 (28.49%) of them were residents of rural areas, with a non-significant difference (P=0.973).

Table (3): Distribution of positive cases according to residency

Residency	Total number	Positive cases		P value
		No.	%	
Urban	179	51	28.65	0.973
Rural	171	49	28.49	

Data shown in table (4) revealed that the mean and SD± levels of serum TGF-β1 in healthy women group was (22.06±10.74), while the mean and SD± levels of serum TGF-β1 in infected patient women group was (97.93±28.6), with a highly significant difference (P<0.001).

Table (4): MeanTGF-β1 levels and SD± in healthy and infected women

Groups	Mean and SD±
Healthy women	22.06±10.74
Patients	97.93±28.6
Calculated P-value	<0.001

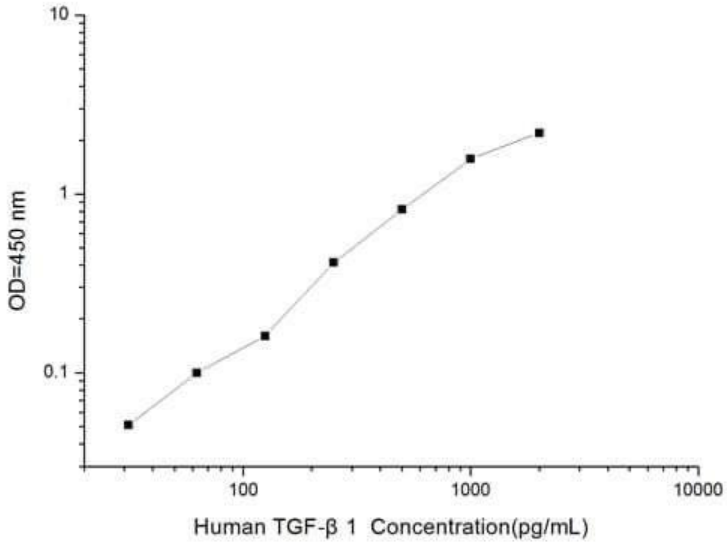

Figure (1): Showing the curve of TGF-β1 concentration estimation by ELISA

Discussion

The epidemiology of Trichomonas vaginalis infection can be influenced by several risk factors such as age, residence, socioeconomic level, education, marital status and the type of contraception method used, presence and type of vaginal discharge, the used drug and history of other sexually transmitted infections [13].

Trichomoniasis poses two major difficulties for public health strategies that seek to contain the disease in the general population. First, unlike other STIs such as chlamydial infection, trichomoniasis was not consistently observed in a particular age group. On contrary to our results, no association was found between age and infection prevalence across the age range 15 to 35 for either women or men [14].

Trichomonas vaginalis infection was shown to be prevalent in 11.5 % of women aged 15 to 49 years old in a previous WHO research conducted in the African region [15]. Similar to our results, the high rate of trichomoniasis was observed in the age group of 26-35 years.We can attribute the highest incidence rate of trichomonasiasis in this age group to the fact that the disease similarly to other sexually transmitted diseases, where the women are in the reproductive period and are sexually active in this age group, which may make it easy to be contaminated by their husbands or partners.This finding was consistent with other previous studies [16,17].Ourresults revealed a non-significant difference between infected women according to residency, which contradicted the findings of [16] who stated that patients who were living in a rural location, having a poor socioeconomic standing, and having only a primary education level were associated with T. vaginalis infection. This discrepancy in findings could be attributed to the difference in the number of participants between the two studies [18].

The present study showed a highly significant difference in the level of TGF-β1 between the women infected with trichomonasiasis and the healthy control women.

To the best of our knowledge, no previous study was done before regarding the levels of this marker (TGF-β1) in trichomonasiasis, thus, our study is the first one to investigate TGF-β1 levels in infected women

However, TGF-β production is upregulated by various factors, such as bacteria, viruses, cytokines, apoptotic cells, and the autocrine/paracrine loop [19].

TGF-β is a homodimeric protein that is part of the TGF-β superfamily and is found in most eukaryotic organisms, including C. elegans, Drosophila, Xenopus, rats, and humans [20]. It is expressed in all cell types and in almost all developmental stages of organisms, playing an important role in the regulation of various biological and cellular responses, including cell proliferation and differentiation, extracellular matrix production, embryonic development, epithelial cell growth, carcinogenesis and apoptosis [21]. In mammalian cells, there are three TGF-β subtypes: 1, 2 and 3. These isoforms are well characterized as small (25 kDa) homodimeric secreted proteins [22].

TGF-β cytokines exert profound effects on lymphocytes, macrophages, and dendritic cells, but these depend on micro-environmental context and vary according to phase of the inflammatory response, such that initially TGF-β exerts pro-inflammatory activity, before later acting to promote the resolution phase. There may be commonality across epithelial tissues in pathways through which TGF-β signaling to epithelial cells strengthens and amplifies direct effects of TGF-β in leukocytes [23].

Finally, all the information mentioned above indicates that the levels of TGF-β increases in inflammatory processes including trichomonasiasis.

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