

Journal homepage: www.sciencearchives.org

ISSN: 2582-6697



Original Research Article

<http://dx.doi.org/10.47587/SA.2020.1309>



Impact of toxoplasmosis on apoptotic activity and natural killer cell cytotoxicity among Iraqi pregnant women

Akeel Shamran Tushy^{1*}, Abdul-A Deem Y. Al.- Barrak², Nawras Noori Al-Alawae¹

¹ Center for Gastroenterology and Hepatology, Clinical Immunology Unit, Ministry of Health, Department of Health, Babylon, Iraq

² Faculty of Medicine, Al-Mustansiriya University, Iraq

*Corresponding author: greetoop@gmail.com

Received: Nov 08, 2020 / Revised: Dec 03, 2020/ Accepted: Dec 16, 2020

Abstract

This study was aimed at assessing NK cell cytotoxicity, soluble Fas ligand (sFasL) serum concentration among Toxoplasmosis patients, and healthy controls. To understanding the role of these parameters in the immunity and pathophysiology of toxoplasmosis, correlations between these parameters were evaluated. NK cell cytotoxicity was estimated by the cultivation of *Candida* cells on Sabouraud's dextrose agar (SDA) plate which had been incubated for two hours with NK cells. Colony-forming inhibition assay (CFIA) by calculating anticandidal index (ACI) has been estimated in two ratios of target: effector (T: E) cells 1:3 (NK R1) and 1:30 (NK R2) for both patients and controls. Enzyme-linked immunosorbent assay (ELISA) kit sFasL were used to estimate serum level in both patients and controls. There is a decrease in sFasL in toxoplasmosis compared to controls.

Keywords Toxoplasmosis, Apoptosis, FAS/FASL, NK Cells, Cytotoxicity

Introduction

Toxoplasma gondii infects a wide range –blooded vertebrate including humans and is one of the world's most successful parasite, as a member of the phylum Apicomplexa (Sibly et al., 2007) The main infection route is ingestion of cyst from raw or badly- cooked meat, ingestion of oocyst from substrates contaminated with the feces of infected feline and congenital transmission by tachyzoites (Lopiset et al., 2007). Natural killer cells are a subset of mononuclear cells, they are nonphagocytic large granular lymphocyte which is cytotoxic for certain tumor cells lines and virally infected cells, NK cells play several important roles in the host defense against certain microorganisms (Denker and Gazzinalli, 1998). Natural killer cells represent an arm of the innate immune system. Cell-mediated immune responses involving CD4+ and CD8+ T-cells and NK cells play a protective role in *T. gondii* primary infection (Laneir, 2005).

Macrophage and NK cells and cytokine are the main component involved in the innate immunity responses against *T. gondii* (Advenson, 2006). Apoptosis or program cell death plays essential roles in the regulation of the immune responses

and as innate and adaptive effects or mechanisms against intracellular pathogens (Luder and Cruoss, 2005). The FAS/FASL system is implicated as an important pathway mediating apoptosis (Arefet et al., 2004). In the immune system FAS/FASL plays an important function in down regulatory immune response and deletion of the autoreactive T-lymphocyte peripheral (Jouet et al., 1998). In the case of infectious diseases, the fas ligand (FSL) triggers an apoptotic waterfall and has a critical role in the effect of the parasites on type I cells which transmitted FAS/CD95, without the use of the mitochondrial loop *T. gondii* death receiver pathways. (Hippeet et al., 2008).

Materials and Methods

Study subjects

The research was performed in the Center Public Health Laboratory/Babylon on patients referred from Babylon Maternity Teaching Hospital and private clinic through the history from January 2019 to July 2019. All these subjects

were with a past abortion and were suspected of having toxoplasmosis.

Patient groups

Screening tests for toxoplasmosis antibodies by using IgM, IgG specific toxoplasma ELISA kit, were done for 30 referred women with a history of abortion. Eighteen patients were found to be with positive IgM, IgG using the ELISA technique. Positive toxoplasma patients with only IgG Immunoglobulin 9 and only IgM was 3, their ages were ranged from 18 - 33 years.

Control groups

Ten, apparently healthy age-matched women with negative toxoplasma antibodies and with a history of abortion were selected as a control group.

Blood sample collection

Four ml of the blood sample was obtained from each patient by vein puncture using a syringe with needle gauge 23, two ml transported to a non-heparinized blood collecting tube and then centrifuged at 1800 XG to separate serum then labeled and stored at -20°C until used, no preservative was added. The other 2 ml were transported to a heparinized (20 U of heparin/ml) vacutainer tube then used for separation of polymorph blood monocyte (PBMC).

Statistical analysis

Statistical analysis was done according to percentages to compare between samples using SPSS V.25 computer software.

Results and Discussion

Ten patients (25%) out of these forty patients were with a history of abortion but with seronegative toxoplasmosis, their age range 20-37 years considered as a control, and 30 (75%) of them showed seropositive toxoplasmosis (IgM+ or IgG+ or both). Table 2, figure 4 showed that out of those 30 positive result, 9 (30%) gave IgG positive and IgM negative toxoplasmosis, 3 (10 %) gave positive IgM and negative IgG, and 18 (60 %) gave both IgG and IgM positive toxoplasmosis.

Table 1. Distribution of the age groups of control and toxoplasmosis aborted women

Age groups (years)	Controls		Toxoplasmosis	
	No.	%	No.	%
<20	-	-	2	6.6
20-29	6	60	19	63.4
30-39	4	40	9	30
Total	10	100	30	100

P=0.199(No significant difference in age using chi-square test)

Toxoplasma infection stimulates humoral immune response as antibody production which includes IgM and IgG (Darcy and Santora, 1994) Serological diagnosis of toxoplasmosis is based

on a variety of techniques the Dye test (DT), the immunofluorescence (IF), and the indirect haemagglutination test (IHAT), each has its limitation, but all are still widely used in clinical medicine (Wielard et al., 1983) these testing for IgM/IgG anti-toxoplasma antibodies may fail to differentiate between a recent and pillar-infection (Iqbal and Nabila, 2007) but for detection of IgM antibody, the ELISA method is preferred because of its greater sensitivity (Jalan, 2009).

Table 2. distribution of the negative (control) and positive toxoplasmosis aborted women according to the IgM, IgG specific toxoplasma ELISA kit

Specific ELISA test	Patients		Control	
	No.	%	No.	%
IgM+ve, IgG-ve	3	10	-	-
IgM-ve, IgG+ve	9	30	-	-
IgM+ve, IgG+ve	18	60	-	-
IgM-ve, IgG-ve	-	-	10	100
Total	30	100	10	100

The different immunoglobulins are considered as marking of the acute or chronic phase of the infection as it is explained next IgM: It is the first antibody in appearing. It is the best activator of the complement, makes an excellent agglutination thanks to its structure, increases the level of cytotoxicity and its main target is the antigens of the surface of the parasite, classically it was considered as a marker of the acute phase of the disease nevertheless at present is known that the titers of IgM can even remain detectable during many months and years after produced the primary infection.

The main value of the IgM is that its absence practically discards the recent infection although it is necessary to consider that in the case of a newborn the answer of IgM antibodies can delay several months after the infection. The presence of IgM on the contrary implies the necessity to continue the study because the simple detection of this antibody is difficult to evaluate if data of the titers of IgG and IgM in series samples or with the results of other tests are not had (IgA and IgE) that suggests recent infection. IgG: This immunoglobulin is second in appearing, facilitates the mechanism of dependent cytotoxicity of antibodies, opzoniza to the antigen, activates to the complement, can cross the placenta and their main target is the antigens of the surface of the parasite, the presence of IgG antibodies implies that at some time of the life the patient has been in contact with the parasite and it is only possible to assure that exists a recent infection if between two separated samples 3-4 weeks a seroconversion of the titer of IgG exists (Filiseti and Candolf, 2004).

Diagnosis of acute infection with the protozoan parasite *Toxoplasma gondii* generally relies on serological methods (Remington and Desmots, 1990). However, serodiagnosis might be indistinct in immune-compromised patients, during pregnancy, or in patients with congenital toxoplasmosis. Whereas immunoglobulin M (IgM) antibodies have been shown to be reliable markers for acute infection, this class of immunoglobulins might have only limited value for diagnosis

in these patients; the observed persistence of IgM antibodies in some female patients might complicate diagnosis, especially during pregnancy.

In contrast, IgM antibodies might not be detectable in patients with congenital toxoplasmosis or during reactivation of a chronic infection in immunocompromised individuals (Fucillo et al., 1987).

The detection of IgM specific antibody can be of major importance in the diagnosis of congenital Toxoplasmosis in the neonate because IgM class antibodies do not cross the placental barrier (Remington, 2015). It is also helpful in differentiating recently acquired (acute) toxoplasmosis from chronic infection. The sensitivity, specificity, and reproducibility of enzyme-linked immunoassays are comparable to other serological tests for antibodies, such as immunofluorescence, complement fixation, hemagglutination, and radio immunoassays (Engwal et al., 2011).

The level of specific IgG antibody in sera was revealed high, after deletion positive cases from it, meant chronic toxoplasmosis between the mothers whose neonates were confirmed in hospital (Kompalic et al., 2004), the chronic toxoplasmosis was considered when only IgG was positive (Peterson et al., 2001), and it's the immunoglobulin was to appears in toxoplasmosis after IgM (Bancroft et al., 2013).

Table 3. Distribution of the IgM and IgG index result in toxoplasmosis patients

Specific ELISA test	Means of IgM or IgG index
IgM+ve,IgG-ve	1.6 IgM
IgM+ve,IgG+ve	1.0 IgM 2.4 IgG
IgM-ve,IgG+ve	3.8 IgG

Table 3 showed that mean toxoplasma IgM index results have a high value with the group of IgM⁺IgG⁻ compared to a decreasing value at the group of IgM⁺IgG⁺, while in the case of IgM⁻IgG⁺, IgM index showed a negative result. The mean level of IgG index showed an increasing value IgM⁻IgG⁺ group compared to that in the group of IgM⁺, IgG⁺.

According to the general concept which states that the acute stage is associated with high IgM, and the transitional stage associated with mixed IgM and IgG followed with a high level of IgG at the chronic stage, it can be concluded that the group of IgM⁺IgG⁻ represents the acute stage, and a group of IgM⁺IgG⁺ represents the transitional stage, while IgM⁻IgG⁺group represents a chronic stage of the disease. NK cells are involved in innate immunity against a broad range of intracellular pathogens, especially *T.gondii*, in the earliest stage of infection (Bancroft et al 2013).

The levels of the NK activity have been found elevated in children with malaria and in mice infected with *Trypanosoma cruzi* and *Toxoplasma gondii*, suggesting a possible effector

role of these cells in parasitic disease (Hatoher et al., 2000). *T. gondii* is capable of triggering the non-specific activation of macrophage and NK cells (Hauser et al., 1983). inhuman congenital toxoplasmosis, elevated circulating NK cell numbers have been linked to protection. Natural killer cytotoxicity is one of the important parameters used in this study to evaluate the natural killer cells' activity in the acute and chronic stages.

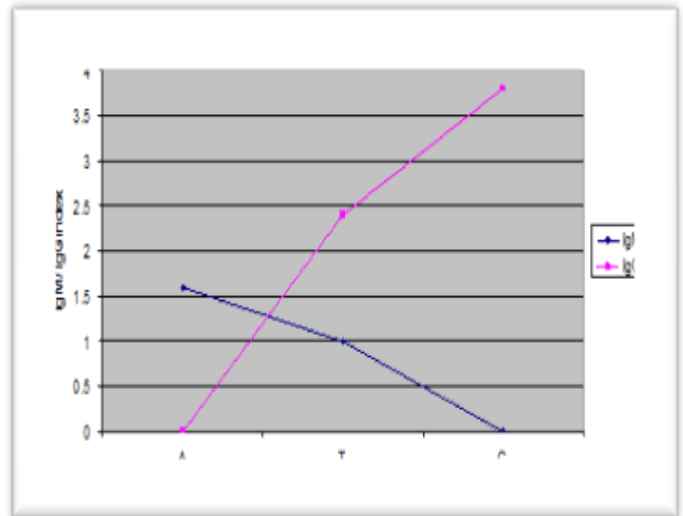


Fig. 1 the IgM and IgG index results in toxoplasmosis patients at different stages

To determine NK cytotoxic activity, CFI (candidal formula index) assay was applied. In this procedure, target cells (T=Candida) were incubated with effector cells (E=NK cell) at different T: E ratios; 1:3 and 1:30 (1:3 called R1 and 1:30 called R2). Figure 3 showed the cells of normal murderers' cytotoxicity in control, acute, chronic, and transitional stages of patients with toxoplasmosis were increased in both ratios R1 and R2 due to an increase in the stimulation of body defense response. Gazzanilli et al. (1998) reported that *Toxoplasmagondii* has the ability to activate the NK cells from the innate compartment of the immune system. Table 4 and figure 4 showed that the cytotoxicity index (CI%) of NK cells in acute toxoplasmosis (IgM⁺, IgG⁻) at ratio 1 (R1) was 64.6 % while in the patient control CI% was 59.5% and it was 99% in the R2 compared with the control patient 84.5 %, from these results it can be concluded that *Toxoplasmagondii* up-regulates the NK cell cytotoxicity in the acute stage of disease more than in control, and also the increase in NK ratio from R1 to R2 lead to change P-value from nonsignificant 0.34 to a significant difference of P = 0.03 which indicates that up-regulation will have a prominent effect when it goes in parallel with the increase in NK cell population. In the chronic stage (IgM⁻, IgG⁺), as in table 5 and figure 3, the NK cells cytotoxicity in R1 increased to 65% in comparison with the control patient 59.5 % and with R2 NK cell cytotoxicity increased to 88.7 % in comparison with control patients 84.5%. Table 6 and figure 6 showed the final stage of the acute infection and the first stage of the chronic infection, the IgM and IgG were both seropositive (IgM⁺, IgG⁺) which represent transitional stage.

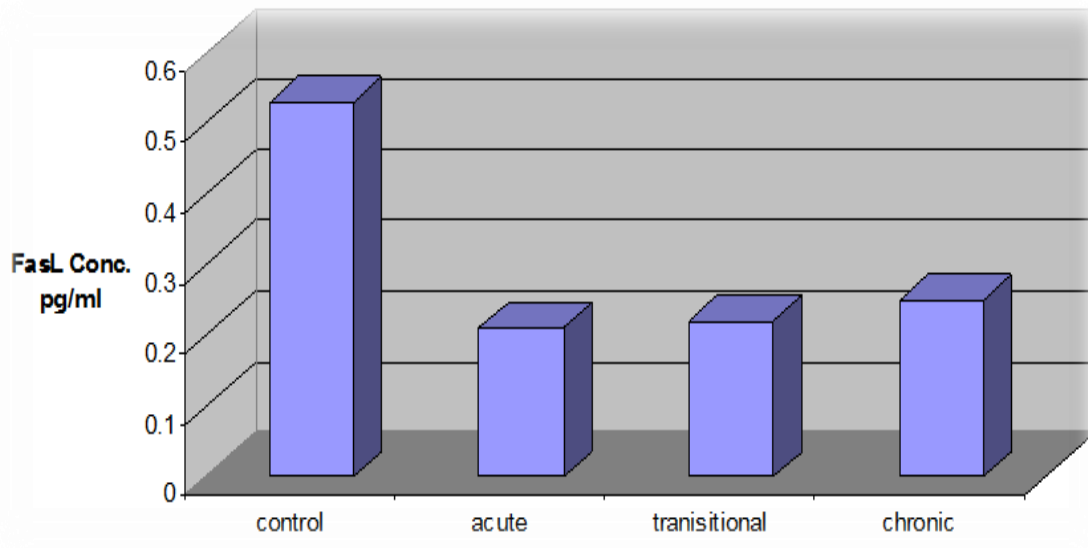


Fig. 2 the number of cases of each toxoplasmosis stage

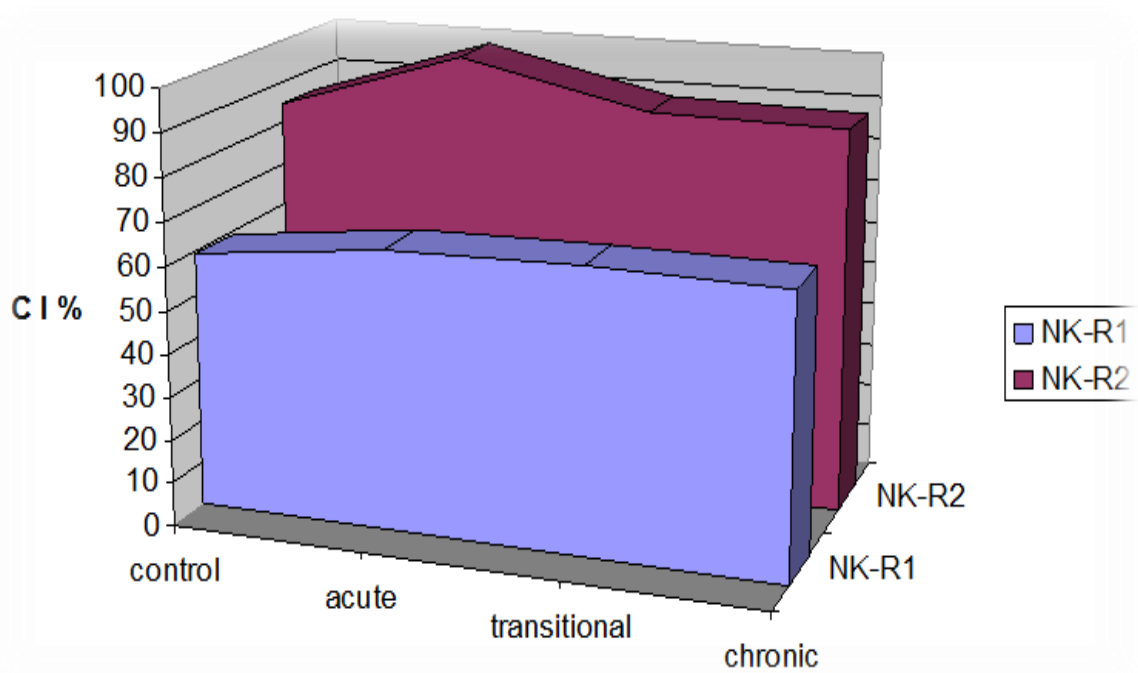


Fig. 3 Natural killer cells cytotoxicity (CI%) in control, acute, chronic and transitional stages in patients with toxoplasmosis. NK-R1, NK-R2=natural killer cell cytotoxicity at 1:3 ,1:30 candidal / NK cell respectively

In this stage both acute (IgM) and chronic (IgG) parameter showed a seropositive result, but when NK cytotoxicity in R2 of the patient (89.3%) compared to NK cytotoxicity at R2 in acute (99%) and chronic stage (88.8%) it is found that NK

cytotoxicity is near to the chronic result than to the acute result. These might be explained on the basis that this stage will proceed to the chronic more than acute and enable this proposal that this is the transitional stage of the disease.

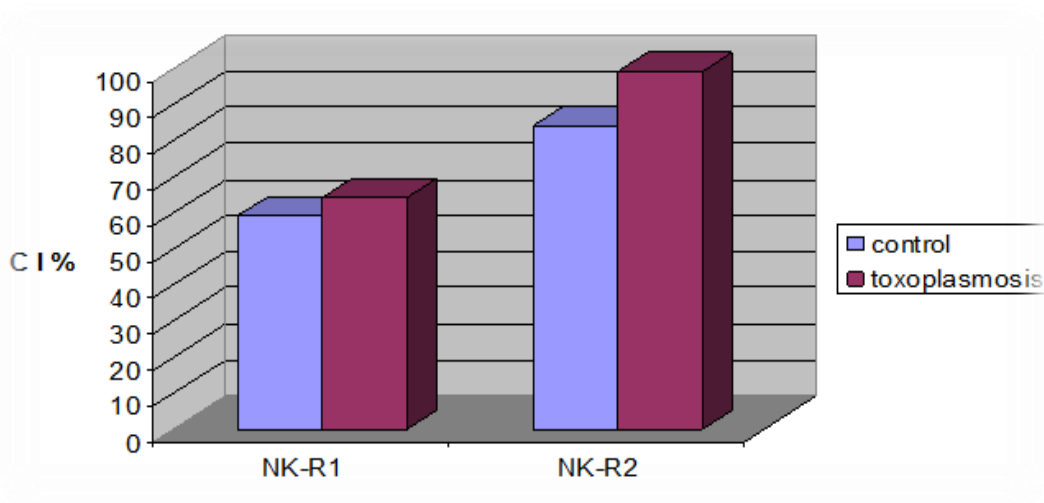


Fig. 4 NK cells cytotoxicity index % (CI %) in the acute stage of toxoplasmosis and control at both ratios R1 and R2

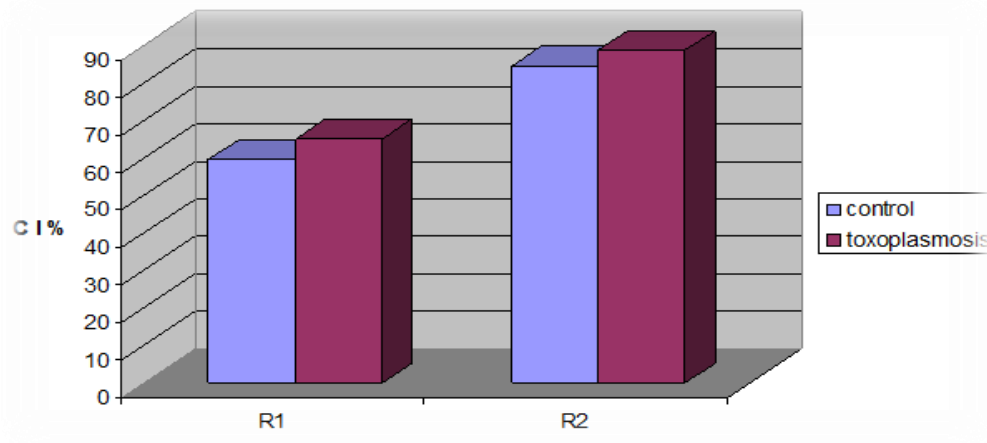


Fig. 5 NK cells cytotoxicity in chronic stage of disease and control

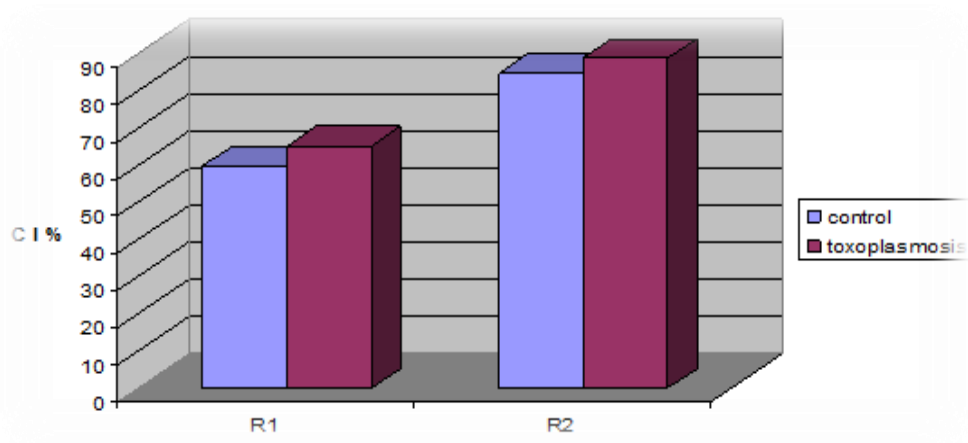


Fig. 6 NK cells cytotoxicity in transitional stage of disease and control

Table 4. the activation of NK cells in acute stage of disease and control

	Controls	Toxoplasmosis	P-value
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	
NK R1	59.50±8.67 (47.00-74.00)	64.66±12.85 (50.00-74.00)	0.43
NK R2	84.50±5.52 (78.00-95.00)	99.00±17.32 (97.00-100.00)	0.03

Table 5. NK cells cytotoxicity in chronic stage of disease and control

	Controls	Toxoplasmosis	P value
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	
ACIR1 %	59.50±8.67 (47.00-74.00)	65.00±6.1 (56.00-74.00)	0.0001*
ACIR2 %	84.50±5.52 (78.00-95.00)	88.78±3.31 (82.00-93.00)	0.06

*Significant difference using t-test for two independent means at 0.01 level of significance.

The difference in CI % between R1 and R2 in the acute stage was 27 while in CI% between R1 and R2 in the chronic stage was 18, which indicates that Toxoplasma infection had a higher impact on CI % of NK cells at the acute stage compare to the chronic stage, as in figure 7, also it reveals that the increasing number rise of NK cells (effector cells) is not a determinative factor in NK cells cytotoxicity but the toxoplasma infection stage.

The FAS / FAS L dysregulation contributes to infectious disease pathogenesis (Nigro *et al.* 1994). FASL activates and plays a critical role in the apoptotic cascading during infectious disease and the effect of the parasite on apoptosis in type I cells translating FAS/CD95 via death receptor pathways without mitochondrial looping need. *Toxoplasma gondii* significantly reduces FAS/CD95 triggered apoptosis by impairing activation of the pro-caspase 8 (Polya *et al.* 2007). And also *Toxoplasma gondii* inhibition FAS/CD95-mediated apoptosis in type II cells primarily by decreasing the apoptogenic function to mitochondria (Hippe *et al.* 2008). In this study, FAS L was determined at three stages; The first stage was acute, the mean value of the result of FAS L in this stage was 0.21 pg/ml, and the second stage (transitional stage) was 0.22 pg/ml, and the third stage (chronic stage) value was 0.25 pg/ml. While the mean value of FASL concentration in the control group was 0.53 pg/ml, as showed in table.7. From these results, it can be concluded that FAS L concentration at both acute and transitional stages showed a decrease in their values compared to the chronic stage. The results also showed that FAS L concentration at the

transitional stage (0.22 pg/ml) was mostly deflected towards the acute stage (0.21 pg/ml) more than chronic stage (0.25 pg/ml).

Table 6. NK cells cytotoxicity in transitional stage of disease and control

	IgM & IgG		P-value
	Controls	Positive	
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	
ACIR1%	59.50±8.67 (47.00-74.00)	65.55±6.40 (56.00-78.00)	0.04
ACIR2%	84.50±5.52 (78.00-95.00)	89.38±5.30 (82.00-100.00)	0.03

Table 7. Fas ligand concentration at different stages of disease compared to control

Fas ligand Concentration (pg/ml)	Controls	Acute stage	Transitional stage	Chronic stage
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)	Mean±SD (Min-Max)
	0.53±0.035 (0.10-0.90)	0.21±0.04 (0.16-0.25)	0.22±0.8 (0.14-0.48)	0.25±0.9 (0.16-0.48)

Table 8. distribution of the negative (control) and positive toxoplasmosis aborted women results (mean of all stage) according to the different variable

	Controls	Toxoplasmosis	P-value
	Mean±SD (Min-Max)	Mean±SD (Min-Max)	
Age (years)	26.30±5.70 (20.00-37.00)	25.70±4.23 (18.00-33.00)	0.724
NK R1	60.90±8.71 (47.00-74.00)	69.00±7.48 (50.00-85.00)	0.0001*
NK R2	84.50±5.52 (78.00-95.00)	93.30±4.49 (82.00-100.00)	0.0001*
sFasL Concentration (pg/ml)	0.53±0.035 (0.10-0.90)	0.22 ± 0.7 (0.12-0.47)	0.0001*

*Significant difference using t-test for two independent means at 0.05 level of significance.

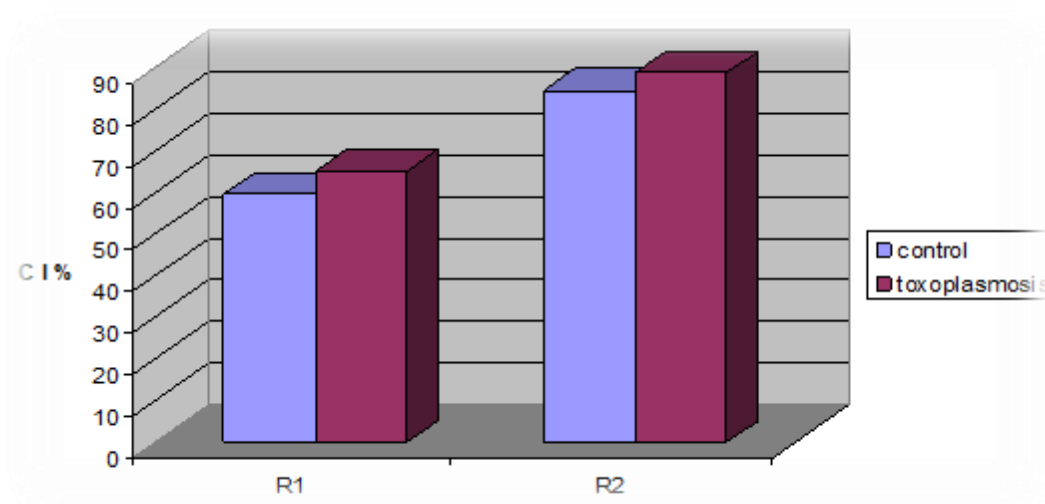


Fig. 6 NK cells cytotoxicity in a transitional stage of disease and control

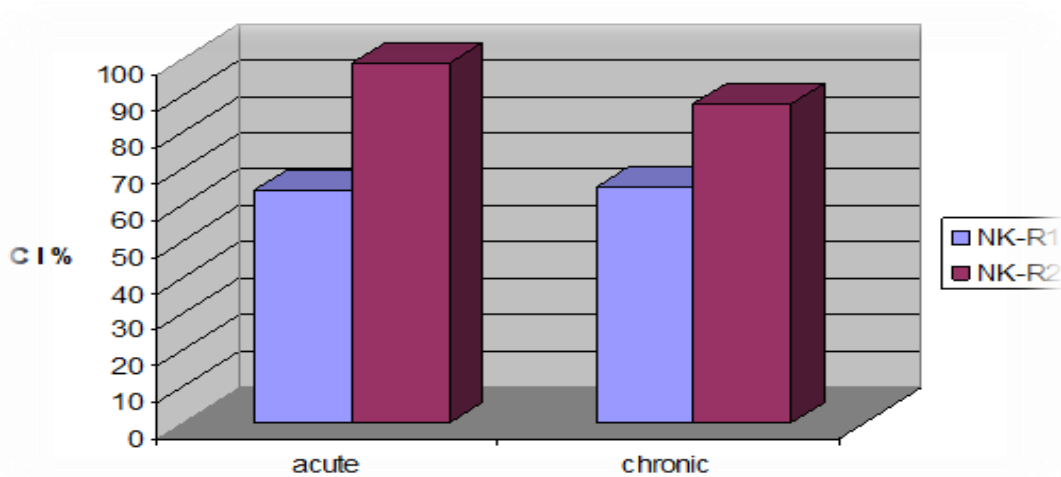


Fig.7 Activation of NK cells in acute & chronic stage of the disease

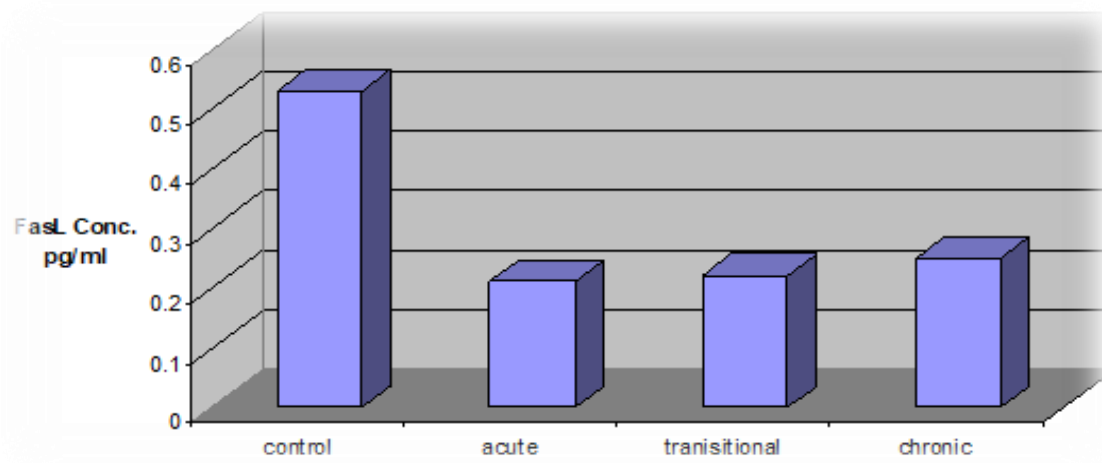


Fig. 8 Fas ligand concentration at different stages of disease and control

The correlation between sFasL and the age groups

Table 7 showed those age groups have a positive correlation with sFasL in the control (r=0.094) and patients with toxoplasmosis (Table 8) have a positive correlation (r=0.030) but not significant. These results could be compared with the result of other studies. Mysliwiec *et al.* 2006, found a positive correlation between sFas and age in Graves' disease patients. No big variations were made in FasL concentrations between those studied groups of patients. However, a negative correlation was formed between FasL and age in all Hashimoto thyroiditis and Graves' disease patients. Goto 2008, showed The sFasL in Werner syndrome (WS), a level comparable to that in healthy elderly ages 83 to 95 years, had significantly increased ($p < 0.05$) compared to that in young healthy individuals ages 15 to 70 years, and Jiang *et al* 2008, showed the plasma sFasL levels were examined as a function of age, There has been a considerable connection between the sFasL and age in the non-age-related macular degeneration (AMD) subjects, and also showed the plasma FasL increased with age and AMD.

Table 9. correlation between age, NK CI% and sFasL among controls

		NK CI%	FasL Concentration (pg/mL)
Age (years)	R	-0.030	0.030
	P	0.877	0.875
	N	30	30
NK CI%	R		-0.062
	P		0.640
	N		30

**Correlation is significant at the 0.01 level (2-tailed).

Table 10 correlation between age, NK CI% and sFasL among toxoplasmosis patients

		NK CI%	FasL Concentration (pg/mL)
Age (years)	R	0.779**	0.094
	P	0.008	0.795
	N	10	10
NK CI%	R		0.148
	P		0.574
	N		10

The correlation between sFasL and the NK CI%.

Table 7 showed those NK CI% in control have a positive correlation with FASL (r =0.14) but not significant (P > 0.01). While in patient with toxoplasmosis (table 8) NK CI% have a negative correlation with FASL concentration, these correlation indicate that any increased in NK activity showed a greater decline in FASL concentration. These results could be

compared with the result of other studies such as: Tanaka *et al* 1996, showed that High levels of sFasL in serum have been generally detected in several hematological diseases including NK-cell leukemia, NK cell lymphoma, and the Peripheral nasal T/NK cell lymphomas coexpress Fas, FasL, and perforin/granzyme. This is in good correlation with the observation that in NK cell lymphoma, mFasL was constitutively expressed, and sFasL was shed, whereas NK cells of healthy volunteers expressed FasL only upon activation.

Kern *et al.* 2000, reported that a significant negative correlation was found between initial sFasL levels on the first day and both total lymphocyte and T-cell counts during the *Plasmodium falciparum* disease course, sFasL levels significantly declined.

Massaro *et al.* 2005, showed that FasL interacting with Fas at NK cell surface causes NK cell suicide, as apoptosis of NK cells was inhibited by blocking FasL/Fas interaction with specific mAbs, and doughty *et al.* 2002, reported that Increased sFasL was associated with a viral infection and lymphoproliferative disease.

Conclusion

When comparing NK R1 to NK R2 the results revealed that NK cell function increase with the increase in number in both patients and controls, but in patients the level of the increase is more than the controls. A negative correlation was detected between sFasL and NK cell cytotoxicity in both toxoplasmosis patients and controls. The positive correlation between sFasL and NK cell cytotoxicity in controls was changed to a negative correlation in Toxoplasmosis. There is a significant positive correlation between NK cell cytotoxicity and age group in controls. While in toxoplasmosis a positive correlation was detected between age group and sFasL and a negative correlation between age group and NK cell cytotoxicity.

Conflict of Interest

The authors hereby declare no conflict of interest.

Consent for publication

The authors declare that the work has consent for publication.

Funding support

The authors declare that they have no funding support for this study.

References

Aref, S., Refaei, M. E., Goda, T., Sakrana, M., & El-Nemre, H. (2004). Accelerated neutrophil apoptosis in neutropenic patients with hepatosplenic schistosomiasis is induced by serum Fas ligand. *The Hematology Journal*, 5(5), 434-439.

Bancroft, G. J., Schreiber, R. D., Bosma, G. C., Bosma, M. J., & Uhanue, E. R. (1987). AT cell-independent mechanism of macrophage activation by interferon-gamma. *The Journal of Immunology*, 139(4), 1104-1107.

- Darcy, F., Santora, S. (1994) Toxoplasmosis. In :Parasitic infection and the immunity system. Ed by kierszenbaum. Academic press. Inc , sandiago, calif, pp 163-201.
- Denkers, E. Y., & Gazzinelli, R. T. (1998). Regulation and function of T-cell-mediated immunity during *Toxoplasma gondii* infection. *Clinical microbiology reviews*, 11(4), 569-588.
- Doughty, L., Clark, R. S., Kaplan, S. S., Sasser, H., & Carcillo, J. (2002). sFas and sFas ligand and pediatric sepsis-induced multiple organ failure syndrome. *Pediatric research*, 52(6), 922-927.
- Edvinsson, B. (2006). *Molecular diagnosis of infection with Toxoplasma gondii in immunocompromised patients*. Institutionen för laboratoriediagnostik/Department of Laboratory Medicine.
- Engvall, E., & Perlmann, P. (1971). Enzyme-linked immunosorbent assay (ELISA) quantitative assay of immunoglobulin G. *Immunochemistry*, 8(9), 871-874.
- Fidan, I., Yüksel, S., Kalkanci, A., Imir, T., & Kustimur, S. (2005). Evaluation of the natural killer cytotoxicity and the levels of cytokines in rats with type I diabetes mellitus. *Memórias do Instituto Oswaldo Cruz*, 100(8), 883-887.
- Filiseti, D., Candolf, E. (2004). Immunorespons to *T.gondii* . *Ann.Istsuper sanito*, 40 (1),71-80.
- Fuccillo, D. A., Madden, D. L., Tzan, N., & Sever, J. L. (1987). Difficulties associated with serological diagnosis of *Toxoplasma gondii* infections. *Diagn.Clin. Immunol.* 5, 8–13.
- Goto, M. (2008). Elevation of soluble Fas (APO-1, CD95) ligand in natural aging and Werner syndrome. *Bio Science Trends*. 2(3), 124-127.
- Hatoher, F. A., Cerrone, M. C., Burton, R. C. (2000). Increased natural killer cells activity in expremintal Amrecan Trypanasomosis. *J. Immuno*, 127, 1126-1130.
- Hauser, W., Sharma, S., Remington, J. (1983). Augmentation of NK cell activity by soluble and particulate fractions of *toxoplasma gondii*. *J. Immunol*, 131 (1), 458-463.
- Hippe, D., Lytorchenko, O., Schimts, I., Luder, C. G. K. (2008). Fas/CD95-mediated apoptosis of type II cells in blocked by *toxoplasma gondii* primary via interference with the mitochondrial amplification loop. *Amrecan Soci Microbiol*, 76 (7), 2905-2912.
- Iqbal, J., Nabila, K. (2007). Detection of acute *toxoplasma gondii* infection in early pregnancy by IgG avidity and P C R analysis. *J. med. Microbiol*, 56, 1495-1499.
- Jalan, A. B. (2009). *Toxoplasma Infection* , Nirman website , 312, Nirman Kendra , sector 17 . vashi , Narinumbai , India . 40060s ,Tel – fax 7891410 .www.Nirman.com
- Jiang, Sh., Moriarty-Craige, S. E., Li Ch, Lynn, M. J., Cai, J., Jones, D. P., Sternberg, P. (2008). Associations of Plasma-Soluble Fas Ligand with Aging and Age-Related Macular Degeneration. *Vis Sci*. 49 1345–1349.
- Juo, P., Kuo, C.J., Yuan, J., Blenis, J. (1998). Essential requirement for caspase -8/FLICE in the initiation of the Fas-induced apoptotic cascade. *Curr. Biol*, 8, 1001-1008.
- Kern, P., Dietrich, M., Hemmer, Ch., Wellinghausen, N. (2000). Increased Levels of Soluble Fas Ligand in Serum in *Plasmodium falciparum* Malaria. *Infection and Immunity*. p 3061–3063
- Kompalic, C. A., Nogueira, S. A., Guedes, A. L., Frota, C., Gonzales, L. F., Brandao, A. (2004). Lack of technical specificity in the molecular diagnosis of toxoplasmosis. *Trans R Soc Trop Med Hyg*, 98(2) 92-5.
- Lanier, L. L. (2005). NK cell recognition. *Annu. Rev. Immunol*, 23, 225-274
- Lopis, F. M. R., Goncalves, D. D., Mitsuka-Bregano, R., Freire, R. L., Navarro, I. T. (2007). *Toxoplasma gondii* infection in pregnancy. *Brazil. J. Infect. Dis*. 11 (5), 496-506.
- Luder, C. G. K. & Gross, U. (2005). Apoptosis and its modulation during infection with *Toxoplasma gondii*. Molecular mechanisms and infection. Griffin, D.E. (ed.) *Curr top Microbiolimmunol*, 289, 219 – 237.
- Massaro, A. M., Negrini, S., Contini, P., Raffaella, M. Z., Pogg, A. (2005). Tumor-Induced Apoptosis of Human IL-2-Activated NK Cells: Role of Natural Cytotoxicity Receptors. *Journal of Immunology*,174, 2653-2660.
- Mysliwiec, J. K., Oklotam, M., Nikolajuk, A., Gorska, M. (2006). Age relatedchanges of soluble Fas, Fas ligand and Bcl-2 in autoimmune thyroiddiseases. *Endocrine Abstracts* 11 941.
- Nigro, G., Pazzi, J., Paesano, T., Mango, S., Pravvedi, S., Capuano, O. Pollastrin, O. (1994). Low lvels of natural killer cells in pregnant women transmitting *toxoplasma gondii*. *Prenat. Diagn* . 9, 401-404.
- Peterson, E., Pollak, A., Reiter-Owona, I. (2001). Reseant trend in research on congenital toxoplasmosis. *International .J. Parasitology*, 31, 115-144.
- Polya, V., Martina, W., Diana, H., Cross, U., Klaus, S.O., Ingo, S., Lunder, C. G. K. (2007). *Toxoplasma gondii* inhibit Fas / CD 95 triggered cell death by inducing aberrant processing and degradation of caspase 8. *Cellular. Microbial*, 9(6), 1556 – 1570.
- Remington, J. S., and Desmonts, G. (1990). Toxoplasmosis. Infectious diseases of the fetus and newborn infant. In J. S. Remington and J. O. Klein (ed.), *The W. B. Saunders Co.*, Philadelphia, Pa. , p. 89–195
- Remington, J. S. (2015). Toxoplasmosis In the Adult. *Bull. N.Y. Acad. Med*.50 211-227
- Scott, P., Trinchieri, G. (1995). The role of the Natural Killer cells in host-parasite interaction . *Curr.Opin.Immunol*, 7, 34-40.
- Sibly, L. D., Charron, A., Hakansson, S., Mordue, D. (2007). Invasion and Intracellular Survival by *Toxoplasma*. Protozoan in Macrophages, edited by Eric Denkers and Ricardo Gazzinelli. Landes Bioscience. P 16-24.
- Tanaka, M., Suda, Haze, K., Nakamura, N., Sato, K., Kimura, F. Motoyoshi, K., Mizuki, M., Tagawa, S., Ohga, S., Hatake, K., Drummond, A. H., Nagata, S. (1996). Fas ligand in human serum. *Nat Med*. 2, 317-32.
- Wielard, F., Gruijthuijsen, H. V ., Duermeijer, W., Joss, A. W. L., Skinner, L. William, H., Vandeven, E. H.(1983). Diagnosis of acute toxoplasmosis by an enzyme immuno assay foe spesificimmunoglobuline M antibodies.

This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/).



How to cite this article:

Tushy, A.S., Abdul, A Deem, Y. Al- Barrak, & Al-Alawae, N.N. (2020). Impact of toxoplasmosis on apoptotic activity and natural killer cell cytotoxicity among Iraqi pregnant women. *Science Archives*, Vol. 1 (3), 123-131.

<http://dx.doi.org/10.47587/SA.2020.1309>