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Relationship between *Toxoplasma gondii* and arthritis among patients in Kirkuk city

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ESR

A B S T R A C T

A study was conducted during 1st of November 2014 to 30th of June 2015 to assess some epidemiological factors of toxoplasmosis among patients with arthritis in Kirkuk city-Iraq. A total of 234 sera were extracted from venous blood of both genders attending rheumatological clinic in Azadi-teaching Hospital and Ibn-Nafies private medical laboratory. Also 30 sera were separated from healthy individuals (control group).The age group of women ranged from year to 90 years and above. ELISA kits wereused for detecting *Toxoplasma* antibodies (IgM and IgG). While for arthritis diagnosis: latex fixation test(direct test) and standard tube agglutination test(titration test STAT) were performed for detecting rheumatoid factor(RF) antibodies and concentration respectively. Also ELISA anti-cyclic citrullinated peptide (anti-ccp-IgG) for confirmation reactivity of (RF) was used. Out of 234 cases screened for arthritis only183 (78.20 %) sera were positive for polyarthritis, 99 sera of them reveal *T. gondii* antibodies 54.09 % which involved 47.54% and 6.55 % of *Toxoplasma*IgM and IgG antibodies respectively $p<0.05$.According to age high rates of *Toxoplasma* were recorded among patients aging from 30 to 40 years and from 1year to 10 years 69.23 % and 57.14 % respectively P.<0.05.Relationship between toxoplasmosis and patients educational levels was significant, while it was not significant with types of water consumption, and environmental contact with the parasite. Back pain 83.61% and knee swelling 86.69 % were dominant symptoms among arthritis patients with no relation to *Toxoplasma* antibodies distribution, $P>0.05$. Frequency of RF was high60.29% among females than55.32 % in males, and relationship between Toxoplasma antibodies distribution and rheumatoid factor was not significant. ESR rate among females with arthritis and toxoplasmosis was high among females aging above 50 years, controversy to higher ESR rate in males aging below 50 years. Positive anti-ccp-IgG antibodies was found in 15 sera (8.19 %) of arthritis patients and *Toxoplasma* antibodies rate was 93.33 % among them before treatment compare to 6.45 % of anti-ccp and complete patients sera exerting 100% of toxoplasmosis with significant increases of *Toxoplasma* IgM after treatment by anti-arthritis drugs, $P<0.05$.The rates of *T. gondii* and poly-arthritis antibodies were high in Kirkuk city. RF test has had low value compare to STAT in diagnosis of arthritis and anti-ccp-IgG ELISA test had strong role in confirming arthritis cases. Relationship between toxoplasmosis and poly-arthritis is significant.

Introduction

Toxoplasmosis is a disease caused by a tissue apicomplexian protozoan parasite called *Toxoplasma gondii* (T.g). It is an intracellular parasite that infects human and other warm-blooded animals (Switaj, 2005). Its distribution is worldwide and about 20 to 90 % of world adult population have serum *Toxoplasma* antibodies (Tawfiq, 2013). Cats and some carnivores are final hosts while most mammals including human being are intermediate hosts. *Toxoplasma* prevalence depends on several factors such as sanitation, cultural levels, age, gender, residency, nutritional habits and modes and cat bearing houses (Al-Jubori, 2005). From clinical view; toxoplasmosis manifested a symptomatically among immune-competent and self-limits in men and unmarried women, with chance of conveying to symptomatic when the female gets infection during pregnancy mostly leads to miscarriages and congenital abnormalities (Pinard, 2003). While in immunocompromised and depleting diseases the picture is sever and life threatening (Boothyroyd, 2000). The parasite can invade cervical lymph nodes, leads to lymphadenopathy most times associate with cervical stiffness, or parasite migration by blood stream and lymphatic system may give rises in serious health problems by invading of other vital organs such as brain, eyes orbit, muscles which mostly leads to stillbirth, encephalitis, microcephaly and hydrocephaly of fetus and neonates, abnormal sight (lateral retino-chorioditis) and myositis respectively (Hegab and Al-Mutawa, 2003). Arthritis is a medical term derived from Greek word “arth” refers to joints in the body and it means inflammation. This inflammation may involve knees, hands, hips and spine, although any joint may be affected. Technically, arthritis is called a degenerative joint disease. The common link between these disorder is painful joints more than 100 types of arthritis (Cho, 2005).

There are two main types of arthritis: inflammatory and non-inflammatory. Rheumatoid arthritis and gout are examples to former one, while osteoarthritis is an example to the later. Distinguishing between them can be based on location, timing, and pattern of joint pain, as well as the presence of swelling and symptoms outside the joint such as rash (Zhu et al., 2011). Also arthritis can be classified into mono arthritis and polyarthritis; examples to former one are septic arthritis, Gout, pseudo-gout and osteoarthritis'. Risk factors include genetics, sex (high dominant in female), past trauma, advancing age, and obesity (Goodman, 2005). While polyarthritis is an arthritis which involves 5 or more joints at the same time. It is usually associated with autoimmune conditions such as rheumatoid arthritis and lupus erythematosus, but can also be caused by infection with viruses. It may be experienced at any age and is not gender specific (Edworthy *et al.,* 2001). Laboratory diagnosis of arthritis is big score require employ of different tests such as: rheumatoid factor, anti-DNA-systemic lupus erythematosus (SLE) antibody test, C. reactive protein (CRP) determination, anti-nuclear factor (ANA) and recently anti-cyclic citrullinated peptide (anti-ccp). Lipid coagulant antibodies such as anti-phospholipid (APL) and anti-cardiolipin (ACL) in addition to assessments of serum levels of uric acid, calcium and inorganic phosphate (Gaddy *et al.,* 2012). Sometimes differential diagnosis of arthritis demands complete blood count for distinguishing acute from chronic and to get assurance from blood elements due to arthritis (Andrea, 2006). The outcome of toxoplasmosis and arthritis is tissue damages and injuries comprehensively due to

toxoplasmosis and particularly joints due to arthritis, so to correlate between toxoplasmosis and arthritis in general because according to our information; there is no study in this regard in Iraq particularly in Kirkuk city the present study was conducted to fulfills the following aim**:** To study some epidemiological aspects of toxoplasmosis among arthritic patients in Kirkuk city. The second aim is to detect relationship between toxoplasmosis and some causative agents of arthritis.

Materials and Methods

Time, location and study design: The present study was cross sectional study involved patients with arthritis and difficulties in movements. Whom they attend department of rheumatology in Azadi teaching Hospital and Ibn-Nafies medical private laboratory in Kirkuk Province-Iraq from 1st of November 2014 to 30th of June 2015.

Blood collections: A total of 234 venous blood samples were collected from patients of both gender attending rheumatology department of Azadi teaching Hospital, private rheumatological clinics and Ibn-Nafies private medical lab. For each patient complete informations were taken using special questionnaire. Patients ages ranged from one year up to 90 years, they were arranged with in three groups as: test groups which includes 183 polyarthritis patients and 21 polyarthritis patients accepted to receive treatments and follow up monthly for about three months. While control group involves 30 healthy individuals without arthritis and other diseases.

Samples collection: Five ml of venous blood has been drawn into gel tube containing clot activator for serum separation. The gel tubes containing blood samples were left for about 10 minutes in water bath at 37°C for complete blood clotting. Then after the tubes were transported into centrifuge that fixed on 3000 rpm for about 5 minutes. Sera after centrifugation were separated from gel tubes and kept in clean unused eppendorff tubes. While the rest part of the sera were kept at -20°C for longer period use.

Laboratory tests: For detecting *Toxoplasma gondii* antibodies ELISA kits both IgM and IgG kits were used according to manufactured company leaflets and including instruction manual. For arthritis diagnosis, latex fixation test was performed using direct agglutination test, which confirmed by standard tube agglutination test (STAT) for detecting rheumatoid factor (RF) antibody titer as follows: clear sera, non hemolysed, non lipemic and non-icteric were chosen and about 25µl of each serum was taken by micropipette on a card test (containing 6 wells) and transferred in to well number 2. The same volume of negative and positive controls was transferred separately in to well 1 and 3. Latex antigen (RF) vial was reconstituted by shaking and about 25µl of this antigen was transferred on each wells. Card test was placed on shaker for about 2 minutes for watching agglutination formation that indicates positive for RF, however absence of agglutinations means negative for RF. Each positive RF serum was seeded for STAT which briefly consists of serial dilutions of sera made by adding phosphate buffer saline (PBS) to sera as initial dilution 1:2 in the first tube was composed of 50µl PBS and 50 µl o suspected positive RF sera. Other 6 tubes has contains 50µl PBS and from tube one 50 µl was transferred in to tube 2 to obtained 1:4 dilution and so on in other tube to obtain 1:8, 1:16, 1:32, 1:64 and 1:128 form last tube 50µl was pulled out and discharged into waste basket for getting accurate dilution. Then after 50µl of RF antigen was added to each tube and all tubes

were agitated for 20 to 30 seconds then transferred into incubator at 37°C for about 2 hours for watching agglutination in the bottom of tubes. The last tube that demonstrates agglutination is presenting RF dilution. RF concentration or titer was determined by multiplying dilution to inverse of final dilution. According to kit titers equal at 8 IU/ml and above were positive for RF. These to tests were done according to instruction manual of manufactured company Spinreact (Girone-Spain). The second test that used for detecting arthritis was anti-cyclic citrullinated peptide (ACCP) using ELISA-IgG sandwich kit purchased by the means of Al-Assala local company in Kirkuk city from Aeskulisa company–German (Schellekens *et al.*, 1998). Also the rate of inflammation due to toxoplasmosis and arthritis was determined using Erythro-sedimentation rate (ESR). All obtained data were arranged in tables and tested statistically using chi-square, t-student test and Fisher test to decide significant differences between study limits at P <0.05.

Results and Discussion

The overall rate of *Toxoplasma gondii* antibodies among patients with arthritis was 54.09**%**, this rate contributed 55.15% in75 sera of women compare to 51.06% in 24 sera of menP >0.05 .Statistical analysis reveal high occurrence of *Toxoplasma* IgG antibodies 48.53% and 44.68% among females and males. Controversy to 6.62% and 6.38% of *Toxoplasma* IgM antibodies among women and men respectively also P<0.05 (Table 1).

Patients enrolled study, their ages ranged from 1 year to over than 51 years, they arranged in 6 age groups. The obtained data from ELISA test was obvious in table 2; which exerting high rate of *Toxoplasma gondii* antibodies 69.23% among patients aging from 31 to 40 years compare to 25 % of *Toxoplasma antibodies* among patients aged from 10 to 20 years, P<0.05. Considering types of *Toxoplasma* antibodies distribution; statistical analysis show high differences in distribution of *Toxoplasma IgG* antibodies 47.55% versus to 6.56% of *Toxoplasma* IgM antibodies P<0.05.Also each type of *Toxoplasma* antibody show high rate of incidence in such age group specially *Toxoplasma* IgM which show high occurrence 14.29% among patients from 1 year to 10 years, while high rate of *Toxoplasma* IgG 64.10% was recorded among patients aged from 31 to 40years, P<0.05.

Table 3 clarifies the role of patients contact with some external factors such as animal, vegetables and meat and *Toxoplasma* antibodies frequencies, via which high rates of *Toxoplasma* IgG antibodies were recorded compare to low rates of *Toxoplasma* IgM antibodies, P <0.05. From statistical analysis it has been found that all three factors of contacts show no differences in *Toxoplasma* distribution in general, P >0.05.

Toxoplsama gondii is water borne disease, for this reason, sera of patients suffering from arthritis were tested by ELISA for *Toxoplasma* antibodies and the results sh high rate ows of *Toxoplasma* IgG antibodies verses to low rates of *Toxoplasma* IgM with clear absence of *Toxoplasma* IgM antibodies in sera of patients consuming well water, P <0.05.All four types of water consumption show no significance in *Toxoplasma* antibodies occurrence when it was analyzed statistically, P >0.05.

The results of *Toxoplasma* antibodies distributions in consider to patients educational levels were tabulated in table 5,

which revel high rate 59.32% of *Toxoplasma* antibodies (IgM + IgG) in sera of patients whom they have primary educational levels compare to40%, 41.66% and41.67% in sera of patients with intermediate, Bachelor and secondary degrees respectively. Also in the same table high rate of *Toxoplasma* IgG 87.88% was recorded comparing to 12.12 % of *Toxoplasma* IgM and the later antibody was recorded in high rate 11.48% in sera of patients with illiterate educational levels, P <0.05.

Mostly arthritis associate with some signs and symptoms in general, that depending on type of arthritis, the more common signs and symptoms that recorded during the present study involved: knee pain 86.89%, followed by back pain83.61%, swelling 78.69 %fever 67.76%, sweating 63.39 % and 53.55 % of difficulties in walking, P > 0.05.In spite of high rate of *Toxoplasma* antibodies 59.18 % that recorded among patients with difficulties in walking but statistical analysis show no differences in *Toxoplasma* antibodies distributions with all signs and symptoms, P >0.05; (Table 6).

From watching the obtained data in table 7, it was obvious that Rheumatoid factor was distributed in both gender without significant differences using direct latex fixation test as the following rates 60.29 % and 55.32 % were recorded in sera of females and males respectively>0, 05. Controversy to the results of standard tube test that exert high titers 26, 22, 7, 1 of I.U of RF in sera of females using serial dilutions 8, 16, 32 and 64 respectively compare to 6.12.1.0 of IU of RF in sera of males with the following dilutions 8, 16, 32 and 64 respectively, P<0, 05.

Direct agglutination test using rheumatoid factor antigen coated on latex particle was applied on 183 sera and the following rates were obtained: 82 sera out of 136 sera from males were positive for RF, the rate was 60.39%, while 26 sera of females from 47 sera reveal RF positive, p>0.05, table 10. Regarding *Toxoplasma* antibodies distributions, statistical analysis show no differences in frequency of *Toxoplasma gondii* antibodies and RF positive in relation with the patients gender P >0.05 (Table 8). On the other hand significant differences were obtained in regard of *Toxoplasma* antibody types and RF positive specially high overall *Toxoplasma* IgG antibodies rate 53.70% compare to 7.41% of *Toxoplasma* IgM, P <0.05.

Erythro-sedimentation rate (ESR) was determined among 137 patients with arthritis from total of 183 patients enrolled the study taken in consider patients gender and age.

The results were arranged in table 9 below which show high rate 66.66% of *Toxoplasma* antibodies among males aging below 50 years, controversy to 84% of *Toxoplasma* antibodies among female aging over than 50 years. In both cases ESR rates were above than normal limits regarding patients ages and gender, P<0.05.

Patients following up within 3 months of treatment with non-steroid anti-inflammatory drugs was shown in table 10, via which anti-ccp antibodies rate 8.19 % was declined into 6.45 % while anti-toxoplasma rate 93.33 % was increased to 100 % with significant differences in *Toxoplasma* IgM high pick after treatment than before treatment, p<0.05. Since 1990 an idea of watching women habitually or spontaneous abortion and the out comes of congenital abnormalities was aroused and warned the gynaecologist in kirkuk health officeand the author also, so several studies were carried on for detecting the prevalence of toxoplasmosis and role of serology in *Toxoplasma* diagnosis (Kadir, 1992,

Salman, 2014a). But correlation between toxoplasmosis and arthritis has not been investigated in Kirkuk city previously.Also informations about arthritis was not present in this city. The all rate of arthritis 78.20 % in present study was high contributing in both gender equally. This result was highlighting the degree of injury exposing the peoples in Kirkuk city due to arthritis. The overall rate of arthritis was higher than 51.2 % reported in Iraq by Abdul-Qahar (2013) and with 0.36 % mentioned by Al-Temmemi (2010) in Saltant Oman.Variances in the rates can be explained by using double laboratory methods (RF and anti-ccp) in the present study as well as confirmatory STAT applying to all RF positive that had role in reducing standered errrors and obtainingcorrect rate. Further more to adequate study size in the present study compare to those in table 2 and 3.

Regarding Knee swelling 86.89% and back pain 83.61% high appearances among patients; these reflect that all cases were poly-arthritis affecting synovial membrane in knee regions and might be attributed to reactive types of arthritis such as presence of infections or parasites that infect the joint surfaces. Stress and psychological factors occasionally play an important role in joint problems as well, mainly by influencing body chemistry. These findings were not agreed with 36 % and 57 % of Knee swelling reported by Nolla (2003) and Raad peacock (2004). Regarding role of laboratory tests employee in diagnosis of arthritis to patient gender; STAT results in women showing 55 sera positive compare to 19 sera in men, might be explained by an excess women exposing to water, contraception, infections (mostly Chlamydia) specially among house makers in Kirkuk city than males (Salman, 2014b). Inflammation rates 58.08 % and 44.68 % in females and males below 50 years respectively than in the same genders aging above than 50 years, this might be due hormonal changes because women give high size of the study and some of them were pregnant and already ESR rate becomes high in gestational periods (Salman, 2014c and Gallef *et al.,* 2015). Elevation of ESR among young age patients finding was seen in Iraq by Mahdi (2012). Regarding toxoplasmosis, this study showed an overall 54.09 % sero-prevalence of anti-*T. gondii* in sera of 99 patients from total of 183 patients with arthritis, this finding was higher than those recorded by Othman (2004) and Al-Jubori (2005) in the same province, whom they record 36.67 % and 33.53 % respectively (Salman 2014b). While it was lower than those recorded in Tunisia 58.45% by Bouratbine *et al.* (2001) and 57.52 % in Egypt by El-Tantawi *et al.* (2014). The variances in *Toxoplasma* rates are factorial: it might be due differences in study size, type of laboratory test, and type of the patients. High incidence of *Toxoplasma* IgG antibodies 47.54% compare to 6.56 % of *Toxoplasma* IgM, this finding is very important because positive IgG means prevention against previous toxoplasmosis forlifelong (Salman, 2014e). On the other hand 6.56% of *Toxoplasma* IgM is significant predisposing the acuteness of toxoplasmosis and the level of the injury that affecting tissues specially that in articular regions.This finding was agreed those recorded in the same city by Salman (2014e), Muhammad and Salman (2014), Salman (2014f) and Salman (2014h). Additionally *Toxoplasma* IgM 14.29 % in table 2 among patients between 1 year to 10 years is very critical, it will altered child development, learning, child motions and mental retardness (Salman and Mustafa, 2014d). High frequency 69.23% of toxoplasmosis among patients aging between 31 to 40 years was vital, particularly5.13 % contribute

Table.1 Distribution of *Toxoplasma gondii* antibodies among patients with arthritis in relation with gender

Genders	Total No.Exam. Toxo. +ve & %		Total No.Exam. IgM +ve & %		Total No. Exam. IgG +ve &%		Total No. Exam. IgM&IgG+ve& %	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
FEMALEs	136	74.32%	9	6.62%	66	48.53%	75	55.15%
Males	47	25.68%	3	6.38%	21	44.68%	24	51.06%
TOTAL	183	100%	12	6.55%	87	47.54%	99	54.09%

Table.2 Frequency of *Toxoplasma gondii* antibodies among patients with arthritis in regard to ages

Age groups years/	Total No. Exam. & %		Total No. Exam. IgM +ve& %		Total No.Exam.IgG +ve ** & %		Total No. Exam. IgM&IgG+ve& %	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
1 to 10	7	3.83%	1	14.29% *	3	42.85%	4	57.14%
11 to 20	8	4.37%	0	0%	2	25%	2	25%
21 to 30	19	10.38%	1	5.26%	8	42.11%	9	47.37%
31 to 40	39	21.31%	2	5.13%	25	64.10%*	27	69.23%*
41 to 50	60	32.79%	3	5%	27	45%	30	50%
51 and above	50	27.30%	5	10 %	22	44.00%	27	54.00%
TOTAL	183	100%	12	6.56%	87	47.54%	99	54.09%

*, ** $p < 0.05$

Table.3 Relationship between *Toxoplasma gondii* antibodies distribution and patients contact with animal, meat and vegetables

Types of contact	TotalNo. Exam. & %		TotalNo. Exam. IgM +ve& %		TotalNo.Exam. IgG +ve * & %		TotalNo. Exam IgM and IgG +ve& %	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Animal	63	34.43%	5	7.94%	33	52.38%	38	60.32%
Meat	137	74.86%	11	8.09%	65	47.45%	76	55.47%
Vegetables	141	77.04%	11	7.80%	68	48.23%	79	56.02%

*$P < 0.05$

Table.4 Roles of types of water consumption in *Toxoplasma gondii* antibody distributions among sera of patients with arthritis

Types of water	Total No.Exam. &%		Total No. Exam. IgM +ve&%		Total No. Exam. IgG +ve * &%		Total No. Exam. IgM&IgG+ve& %	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Mineral	65	35.52%	4	6.15%	37	56.92%	41	63.07%
Portable	21	11.48%	1	4.76%	13	61.90%	14	66.66%
Tank	129	70.49%	12	9.31%	57	44.19%	69	53.48%
Well water	13	7.10%	0	0%	8	61.53%	8	61.53%

* P< 0.05

Table.5 Correlation of patients educational levels with distribution of *Toxoplasma gondii* antibody in sera of patients with arthritis

Educational levels	Total No.Exam & %		Total No. IgM +ve & %		Total No. IgG +ve & %		TotalNo. IgM&IgG+ve & %	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Illiterate	61	33.33%	7	11.48% *	28	45.90%	35	57.38%
Literacy	3	1.64%	0	0%	3	100%	3	100%
Primary	59	32.24%	4	6.78%	31	52.54%	35	59.32% *
Intermediate	20	10.93%	0	0%	8	40.00%	8	40.00%
Secondary	12	6.56%	0	0%	5	41.67%	5	41.67%
Institute	16	8.74%	0	0%	8	50%	8	50%
College	12	6.56%	1	8.33%	4	33%	5	41.66%
TOTAL	183	100%	12	12.12	87	** 87.88%	99	54%

*, ** P<0.05

Table.6 Some signs and symptoms among arthritis patients in relation to *Toxoplasma gondii* antibodies distribution

signs and symptoms	Total No.Exam. and %		Total No.IgM +ve and %		Total No.IgG +ve and %		Total No..IgM&IgG+ve and %	
	No.	(%) *	No.	(%)	No.	(%)	No.	(%)
Back pain	153	83.61%	10	6.54%	71	46.41%	81	52.94%
Difficulties in walking	98	53.55%	8	8.16%	50	51.02%	58	59.18% *
Fever	124	67.76%	11	8.87%	59	47.58%	70	56.45%
knee pain	159	86.89%	12	7.55%	77	48.43%	89	55.97%
Swelling	144	78.69%	11	7.64%	68	47.22%	79	54.86%
Sweating	116	63.39%	9	7.76%	53	45.69%	62	53.45%

P>0.05

Table.7 Frequencies of Rheumatoid factor antibody RF using Latex fixation test and RF titers using standard tube test in relation to gender of arthritis patients

Gender	Total No. Exam & %		No.Exam. RF+ve&%		Titers IU/ml RF titers using dilutions					
	No.	(%)	No.	(%)	2	4	8 *	16	32	64
Females	136	74.32%	82	60.29%	6	20	26**	22**	7**	1**
Males	47	25.68%	26	55.32%	3	4	6	12	1	0
Total	183	100%	108	59.02%	**9**	24	32	34	8	1

This dilution is the initial of positive for RF. IU mean international unit
** P <0, 05

Table.8 Distribution of Rheumatoid factor (RF) and *Toxoplasma gondii* antibodies in relation to patients gender

Gender	Total No. Exam & %		Total No. RF+ve & %		*Toxoplasma gondii* No. IgM +ve& %		No. IgG +ve & %		No. IgM&IgG+ve & %	
	No.	(%)	No.	(%)*	No.	(%)	No.	(%)	No.	(%)*
Females	136	74.32%	82	60.29%	6	7.32%	44	53.66%	50	60.98%
Males	47	25.68%	26	55.32%	2	7.69%	14	53.85%	16	61.54%
Total	183	100%	108	59.02%	8	7.41%	58	53.70%**	66	61.11%

*P > 0.05 **P < 0.05

Table.9 Correlation between *Toxoplasma gondii* distribution and erythro-sedimentation rate (ESR) among patients with arthritis

SEX / ESR <50 Years	Total No. Exam & %		Toxo. IgM +ve & %		Toxo. IgG +ve & %		Total IgM IgG +ve& %	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Female ESR >12	79	58.08%	1	1.27%	38	48.10%	39	49.37%
Male ESR>10	21	44.68%	2	9.52% *	12	57.14%	14	66.66%
Sex /ESR>50 years								
Female ESR>25	**25**	**18.38 %**	**5**	**20%**	**16**	**64.4 %**	**21**	**84%**
Male ESR>20	**12**	**25.53 %**	**0**	**0**	**5**	**41.66 %**	**5**	**41.66%**

*P<0.05

Table.10 Following up of anti-ccp antibody and *Toxoplasma gondii* antibodies distributions before and after treatment

Lab. test	Before taking the treatment							
	Total positive		Toxo-IgM +ve		Toxo-IgG +ve		Total Toxo (IgM+IgG) +ve	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
ACCP *	15	8.19%	2	13.33%	10	66.67	12	80%
Toxo	14	93.33%	0	0%	14	100%	14	100%

Lab. test	After taking the treatment							
	Total +ve		Toxo-IgM +ve		Toxo-IgG +ve		Total Toxo (IgM+IgG) +ve	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
ACCP	12	6.45%	3	**25% ***	7	58.33%	10	83.33%
Toxo	15	100%	4	26.67%	11	73.33%	15	100%

$p<0.05$

Toxoplasma IgM that will interfere life style and patients low outcomes due to acute illness of arthritis associated with toxoplasmosis (Tabbara and Saleh, 2005). In spiteof statistical analysis exerting non significance relation of environmental contacts (water, meat and vegetables) with toxoplasmosis, but frequencies of *Toxoplasma* antibodies both IgM and IgG were high and reflecting degree of environmental contamination due to instability of Iraq as continuous wars, economic sanctions, poverty due to displaced peoples, whom they migrates from their provinces to Kirkuk city. All of these factors had role in increasing the rate soil, water and vegetable contamination by the oocysts of *Toxoplasma* parasite (Kadir, 1992). This finding not in agreement with that recorded by Al-attar, 2000 and Al-Jobori (2005). The results considering patient educational levels and frequency of *Toxoplasma* antibodies were very important to scientific workers in community diseases, particularly patients with low educational levels (illiterate, literacy and primary level) and reflect poor hygienic condition and low level of sanitation in Kirkuk community. This condition demands vital plans to increase levels of educations by continues teaching and improving health conditions in Iraq particularly of Kirkuk. Anti-cyclic citrullinated peptide (anti-CCP) antibody testing is particularly useful in the diagnosis of rheumatoid arthritis, with high specificity, presence early in the disease process, and ability to identify patients who are likely to have severe disease and irreversible damage. However, its sensitivity is low, and a negative result does not exclude disease (Niewold, 2007). The follow-up of 21 patients before and after treatment shows the benefit of confirming anti-ccp-IgG ELISA test in demonstrating rheumatoid arthritis positive cases for RF than using STAT. Patients with RA show much variability in disease activity, which can be difficult to predict at the onset of disease. Anti-CCP antibodies have proven useful in identifying those patients who are likely to have

clinically significant disease activity (Yetteberg, 1994). In 21 patients with long-standing RA, a strong correlation was found between greater disease activity and anti-CCP positivity specially reduction the rate of anti-ccp from 8.19% before treatment in to 6.45 % after treatment. On the hand *Toxoplasma* IgM was raised from 13% in to 25 %, this finding was highlighting that anti-arthritis drugs produce cure in 2 patients from total 15 positive for anti-ccp, but not affect toxoplasmosis. Furthermore this is a prone for *Toxoplasma* predisposing more tissue injury in future particularly synovial tissue.

Conclusions

The rate of arthritis particularly poly-arthritis is high in Kirkuk city. Frequency of *Toxoplasma* IgM among arthritic patients also high. Anti-CCP antibodies tend to remain stable or decline slightly with treatment, and have not been found often in non-RA inflammatory or arthritic diseases. Relationship between toxoplasmosis and arthritis (polyarthritis) is significant.

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