



EFFECT OF TOXOPLASMOSIS AND ITS TREATMENTS ON MALE RAT REPRODUCTIVE FUNCTIONS

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ABSTRACT

In comparison with the non infected male rats, toxoplasmosis significantly decreased serum FSH 79.7 ± 8.2 ng/ml ($P < 0.01$), LH 3.62 ± 0.6 ng/ml ($P < 0.05$), testosterone 0.96 ± 0.1 ng/ml ($P < 0.01$), sperm count / mg of epididymal cauda $253 \pm 12 \times 10^6$ ($P < 0.01$), sperm viability percent $28.8 \pm 1.8\%$ ($P < 0.01$), the relative weight of the testis and seminal vesicle ($P < 0.001$), prostate ($P < 0.01$) and epididymis ($P < 0.05$), pregnancy rate 86% ($P < 0.01$), litter size 6.29 ± 0.92 ($P < 0.001$), fetal weight 0.367 ± 0.038 g ($P < 0.05$) and placental weight 0.282 ± 0.012 g ($P < 0.05$); while it significantly increased sperm malformation percent $1.6 \pm 0.3\%$ ($P < 0.001$), fetal resorption rate 2.222% ($P < 0.05$) and early fetal death percent 8.07% ($P < 0.01$). Sulphadiazine or pyrimethamine can enhance some of the fertility parameter in toxoplasma infected rats, but they were not free from adverse effects which decreased pregnancy rate, litter size, fetal weight and increased fetal resorption and early fetal death.

Key words: Fertility, Reproductive functions, Rats, Toxoplasmosis, Sulphadiazine, Pyrimethamine.

INTRODUCTION

Toxoplasmosis is caused by an obligate intracellular protozoan parasite *Toxoplasma gondii*. Approximately one-third of the world's population is exposed to this parasite. Feline including domestic cat act as definitive host and various warm-blooded animals as well as human, act as an intermediate host. The infection in human generally occurs through consuming food or drink contaminated with oocysts or tissue cysts. Congenital transmission and organ transplantation are other routes of the infection [1-2]. After ingestion of parasite and proliferation of tachyzoites during acute stage, the parasite is usually localized in different organs including male and female reproductive organs of intermediate hosts [3-6].

Many studies correlated between reproductive performance and Toxoplasmosis [3-4,7]. *Toxoplasma gondii* deteriorated the male and female reproductive performance in many experimental animals [8-12]. Toxoplasmosis also caused profound adverse effect on human reproductive functions [14]. Acute toxoplasmosis infection caused hypogonadotropic gonadal insufficiency in male patients regardless of the course of the disease [15]. The women with toxoplasmosis may complain spontaneous abortions, stillbirths, intrauterine growth retardation, preterm deliveries, or fetal anomalies [16-17]. *T. gondii* infection is of particular public health interest due to the

ability of this parasite to cause infertility; therefore this study was carried out to verify the effects of toxoplasmosis on male rat reproductive functions.

MATERIAL AND METHODS

The study was carried out on 84 male rats (*Rattus norvegicus*) ranging in weight from 250 to 300g, all rats were housed in an air-conditioned animal room at an ambient temperature of 23 ± 2 °C and in a 12h light 12h dark cycle. Half of the males were infected intraperitoneally with 100 tissue cysts of *T. gondii* intraperitoneally [18].

Infected group was examined for documentation of the infection with the using of real-time PCR. Each, infected group (42 males) and non infected group (42 males) were divided into 3 subgroups (14 males each) and treated with DMSO, sulphadiazine 200 mg/kg or pyrimethamine 12.5 mg/kg. Sulphadiazine and pyrimethamine were given in DMSO as a single oral daily dose for 60 days. At the end of the treatment period, blood samples were collected for hormonal analysis ELISA by cardiac puncture from half of animals in each subgroup, and then they were killed by neck dislocation after light anesthesia.

Left testis, left epididymis, seminal vesicle and prostate were weighed, then left testis and left epididymis were fixed in formalin for histological examination. Right epididymis was used to estimate sperm count/ mg of the epididymal cauda, sperm malformations % and sperm viability% [19-21].

Other half of males in each subgroup were mated with females (with 2 regular estrus cycles) 1 male/1 females, during proestrus and for 24 hrs. Recovery of sperms in the vaginal smears was considered as day one of pregnancy. Females were killed at day 15 of gestation by cervical dislocation after light anesthesia. Fetuses were counted, weighted and examined for identification of resorption rate [22-24].

The significant differences among subgroups were determined by single sided student t-test and Chi square test.

RESULTS

Hormonal analysis

The serum FSH level of non infected male rats treated by DMSO was 127.3 ± 13.2 ng/ml. Treatment of non infected rats with sulphadiazine or pyrimethamine didn't induced significant changes in serum FSH levels. However, serum FSH level in toxoplasma infected male rats treated by DMSO was 79.7 ± 8.2 ng/ml, it was significantly less than that in non infected rats ($P < 0.01$). Sulphadiazine and pyrimethamine treatment normalized serum FSH level in infected male rats (128.8 ± 11.6 and 125.8 ± 13.5 ng/ml respectively). Serum LH level followed the same style, it was significantly decreased in the infected male rats treated with DMSO 3.62 ± 0.6 ng/ml in comparison with non infected male rats 4.23 ± 0.9 ng/ml ($P < 0.05$). Sulphadiazine and pyrimethamine didn't change serum LH level in non infected rats, but they normalized its level in the infected rats. Serum testosterone level in non infected rats treated with DMSO was 2.64 ± 0.2 ng/ml. Treatment with sulphadiazine didn't change serum testosterone level significantly, while pyrimethamine significantly decreased testosterone level 0.84 ± 0.2 ng/ml in non infected male rats ($P < 0.01$). Toxoplasma infection was significantly decreased serum testosterone level 0.96 ± 0.1 ng/ml in comparison with non infected rats ($P < 0.01$). Sulphadiazine 1.32 ± 0.3 ng/ml and pyrimethamine 1.93 ± 0.7 ng/ml, were significantly ($P < 0.05$) increased serum testosterone level, but it didn't reach the normal limit in the non infected group (table 1).

Semen quality

The sperm count / mg of epididymal cauda in non infected males treated by DMSO was $333 \pm 12 \times 10^6$, it was significantly declined in non infected males treated with sulphadiazine to $325 \pm 26 \times 10^6$ ($P < 0.05$) and in pyrimethamine treated non infected rats to $323 \pm 28 \times 10^6$ ($P < 0.05$). The sperm count / mg of epididymal cauda in toxoplasma infected male rats treated with DMSO was $253 \pm 12 \times 10^6$, it was significantly less than that in non infected

rats ($P < 0.01$). The sperm count / mg of epididymal cauda was increased significantly in sulphonamide 280 ± 18 ($P < 0.05$) and pyrimethamine 278 ± 16 ($P < 0.05$) treated infected rats in comparison with infected rats treated by DMSO, but in both groups the sperm count didn't reached the level of sperm count in non infected group.

The sperm viability percent in non infected males treated by DMSO was $58.6 \pm 3.6\%$, it was declined in non infected males treated with sulphadiazine to $49.9 \pm 4.2\%$ ($P < 0.05$) and in pyrimethamine treated non infected rats to $45.0 \pm 4.6\%$ ($P < 0.05$). The sperm viability in toxoplasma infected male rats treated with DMSO was $28.8 \pm 1.8\%$, it was significantly less than that in non infected rats ($P < 0.01$). The sperm viability was significantly increased in sulphonamide $41.0 \pm 4.2\%$ ($P < 0.05$) and pyrimethamine $34.7 \pm 2.6\%$ ($P < 0.05$) treated infected rats in comparison with infected rats treated by DMSO.

The sperm malformation percent in non infected males treated by DMSO was $0.02 \pm 0.01\%$, it was insignificantly increased in non infected males treated with sulphadiazine to $0.05 \pm 0.02\%$, while, it significantly increased in pyrimethamine treated non infected rats to $0.96 \pm 0.08\%$ ($P < 0.05$). The sperm malformation ratio in toxoplasma infected male rats treated with DMSO was $1.6 \pm 0.3\%$, it was significantly more ($P < 0.001$) than that in non infected rats, sulphadiazine was not induce further increase in the sperm malformation ratio, while pyrimethamine induced further significant increase $2.5 \pm 0.4\%$ ($P < 0.01$) in the sperm malformation percent in comparison with infected rats treated by DMSO (table2).

Reproductive organs weight

The relative weights of testis, epididymis, seminal vesicle and prostate in non infected male rats treated by DMSO were 0.398 ± 0.062 , 0.154 ± 0.012 , 0.480 ± 0.086 and 0.275 ± 0.052 g. Sulphadiazine treatment didn't induce significant changes in the relative weights of these organs in non infected male rats, while, pyrimethamine was significantly decreased the relative weight of testis, epididymis and prostate. However, infection with toxoplasmosis significantly decreased the relative weight of the testis and seminal vesicle ($P < 0.001$), prostate ($P < 0.01$) and epididymis ($P < 0.05$), while treatment of infected male rats with sulphadiazine and pyrimethamine significantly increased the weights of testis and seminal vesicle, but not epididymis and prostate.

Fetal characteristics

The percent of pregnancy in healthy female fertilized by non infected males treated by DMSO was 100%, while, the rate of pregnancy was declined in females fertilized by non infected males treated by sulphadiazine to 71% ($P < 0.01$) and pyrimethamine to 43% ($P < 0.001$). The rate of pregnancy in females fertilized by infected males treated by DMSO was 86%, it was significantly less than that in females fertilized by non

infected males treated by DMSO ($P < 0.01$). However, pregnancy rates in females fertilized by infected males treated by sulphadiazine was further declined to 71% ($P < 0.05$), and in pyrimethamine to 57% ($P < 0.01$) in comparison to females fertilized by infected males treated by DMSO.

The litter size in healthy females fertilized by non infected males treated by DMSO was 11.29 ± 1.20 fetus/dam, the litter size of females fertilized by non infected males treated by sulphadiazine was decreased to 5.00 ± 0.82 ($P < 0.001$) and pyrimethamine to 3.14 ± 0.22 ($P < 0.0001$). The litter size of the females fertilized by infected males treated by DMSO was 6.29 ± 0.92 , it was significantly less than litter size of females fertilized by non infected males treated by DMSO ($P < 0.001$). Litter size of females fertilized by infected males treated by sulphadiazine was 4.57 ± 0.83 and of those treated by pyrimethamine was 3.14 ± 0.12 in comparison with litter size of females fertilized by infected males treated by DMSO ($P < 0.05$ and $P < 0.01$ respectively).

The mean fetal weight of healthy female fertilized by non infected males treated by DMSO was 0.469 ± 0.064 g, while the mean fetal weight of healthy female fertilized by infected male treated by DMSO was decreased significantly to 0.367 ± 0.038 g ($P < 0.05$). Sulphadiazine treatment didn't change the mean fetal weight of healthy female either fertilized by infected or non infected male rats, But pyrimethamine decreased significantly ($P < 0.05$) the mean weight of fetuses of healthy females fertilized by non infected, and ($P < 0.01$) infected male rats.

The mean placental weight of healthy female fertilized by non infected male treated by DMSO was 0.323 ± 0.035 g, while the mean placental weight was decreased significantly in females fertilized by infected male treated by DMSO ($P < 0.05$), as well as those fertilized by non infected and infected males either treated by sulphadiazine or pyrimethamine ($P < 0.05$).

The fetal resorption percent in healthy females fertilized by non infected males treated by DMSO was 0.00%, while, it was increased in females fertilized by non infected males treated by sulphadiazine to 2.778% ($P < 0.05$) and pyrimethamine to 4.347% ($P < 0.05$). The fetal resorption in females fertilized by infected males treated by DMSO was 2.222%, it was significantly more than that in female fertilized by non infected males treated by DMSO ($P < 0.05$). However, the mean of fetal resorption percent in females fertilized by infected males treated by sulphadiazine and pyrimethamine was further increased significantly ($P < 0.01$ and $P < 0.01$ respectively) in comparison to females fertilized by infected males treated by DMSO.

The early fetal death percent in healthy females fertilized by non infected males treated by DMSO was 0.00%, while, it was significantly increased in females fertilized by non infected males treated by sulphadiazine to 7.33% ($P < 0.01$) and pyrimethamine to 11.11% ($P < 0.001$). The early fetal death in females fertilized by infected males

treated by DMSO was 8.07%, it was significantly more than that in females fertilized by non infected males treated by DMSO ($P < 0.01$). However, the early fetal death percent in females fertilized by infected males treated by sulphadiazine was significantly decreased, but pyrimethamine didn't show significant changes in comparison to females fertilized by infected male treated by DMSO (table 4).

Histology

The sections of the testis of non infected male rats treated with DMSO showed normal histological structures. The seminiferous tubules were intact with normal appearance of basement membrane, primary and secondary spermatocytes. The lumen was full with sperms, with intact Sertoli cells. The seminiferous tubules appeared adjacent to each other with regular outlines. The interstitial tissues were intact. Also there were no histological changes in the non infected male rats treated with sulphadiazine or pyrimethamine.

The testis section of toxoplasma infected male rats showed vacular degeneration of spermatogonia and spermatocytes. The seminiferous tubules revealed sever degeneration, shrinkage, necrosis, hemorrhages with disappearance of epithelial lining of the majority of seminiferous tubules. They were also appeared separated with an irregular outlines and surrounded by fibrin. Seminiferous tubule lumen contained little amount of sperm with appearance of giant cells, polymorph nuclear leukocyte and exfoliated cellular debris. Scattered areas of edema and necrosis were noted in Sertoli cells. Sloughing of Leydig cells was also recorded. Parasitic cyst was also noted in the testicular tissue.

The sections of the testis of infected male rats treated with sulphadiazine or pyrimethamine showed improvement of testicular structure. The section appeared with less or absent of vacular degeneration, necrosis and hemorrhages. The seminiferous tubules appeared with intact epithelial lining and the lumen full with sperms. The interstitial tissues also appeared intact with almost normal structure. It appeared that pyrimethamine was more effective than sulphadiazine in attenuation of the testicular histological changes associated with toxoplasmosis.

The epididymal sections of non infected male rats treated with vehicle, sulphadiazine, or pyrimethamine, showed that the epididymal duct was lined with an epithelium composed of principal and basal cells. Other cells, such as apical and halo cells, were also present in the duct in a segments specific manner. The luminal diameter and the thickness of the peritubular smooth muscle increases from the proximal to the distal regions. Few sperm are found in the initial segment, but a large mass of sperm aggregates are located in the cauda.

The epididymal sections of *Toxoplasma gondii* infected untreated male rats showed decreasing of the epithelial cell high and ducts diameters with infiltration of mononuclear and multinucleated giant cell. Epididymal

sections also showed hyperplasia of duct lining which appeared as papillary projections into duct cavity. As a result of decreased duct diameter and hyperplasia, sperms appeared impacted in the lumen along with desquamated cellular debris. However, some epididymal ducts appeared atrophied with low amount of sperms.

The epididymal sections of *Toxoplasma gondii* infected male rats which treated with sulphadiazine, or pyrimethamine revealed only slight degeneration, in the majority of the sections, the ducts appeared with normal diameter and epithelial lining and the cavity was full with sperms.

Table 1. Serum level of FSH, LH and testosterone (ug/ml) of non infected and *Toxoplasma gondii* infected male rats treated with DMSO, sulphadiazine 200 mg/kg and pyrimethamine 12.5 mg/kg for 60 days.

Groups	FSH (SSH) (ug/ml)	LH (ICSH) (ug/ml)	Testosterone (ug/ml)
Non infected treated with DMSO	127.2±13.2 ^a	4.23±0.9 ^a	2.64±0.2 ^a
Non infected treated with sulphadiazine	124.8± 12.4 ^a	4.34±0.8 ^a	2.02±0.3 ^a
Non infected treated with pyrimethamine	124.0±16.6 ^a	4.32±0.8 ^a	0.84±0.2 ^b
Infected treated with DMSO	79.7±11.2 ^b	3.62±0.6 ^b	0.96±0.1 ^b
Infected treated with sulphadiazine	126.8±11.6 ^a	4.36±0.9 ^a	1.32±0.3 ^c
Infected treated with pyrimethamine	125.8±13.5 ^a	4.32±0.7 ^a	1.93±0.7 ^c

Vertically, similar letter means not significant

Table 2. Sperm/ mg of epididymal cauda X 10⁶, sperm viability % and sperm malformations % of non infected and *Toxoplasma gondii* infected male rats treated with DMSO, sulphadiazine 200 mg/kg and pyrimethamine 12.5 mg/kg for 60 days.

Groups	Sperm/ mg of epididymal cauda X 10 ⁶	Sperm viability %	Sperm malformations %
Non infected treated with DMSO	333±12 ^a	58.6±3.6 ^a	0.02±0.01 ^a
Non infected treated with sulphadiazine	325±26 ^b	49.9±4.2 ^b	0.05±0.02 ^a
Non infected treated with pyrimethamine	323±28 ^b	45.0±4.6 ^b	0.96±0.08 ^b
Infected treated with DMSO	253±12 ^c	28.8±1.8 ^d	1.6±0.3 ^c
Infected treated with sulphadiazine	280±18 ^d	41.0±4.2 ^c	1.6±0.4 ^c
Infected treated with pyrimethamine	278±16 ^d	34.7±2.6 ^d	2.5±0.4 ^d

Vertically, similar letter means not significant

Table 3. Relative weights (g/ 100 g body weight) of testis, epididymis, seminal vesicle and prostate of non infected and *Toxoplasma gondii* infected male rats treated with DMSO, sulphadiazine 200 mg/kg and pyrimethamine 12.5 mg/kg for 60 days.

Groups	Relative weights g/ 100 g body weight			
	Testis	Epididymis	Seminal vesicle	Prostate
Non infected treated with DMSO	0.398±0.062 ^a	0.154±0.012 ^a	0.480±0.086 ^a	0.275±0.052 ^a
Non infected treated with sulphadiazine	0.376±0.073 ^a	0.150±0.016 ^a	0.477±0.092 ^a	0.288±0.065 ^a
Non infected treated with pyrimethamine	0.347±0.052 ^b	0.138±0.021 ^b	0.461±0.088 ^a	0.226±0.048 ^b
Infected treated with DMSO	0.266±0.034 ^c	0.139±0.028 ^b	0.236±0.042 ^b	0.203±0.032 ^c
Infected treated with sulphadiazine	0.330±0.042 ^d	0.146±0.026 ^b	0.480±0.093 ^a	0.218±0.036 ^{cb}
Infected treated with pyrimethamine	0.300±0.038 ^{bd}	0.142±0.024 ^b	0.475±0.089 ^a	0.208±0.038 ^{cb}

Vertically, similar letter means not significant

Table 4. Pregnancy%, litter size, fetal weight/ g, placenta weight/ g, fetal resorption ratio and early fetal lost ratio of healthy female rats fertilized by non infected and *Toxoplasma gondii* infected male rats treated with DMSO, sulphadiazine 200 mg/kg and pyrimethamine 12.5 mg/kg for 60 days.

Groups	Pregnancy%	Litter size Fetuses/dam	Fetal weight/ g	Placenta weight/ g	Fetal resorption ratio	Early fetal lost ratio
Non infected treated with DMSO	100% ^a	11.29±1.20 ^a	0.469±0.064 ^a	0.323±0.035 ^a	0.00% ^a	0.00% ^a
Non infected treated with sulphadiazine	71% ^c	5.00±0.82 ^b	0.433±0.058 ^a	0.296±0.018 ^b	2.778% ^b	7.33% ^b

Non infected treated with pyrimethamine	43% ^d	3.14±0.22 ^c	0.326±0.032 ^b	0.267±0.016 ^b	4.347% ^c	11.11% ^c
Infected treated with DMSO	86% ^b	6.29±0.92 ^b	0.367±0.038 ^b	0.282±0.012 ^b	2.222% ^b	8.07% ^b
Infected treated with sulphadiazine	71% ^c	4.57±0.83 ^c	0.350±0.036 ^b	0.260±0.014 ^b	5.882% ^c	5.71% ^d
Infected treated with pyrimethamine	57% ^d	3.14±0.12 ^c	0.280±0.024 ^c	0.246±0.015 ^b	8.333% ^d	9.06% ^b

Vertically, similar letter means not significant.

DISCUSSION

Our study showed that toxoplasmosis decreased serum FSH, LH and testosterone levels, it also decreased sperm contents of epididymal cauda, sperm viability% and increased sperm malformation ratio. In addition, toxoplasmosis also decreased relative weights of sex and secondary sex organs. Abdoli *et al.*, found that toxoplasmosis deteriorated reproductive function in male rats. Sperm motility, viability and concentration rates were significantly decreased after infection up to 70 days. Sperm abnormality was also increased, serum testosterone and intra-testicular testosterone levels were significantly decreased in the infected group[8]. The level of LH in the urine of *Toxoplasma gondii* infected mice was lower compared to the control. In direct correlation with the hormone level, testicular function and sperm production was also significantly lower in *Toxoplasma gondii* positive group using sperm count and histometric analysis as a marker [9]. Reproductive parameters (sperm motility, concentration and morphology), weight of the epididymis, sperm concentration and sperm motility were significantly decreased, while, sperm abnormalities was significantly increased in male rats with toxoplasmosis[10].

Interleukin-1b (IL-1b) levels were found to increased in toxoplasmosis. The levels of IL-1b correlated significantly in a negative manner with FSH, LH, free testosterone (FT), total testosterone (TT) in all patients with acute toxoplasmosis[15]. Interleukin-1b was known to suppress the hypothalamic- pituitary- gonadal (HPG) axis, directly or indirectly through increased corticotrophin-releasing hormone (CRH) and/or cortisol [25]. It was also postulated that cytokines released peripherally in response to the parasite, were reached the hypothalamus and initiated a sequence of events that inhibited the pulsatile release of gonadotropin-releasing hormone (GnRH), leading to the subsequent impairment of the pituitary-ovarian axis[11]. By this mechanisms, toxoplasmosis could interfered with hypothalamic-pituitary-gonad axis and decreased FSH and LH secretion, while, the decreasing of testosterone level could be occurred as a result of decline of LH secretion.

The histological changes found in testis and epididymis in this study were also recorded previously, the histopathological study of the reproductive system (testicles and epididymis) of male dogs experimentally infected with *Toxoplasma gondii* showed mononuclear inflammatory infiltrate in the epididymis, moderate cellular

edema, hydropic degeneration and moderate interstitial fibrosis in seminiferous tubules[26]. The deterioration of semen quality, sex and secondary sex organ weights and histological findings could be attributed to deterioration of hypothalamic-pituitary-gonads axis and the absence of the effect of LH and FSH on testis and other reproductive organs.

Our study showed that sulphadiazine and pyrimethamine didn't induced significant changes in the serum level of FSH, LH and testosterone in non infected rats (except pyrimethamine on testosterone). Furthermore, they didn't induced histological changes and didn't significantly altered the relative weight of sex and secondary sex organs, but they induced slight declined in the sperm contents of epididymal cauda and sperm viability%, with slight increase in the sperm malformation%. Many previous studies showed that sulphonamides and pyrimethamine didn't affected hypothalamic- pituitary – gonads axis[27-28]. All semen quality measurements were similar ($p>0.10$) for untreated and sulphonamides or pyrimethamine treated stallions during baseline and throughout the study. Testicular volume and sperm production efficiency were not affected by treatment ($p > 0.05$). There were no differences due to treatment in the erection latency, mount readiness latency, or erection rigidity score [29]. Awoniyi *et al.*, mentioned that pyrimethamine 100 mg/kg/day did not alter the testicular and epididymal sperm counts of the male rats. Treated males showed the same capability of the intact controls to impregnate females. Histological picture of the testis of the treated male was indistinguishable from controls[28]. Tumkiratiwong *et al.*, found that there was no significant differences ($P>0.05$) in numbers of spermatids, epididymal spermatozoa, sperm motility and viability of epididymal spermatozoa, induced by pyrimethamine, sulfanilamide, and their combination on day 7 of the treatment. Histological study of seminiferous tubules of rats treated by of pyrimethamine and sulfanilamide combination showed that the this combination produced less desquamation and fewer multinucleated giant cell infiltration[30].

In the toxoplasma infected rats, sulphadiazine and pyrimethamine improved reproductive parameter (serum level of FSH, LH and testosterone; histological changes, sperm contents of epididymal cauda and sperm viability%, sperm malformation%; and relative weights of reproductive

organs), and can partially alleviate the reproductive toxicity of toxoplasmosis. This could be attributed to the therapeutic efficacy of these drugs in toxoplasmosis.

The decreasing of pregnancy rate associated with toxoplasmosis could be attributed to decline of fertility of the infected male, the decreasing of litter size, fetal and placental weight, increasing of fetal resorption and early fetal death, may result from the mutagenic effects in the sperms in toxoplasma infected males. A pilot epigenetic study on testicular methylation, revealed that toxoplasmosis impaired the DNA methylation of selected genes [9,31].

However, the decreasing of pregnancy rates, litter size, fetal weight and increasing of fetal resorption and early fetal death of healthy female fertilized by either non-infected or toxoplasma infected male rats treated by either sulphadiazine or pyrimethamine, could be attributed to the mutagenic characteristics of these drugs [29,32-33]. Furthermore, pyrimethamine was found to produce a significant increase in structural chromosomal aberrations after acute treatment in bone marrow cells of mice

($P < 0.001$). It also induced chromosome abnormalities in spermatogonial cells ($P < 0.05$) at the highest dose [34]. Many sulphonamides were also mutagenic and cause fetal growth retardation [35].

CONCLUSION

According to these results, we can conclude that toxoplasmosis deteriorated male reproductive functions, while sulphadiazine or pyrimethamine can enhance some of the fertility parameters in toxoplasma infected rats, but they were not free from adverse effects which decreased pregnancy rate, litter size, fetal weight and increased fetal resorption and early fetal death.

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Nil

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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