ORIGINAL RESEARCH

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Effect of *Toxoplasma gondii* infection on the level of NLRP3 in women with Polycystic Ovary Syndrome

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Abstract

In this study, 120 women were assessed and split into four different categories. The first group included women who had been exposed to the T. gondii parasite. The second group included women possibly infected with the T. gondii parasite and PCOS. The third group was made up of women who had PCOS. The first three groups were hospitalized, while the fourth group was healthy. Blood was drawn from all groups, serum was isolated, and the level of NLRP3 was measured for all groups. The present investigation displayed that the concentration of NLRP3 in women infected with T. gondii parasite and polycystic syndrome increased significantly ($P<0.05$) (0.2250 + 6.698 ng/ml) compared to women infected with polycystic ovary syndrome (0.2141 +5.114 ng/ml) and women infected with the parasite (0.2200 + 0.2200). 5.255 ng/ml) compared with the control group (0.1065 + 2.021 ng/ml). This significant increase in the level of concentration NLRP3 (0.2250 + 6.698 ng/ml) in women infected with T. gondii parasite and polycystic syndrome can be adopted as an indicator of co-prepayment, or it may be dependent as an indicator of the occurrence of polycystic ovary syndrome due to prior infection with the parasite.

Keywords

Toxoplasma, T. gondii parasite, Polycystic, Ovary Syndrome

Imprint

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Introduction

Toxoplasmosis is an extremely prevalent zoonotic disease that results from an infection with the intracellular parasite *Toxoplasma gondii* [1]. This parasite has a complicated life cycle. It requires two hosts: definitive, which manifests in the feline family, particularly cats, and intermediate, which includes humans and other endothermic mammals and birds[3]. Most infections are asymptomatic in immunocompetent hosts because the host's immune system can inhibit the parasite's multiplication and the production of tissue cysts in most body tissues, notably the central nervous system and the skeletal and cardiac muscles, with no symptoms arising [2]. As for people who suffer from immunocompromised diseases, they have a reactivation of the latent infection of the parasite, and in the case of infection in women during pregnancy and its transmission to the fetus through the placenta, it causes great danger to the fetus. It may occur miscarriage or death of the fetus inside the womb, and the transmission of the disease increases as fetal age progresses [4]. Polycystic ovary syndrome (PCOS) is a frequent cause of placental anovulation and ovulatory dysfunction. Infertility is viewed as a frequent endocrine condition in women of reproductive age and menopause-related to metabolic illness. Moreover, the syndrome is the main cause of ovarian dysfunction that leads to associated anovulation, resulting in infertility, as 5%-10% of women of childbearing age are affected by this syndrome[5]. Some modern immunological and laboratory criteria were used to diagnose infection with the parasite *T. gondii*, which causes cat disease, to determine the level of anti-Mullerian Hormone (AMH) in women with Polycystic Ovary Syndrome (PCOS), and to investigate some common factors among them and their impact on the presence of the parasite[6].

Moreover, PCOS disease, as the Minividas test was used to test the enzyme-linked fluorescence test (ELFA), which is one of the modern tests that investigate IgM, IgG, and enzyme-linked immunosorbent assay (ELISA) [20]. Anti-Mullerian Hormone (AMH) is a hormone released by tiny follicles in the ovaries smaller than 4 mm. Hormone secretion decreases and then stops in follicles more prominent than 8 mm, and an AMH analysis can be done on any day of the cycle with a fixed value. As the value of this analysis in the blood reflects the total number of eggs still in

the ovaries, it is regarded as one of the most important fertility tests [7]. As age advances, the quantity of eggs left in the ovaries reduces, and so does hormone output. The value of the analysis also increases in women who suffer from polycystic ovary syndrome due to the increase in the number of small follicles, which is less than 8 mm in the ovaries[19].

MATERIALS AND METHODS

Blood samples were obtained from 120 people and split into four groups of 30.There were four groups of women: those with PCOS, those with PCOS and a probable *T. gondii* infection, those with PCOS and no PCOS, and a control group of healthy women. Patient samples were collected from women suspected of having the disease and who were seen at Al-Zahra Maternity and Children Hospital, Al-Hakim Hospital, and various outpatient clinics in the Al-Najaf Governorate between July 2022 and November 2022.The patients' ages ranged from 19 to 45 years old. IgG & IgM in serum, measuring ovarian reserve hormone (AMH) in women with polycystic ovary syndrome and observing some clinical signs such as obesity, irregular or amenorrhea, and acne, in addition to confirming PCOS using ultrasound examinations[8]. 5 ml was drawn for each sample of venous blood from women for all groups. The blood samples were taken to the centrifuge at 3000 rpm for 5 minutes to isolate the serum and distributed into three parts, each frozen at a temperature of -20 ° C until used for serological testing. Record the age, sex, and marital status information for each sample[18]. Detection of *T. gondii* using the VIDAS method: a quantitative test used to estimate the amount of *T. gondii* antibodies in serum by enzyme link fluorescent assay (ELFA). Detecting VIDAS (AMH) [9] A quantitative test used to help estimate ovarian follicle reserve in women and young girls over 12 years of age and detects ovarian dysfunction in women with PCOS and is a test of the VIDAS (AMH) family of ovarian reserve hormone using ELFA enzyme fluorescence assay technique. Detection of human NLRP3 by using ELISA KIT[21].

Statistical Analysis: The findings were statistically evaluated using version 20 of SPSS. The mean and standard deviation were determined, and the T-test was performed to determine whether or not there were significant differences between the means at the probability level P<0.05[17].

Results

1- Estimation of NOD-Like Receptor Pyrin NLRP3(pg/ml) ELISA KIT in *T. gondii* infected women: The current study found that NLRP3 concentrations in women infected with the T. gondii parasite rose considerably (P0<05) (0.2200 + 5.255 ng/ml) comparing to the control group (0.1065 + 2.021 ng/ml).

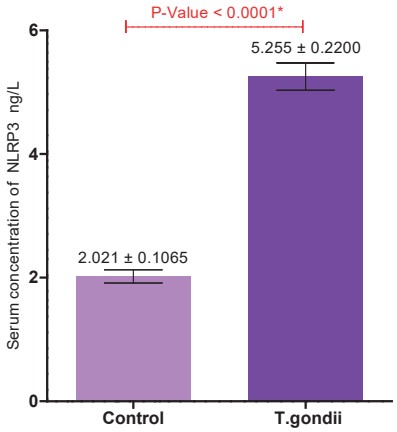

Figure 1: Concentration of NLRP3 (pg/ml) in serum of infected women infected with *T. gondii*

2-Estimation of NLRP3(pg/ml) ELISA KIT in Women with (PCOS): In contrast to the control group (0.1065 + 2.021 ng/ml), the current study found that the concentration of NLRP3 rose considerably (P<0.05) in the blood serum of PCOS patients (0.2141 + 5.114 ng/ml).

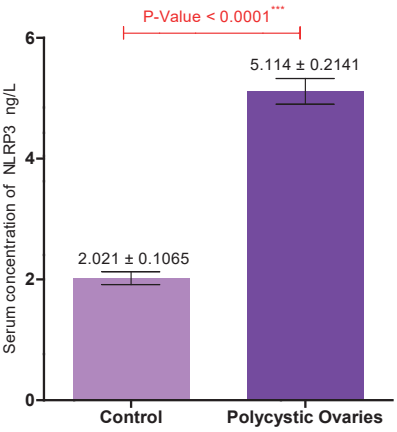

Figure 2: Concentration of NLRP3 (pg/ml) in serum of PCOS patients.

3- Estimation of NLRP3(pg/ml) by ELISA KIT in women infected with *T. gondii* and PCOS: The results of the current investigation revealed that, when compared to the control group (0.1065 + 2.021 ng/ml), women with PCOS and *T. gondii* infection had substantially higher blood levels of NLRP3 (P<0.005).

The current investigation found that the quantity of NLRP3 in the serum of women infected with *T. gon-*

dii and PCOS was substantially higher (P<0.005) than in the control group (0.1065 + 2.021 ng/ml).

The current study showed that the concentration of NLRP3 was considerably increased (P<0.005) in the serum of women infected with the parasite *T. gondii* and PCOS (0.2250 + 6.698 ng/ml) compared with the control group (0.1065 + 2.021 ng/ml).

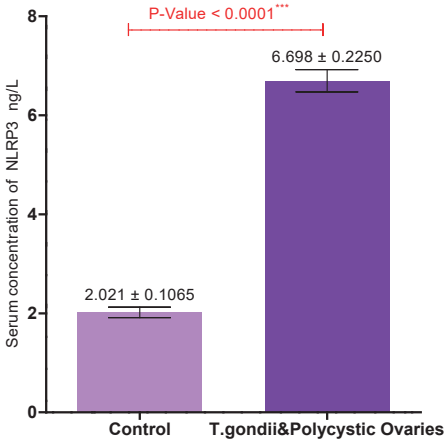

Figure 3: Concentration of NLRP3 (pg/ml) in the blood serum of *T. gondii* and polycystic syndrome females

4-NLRP3 concentration (pg/ml) in women infected with *T. gondii* parasite and polycystic ovarian syndrome and co-infection between them: The present investigation displayed that the concentration of NLRP3 in women with *T. gondii* parasite and polycystic syndrome increased significantly (P<0.05) (0.2250 + 6.698 ng/ml) compared to women infected with polycystic ovary syndrome (0.2141 +5.114 ng/ml) and women infected with the parasite (0.2200 + 0.2200). 5.255 ng/ml).

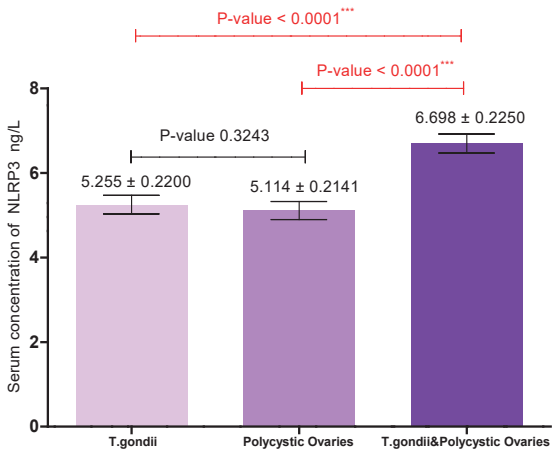

Figure 4: NLRP3 concentrations (pg/ml) in the blood serum of women infected with *T. gondii* and PCOS and their co-infection.

Discussion

A significant elevation of NLRP3 was observed in the present investigation. This increase may be attributed to the occurrence and activation of the inflammatory process due to pathogens as an intracellular mechanism to initiate the immune response to these factors, which is the participation of NLRP3 inflammasomes in the development of obesity and insulin resistance, in which NLRP3 and ASC were increased for women. The ovaries of women with PCOS are abnormal, and they produce more caspase-1 and IL-1β from being activated. Our results suggest that NLRP3 inflammasomes have a role in initiating immunological responses throughout the progression and management of PCOS. Folliculogenesis, oocyte maturation, steroidogenesis, and oligolysis are all reproductive processes negatively impacted by oxidative stress in women[10]. Possible causes for this increase include pathogen-induced activation of the adaptor molecule ASC (inflammasome), caspase-1 activation, the release of active versions of IL-1β and IL-18, and the triggering of the programmed death pathway[17]. Diseases by inflammasomes form a critical host innate immune mechanism to select invading microorganisms. The host produces IL-1 β and IL-18 in response to the parasite *T. gondii*, and research has demonstrated that this response is triggered by NLRP1.*T. gondii's* stimulation of IL-12 production is critical for inducing a strong CD4+ IFN- response. TH1, triggering the activation of IFN- γ mediated genes essential for parasite elimination[11]. A deficiency of NLRP3, ASC, or Casp1/11 will significantly deactivate IFN-γ derived from CD4+ T cells, leading to rapid death of the host. The absence of NLRP1 or NLRP3 inflammasomes increases parasite burden, leading to host death, although both IL-1β and IL-18 play a role in increased IFN-γ production during infection with *T. gondii*[12]. Required for antiparasite resistance is the CCL2-dependent activation of monocytes, NLRP1, NLRP3, ASC, and caspase-1, which enables the release of IL-1β and IL-18 by parasitic cells [13]. Oxidative stress may contribute to the inflammation-inducing state and induce insulin resistance and hyperandrogenism in PCOS. Oxidative stress also triggers the activation of NLRP3 inflammasomes in various cardiovascular, metabolic, and renal diseases[14]. Due to insulin resistance, free fatty acid levels rise, producing reactive oxygen species and oxidative stress, both of which can stimulate the activities of AMH-forming enzymes in the ovaries and increase androgen synthesis [15]. The role of Inflammasomes NLRP3 in initiating the immune response in PCOS patients, as well as the oxidative stress, has an essential role in activating it, and then leads to ovarian dysfunction in PCOS, including polycystic ovaries, increased androgens in the ovaries, and increased insulin resistance[16].

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