Research Article



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Comparative Hormonal and Immunoglobulin Profiles of Aborted Women with or without Toxoplasmosis

Hassanain MA¹, Elfadaly HA¹, Abd El Wahab WM² and Abo El-Maaty AM^{3*}

¹Department of Zoonosis, National Research Center, El-Tahrir Street, Egypt ²Faculty of Medicine, Beni- Suef University, Egypt ³Animal Reproduction and Artificial Insemination department, Egypt

Abstract

Background: Toxoplasmosis is a worldwide disease that causes abortions in human and animals.

Objective: This study assumed that abortions due to toxoplama is associated with increased IgM and IgG immunoglobulins results from disrupting estrogen, progesterone, cortisol and prolactin hormones.

Methods: Blood samples of *T. gondii* sero-positive (n = 25) and sero-negative (n = 10) aborted women at the three gestational trimesters were subjected to ELISA IgM and IgG serological assays and hormone assaying. Simple one way ANOVA was used to test the effect of trimester on hormone concentrations and independant sample t-test was used to study the effect the sero-typing.

Results: Aborted *Toxoplasma* sero-positive women were younger (*P*=0.004) and had (*P*=0.0001) high IgG, IgM and estrogen (*P*=0.02) but low cortisol (*P*=0.029) and prolactin (*P*=0.005).

Conclusion; the alterations in estrogen, cortisol and prolactin hormones possibly predispose latent opportunistic toxoplasmosis during pregnancy in carrier women.

Introduction

Toxoplasma gondii is an intracellular opportunistic protozoan and is one of the most prevalent acute or latent abortifacient zoonosis [1]. The soil sporulated oocyst infective stage develop only in the feline's gut with contaminating food or water [2]. The acute tachyzoites stage is responsible for the materno-fetal diffusion. While the bradyzoite stage persists viable in dormant tissue as cyst and can reactivate to latent acute tachyzoites order to sharp shift of hormones or corticosteroids therapy during pregnancy resulting in temporary gravidity hyperglycemia [3,4].

Women aborted sequence to *T. gondii* infection during pregnancy (recent or primary infection), mainly with predominant IgM titer [5], or through latent opportunistic dynamics stimulating bradyzoites-tachyzoites re-conversion, chiefly with major IgG titer [6]. Latent *toxoplasmosis* is potentially serious, carries the risk of fetal transmission in about 30% of cases, with severe complications depending on the stage of pregnancy, mostly abortion and fetal death [7].

Estrogen and progesterone are synthesized mainly in the ovary and heir fluctuations correspond to the phase of the menstrual cycle [8]. Cortisol rise following exposure to stressors and its concentrations are higher among females than males [9]. Prolactin (PRL) as cytokinelike regulates immune response and increases 10 to 20 times during pregnancy to produce milk [10]. Alterations in ovarian hormones due to *T. gondii* infection were studied in women [11]. The size plus maturity of the placenta, as well as the embryonic/fetal immune response affected the ability to fight *T.gondii* invasion [12].

The current study aimed to evaluate the relationship amongst levels of estrogen, progesterone, prolactin and cortisol hormones in *T*.

gondii sero-positive and sero-negative aborted women during the three trimesters of pregnancy.

Materials and Methods

The study population included 35 women of age range from 22 to 37 years were admitted to Gynecological Department, Beni-Suef general hospital, presented with complicated pregnancy at different trimesters. Patients were subdivided according to the stage of pregnancy into G1 (n=18) include cases aborted during the first 12 weeks of gestation, G2 (n=7) included patients with abortions from 13 to 26 weeks of gestation), and G3 (n=10) corresponding to patients encountered intrauterine fetal death. The procedures followed were in accordance with the ethical standards and the Institutional Ethics Committee of National Research Centre and Faculty of Medicine, Beni- Suef University. Patients allowed sampling needed for the study and a written consent was obtained from each participant

Blood sampling and hormonal assaying

Three ml of blood samples were collected from each woman in the immediate post abortion period. Sera were separated and stored

*Correspondence to: Amal M Abo El-Maaty, PhD, National Research Centre, Veterinary research Division, Animal Reproduction and Artificial Insemination department, 33 Elbehouth, Dokki, Giza, Egypt, E-mail: amalaboelmaaty1@yahoo.com

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at -20°C. Serological screening for *Toxoplasma* antibodies was done through ELISA IgM and IgG commercial kits (Clinotech Diagnostics and Pharmaceuticals, Richmond, Canada). Progesterone and estrogen were assayed using commercial ELISA (DRG, International, Inc., USA). Prolactin was assayed using commercial ELISA kit (BioCheck, Inc. Foster City, CA). Sensitivity, intra- and inter-assay percisions were 0.045 ng/mL, 6.86 and 5.59% for progesterone; 9.714 pg/mL, 2.71 and 6.72% for estradiol; 2.0 ng/mL, 4.6% and 7.4% for prolactine. Cortisol was assayed using EIA (Xema-Medica Co., Ltd., Moscow, Russia), and sensitivity of the assay was 12 nmol/l.

Statistical analysis

Data are presented as mean \pm SD. Simple one way ANOVA was used to study the effect of trimester on different parameters within sero-positive and sero-negative cases. Duncan's Multiple's range test was used to differentiate between significant means. Independent sample t-test was used to study the effect of sero-type within trimester using SPSS version 20 (IBM, Armonk, NY, USA). Significance levels was set at P<0.05.

Results

The serological tests of aborted women (N=35) revealed that the number of sero-positive cases is 25 patient and sero-negative patients is 10 (Figure 1). Aborted sero-positive women were younger (P =0.004) and had significantly high IgM (P = 0.0001), IgG (P = 0.0001), and estrogen (P = 0.02), but low prolactin (P = 0.005), and cortisol (P = 0.029). Age of sero-positive cases varied significantly (P=0.001) between the three trimesters (Table1). Sero-positive women aborted during the first trimester were younger (P = 0.002) than sero-negative ones. Both IgM and IgG of sero-positive (P= 0.028; 0.005), and seronegative (P= 0.001; 0.0001), cases varied significantly. Sero-positive cases had significantly higher IgM (P= 0.0001) during the first and second trimesters. Sero-positive patients had high IgG during the three trimesters. Estrogen concentrations of sero-positive and negative cases increased (P= 0.0001) during the third trimester. Sero-positive patients had (*P*= 0.001) higher estrogens during their first trimester (Table 1). Progesterone of sero-positive and sero-negative cases increased (P= 0.0001) from the first to the third trimesters. Prolactin concentrations of sero-negative cases decreased linearly (P=0.0001) from first to third trimester of sero-negative women but those of sero-positive cases reached (P= 0.0001) minimum values during the second trimester with an obvious (P= 0.0001) decrease in sero-positive compared to seronegative cases in the first trimester and a tended (P=0.08) to be low in sero-negative cases during the third trimester. Sero-positive (P=0.006) and sero-negative (P= 0.0001) cases had high cortisol during the third



Figure 1. Numbers of different sero-group conditions of the studied cases.

trimester but sero-positive cases tended (P= 0.06) to have low cortisol during the first trimester compared to sero-negative cases (Table1).

Discussion

The real answer of the question, Why toxoplasmosis is more prevalent within pregnant women? is that pregnant women consider at exceptional immune-compromised condition attributable to hormonal alteration. Though pregnant and non-pregnant women are equally exposed to the same incidence of T. gondii infective sources, but pregnant and non-pregnant women vary through hormonal curve and the possible materno-fetal diffusion through bradyzoites-tachyzoites re-conversion [13]. So, pregnant women have 2.2 times higher risk of sero-converting than non-pregnant ones [14]. Also, pregnant mice are more susceptible to Toxoplasma infection and progress more severe brain cysts with higher mortality rate than similarly infected nonpregnant ones [15]. Though Galván-Ramírez et al. [16] reported that estrogen did not exhibit significant differences between both chronic and uninfected women, the current study noticed that estrogen act as stimulus for superior susceptibility to T. gondii latent opportunistic abortion, which characterized via high significant (P=0.02) in aborted women. The current results agree with Aabasian et al. [17] who detected significant relationship between estrogen and Toxoplasma positive women. As well as, administration of pharmacological estrogen in guinea pigs and mice increase T. gondii susceptibility and the cysts number [18]. In mice, the tissue cysts were lowering in the absence of estrogen due to ovariectomy [19]. The increase of gestational estrogen (E2) in sero-positive women aggravate the prevalence of Toxoplasma infection increases leading to weakened immune cells through destroy the Natural killer (NK) cells activity and cause neutrophil dysfunction [20]. Increased estrogen shifts the maternal immune response towards Th2 phenotype to facilitate embryo implantation which is opposed with what required for controlling Toxoplasma, possibly progress T. gondii replication and increase the likelihood of trans-placental transmission [20]. Also, sharp deviation of E2 level stimulates recurrent acute symptomatic stage through bradyzoites -tachyzoites re-conversion [3,21].

In the present study; cortisol hormone, sero-positive patients tended to have low cortisol during the first trimester and all seropositive women had significantly low cortisol compared to sero-negative patients. In contrast, Shirbazou et al. [22] showed that serum level of cortisol was higher in Toxoplasma positive women than control group with statistically significant correlation (P<0.0001), and significant relation was found between Toxoplasma and stress (P<0.0001) and anxiety (P=0.04). Moreover, Mahbodfar et al. [23] showed that cortisol level in the infected women was higher than uninfected ones. Stressful behavior that results from cortisol increase acts as immune suppressor factor, motivating recurrent acute toxoplasmosis thru double upturn number of T. gondiitachyzoites and brain cysts [22] Cortisol was suggested to acts via inducing T. gondii higher susceptibility and elevating sequence to Toxoplasma infection that is likely considered as an important stress stimulus irritate blood cortisol upturn [24]. So, significant correlation of cortisol level in the current study might be sequence to stress dynamic of toxoplasmic abortion rather than the normal physiological upturn.

The results in the present study symbolized statistically insignificant change of pprogesterone and this is agreed with Galván-Ramírez *et al.* [16] and Aabasian *et al.* [17].

Prolactin (PRL) stimulates T cell proliferation and releases various protective cytokines as TNF- α which control efficiently the course of *T. gondii* infection. So, PRL should be reducing *T. gondii*

Parameters	Sero-type	Trimester			Davahara	T-4-1
		G1	G2	G3	r-value	rotai
Age/year	positive	$23.79 \pm 3.10^{a^{**}}$	$26.50\pm4.93^{\mathrm{b}}$	$29.43\pm 6.01^\circ$	0.001	$25.80 \pm 4.99^{**}$
	negative	27.00 ± 4.44	28.67 ± 1.30	30.00 ± 5.59	0.18	28.40 ± 4.30
IgM titre	positive	$0.62\pm 0.22^{ab^{**}}$	$0.74 \pm 0.24^{\texttt{b}^{**}}$	$0.51\pm0.36^{\rm a}$	0.028	$0.61 \pm 0.28^{**}$
	negative	$0.32 \pm .12^{b}$	$0.24\pm0.05^{\rm a}$	$0.38\pm.08^{\rm b}$	0.001	0.31 ± 0.11
IgG titre	positive	$1.24\pm0.78^{\rm b^{**}}$	$0.77 \pm 0.86^{a^{\ast}}$	$1.55\pm 0.61^{\tt b^{**}}$	0.005	$1.25 \pm 0.26^{**}$
	negative	$0.33\pm0.03^{\rm a}$	$0.19\pm0.03^{\rm a}$	$0.24\pm0.07^{\rm b}$	0.001	0.26 ± 0.07
Estrogen pg/mL	positive	$406 \pm 219^{a^{**}}$	$339\pm212^{\rm a}$	$592\pm254^{\rm b}$	0.001	$448 \pm 245^{*}$
	negative	$199\pm210^{\mathrm{a}}$	$273\pm287^{\rm a}$	584 ± 211^{b}	0.001	337 ± 284
Progesterone ng/mL	positive	$10.038 \pm 5.12^{\rm a}$	17.41 ± 0.83^{b}	$20.0\pm7.43^{\rm b}$	0.001	14.08 ± 7.43
	negative	$8.79\pm2.67^{\rm a}$	$11.38\pm8.75^{\rm a}$	$19.87\pm6.88^{\rm b}$	0.001	12.89 ± 7.78
Prolactin ng/ml	positive	$7.03\pm 8.99^{\rm ab^{**}}$	$0.77\pm0.02^{\rm a}$	$16.03 \pm 23.97^{\text{b}}$	0.031	9.41 ± 15.51**
	negative	$36.37 \pm 18.00^{\text{b}}$	$10.90 \pm 15.17^{\rm a}$	$3.59\pm4.20^{\rm a}$	0.001	18.89 ± 7.78
Cortisol nmol/l	positive	$314\pm101^{\mathtt{a}}$	356 ± 35^{ab}	$369\pm28^{\rm b}$	0.006	$336\pm82^*$
	negative	$361\pm16^{\rm a}$	354 ± 20^{a}	$382\pm13^{\text{b}}$	0.001	365 ± 20

Table 1. Mean ± Standard deviation (SD) of age/year, IgM titre, IgG titre, Estrogen pg/mL, Progesterone ng/mL, Prolactin ng/ml and Cortisol nmol/l in different cases during their gestation.

replication due to limited capacity of the parasites to penetrate host cells [12,13]. Also, serum human prolactin has the capacity to bind to live RH tachyzoites (type I) and ME49 (type II) strains to inhibit their penetration ability [25]. Concerning PRL, the significant low levels recorded in sero-positive patients of the present study compared to sero-negative women disagreed with Mahbodfar *et al.* [23], but agreed with the results of Dzitko *et al.* [25] who documented that women with hyperprolactinemia showed lower *T. gondii* prevalence.

Conclusions

Sero-negative pregnant woman requires regular check for possible sero-conversion. However, infection could be acquired at the end of pregnancy, with the mother still sero-negative at delivery. The risk of fetal transmission during this period is 70% with no clinical symptoms at birth. So, it is recommended to do further serological test after delivery for all sero-negative pregnant women or for newborns.

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Conflict of interest

The authors declare that they don't have any conflict of interest

Author Contributions

Hassanain funded two hormones, Elfadaly funded the immunoglobulins, Abo El-Maaty funded two hormones,

Authorship and contributorship

Hassanain designed, wrote revised the manuscript. Elfadaly measured immunoglobulins, collected the data and wrote the manuscript. Abd ElWahab conducted blood sampling; and helped in measuring the hormones. Abo El-Maaty assayed all the hormones, made statistical analysis, prepared the manuscript in the journal format and submitted it. Abd El Wahab conducted blood sampling, measured immunoglobulins and helped in measuring the hormones.

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