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IL10 Gene Polymorphism and Its Association with Ocular Toxoplasmosis Susceptibility.

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Abstract

Toxoplasmosis of the eye can induce visual changes, retinochoroiditis, and in some cases, blindness. Infection with T. gondii stimulates T helper 1 cells to produce IL-10, a cytokine implicated in toxoplasmosis resistance. The association between OT and the GG genotype at the IL-10 promoter SNPs suggests that abnormalities in the genetic regulation of cytokine levels may have an impact on the human immune response in OT. IL-10 is an anti-inflammatory and immune-regulatory cytokine that induces T cell anergy by downregulating the expression of genes encoding the costimulatory molecule B7-1/B7-2, major histocompatibility complex (MHC) class II, proinflammatory cytokines (IFN-, TNF-, and IL-12), and chemokines secreted by activated macrophages. The serum level of IL-10 of the group was highly significant increased in O.T. patients than controls, (264.65 ± 19.8 vs. 123.77 ± 6.1 pg/ml), (*P*= < 0.001), As well as, the serum level of IL-10 of the group was non-significantly increased in A.T. patients than controls, (156.82 ± 16.3 vs. 123.77 ± 6.1 pg/ml), (*P*= 0.048), On the other hand, the serum level of IL-10 of the patients groups was highly-significant increased in O.T. patients than in A.T., (264.65 ± 19.8 vs. 156.82 ± 16.3 pg/ml), (*P*= < 0.001) .

Gene polymorphism: The frequency of T allele (dominant allele) was 30 %, 54 % and 75% in OT, AT patients and control group respectively, G allele (recessive allele) was 70%, 46 % and 25% in asthmatic patients and 18.33 % in OT, AT patients and control group respectively. The mutant C allele was higher incidence in OT group (χ^2 = 8.0, *P* = 0.004), while T allele was higher incidence in each of AT patients (χ^2 = 0.076, *P* = 0.78) and control groups (χ^2 = 15.0, *P* = 0.001).

Key words: Toxoplasmosis , O.T. , Uveitis (A.T.) , Gene polymorphism and IL-10.

Introduction

Toxoplasma gondii is a ruthless intracellular parasite belonging to *Coccidae*. *T. gondii* occurs in three forms: tachyzoites, bradyzoites (in tissues), and sporozoites. The parasite locates in the brain, heart, lungs, and most frequently in the lymph nodes. (ADEGBEHINGBE, 2020).

Control of O.T. and response to medication varies among patients based on a number of factors, including their genetic profile. It has been shown that polymorphisms in genes encoding various cytokines are associated with susceptibility to parasitic diseases. The identification of gene-gene interactions could increase the predictive potential and accuracy of a complex disorder (Fehrmann et al., 2011).

The effect of cytokine gene polymorphisms on gene expressions and disease has captured the interest of researchers, and numerous studies have been published in this area. studied the association between cytokines and cytokine gene polymorphisms and O.T. susceptibility (Naranjo et al., 2018). The majority of polymorphisms are located in enhancer, promoter, or other regulatory sequences of cytokine genes (Pravica et al., 2000). Several studies have investigated the relationship between cytokine gene polymorphisms and O.T. risk (Naranjo et al., 2018; Mantilla et al., 2020).

Single nucleotide polymorphisms (SNPs) are valuable for identifying polymorphisms associated with disease susceptibility. Natural selection has favored the introduction of biallelic SNPs into cytokine loci, resulting in variation in protein production and quantity rather than variation in protein quality (Marino et al., 2020).

The human IL-10 gene has been mapped to the junction between 1q31 and 1q32 on chromosome 1 (Turner et al., 1997). Gene polymorphisms provide a genetic

susceptibility to ocular involvement during Toxoplasma infection, which may help explain why some Toxoplasma-infected individuals develop ocular involvement. Despite the fact that the eye has immune privilege, the ocular immune response is linked to the peripheral immune response. The peripheral immune responses of patients with ocular toxoplasmosis differ from those of patients without ocular involvement (De-la-Torre et al., 2014).

Methodology

The research was conducted between February / 2022 and January /2023 on 80 sample (50 patients and 30 controls) ranging in age from 20 to 69 years. The current study included 30 participants who appeared to be in good health and whose ages ranged from (20-40) years. None of them had any matter, and none of them have any chronic or systemic diseases. The 50 patients are divided into two groups (25 are infected with Ocular toxoplasmosis (O.T.) and 25 are infected with Uveitis A.T.) based on the results of an ELISA serological test (IgG and IgM).

human blood was collected intravenously from patient and control groups using. Put in clot activator gel tubes for serum separation and the serum was immediately separated into small equal portions in Eppendorf tubes, which will measure levels (IL-10 ELISA kits) and stored at -20 degrees Celsius until use. And 2ml put it in EDTA tube for molecular analysis (Gene Polymorphisms) also stored in deep freeze.

Genomic DNA was extracted from the peripheral blood leukocytes (frozen EDTA blood samples) by *EasyPure*® Genomic DNA Kit (TRANS/China).

Result and Discussion

The serum level of IL-10 of the group was highly significant increased in O.T. patients than controls, (264.65 ± 19.8 vs. 123.77 ± 6.1 pg/ml), (*P*= < 0.001), as shown in table (1). As well as, the serum level of IL-10 of the group was non-significantly increased in A.T. patients than controls, (156.82 ± 16.3 vs. 123.77 ± 6.1 pg/ml), (*P*= 0.048), as shown in table (2). On the other hand, the serum level of IL-10 of the patients groups was highly-significant increased in O.T. patients than in A.T., (264.65 ± 19.8 vs. 156.82 ± 16.3 pg/ml), (*P*= < 0.001), as shown in table (3).

Table 1 : Serum Levels of IL-10 in O.T. patients and control group.

IL-10 (pg/ml)	Patient (No. = 25)	Control (No. = 30)
Mean ± S.E.	264.65 ± 19.8	123.77 ± 6.1
P-value	< 0.001** HS	
- (**) Highly Significant increase *P* < 0.01 compare to control. - S.E: Standard Error, No: Number, *P*: Probability.		

Table 2 : Serum Levels of IL-10 in A.T. patients and control group.

IL-10 (pg/ml)	Patient (No. = 25)	Control (No. = 30)
Mean ± S.E.	156.82 ± 16.3	123.77 ± 6.1
P-value	0.048*	
- (*) Significant increase *P* < 0.05 compare to control. - S.E: Standard Error, No: Number, *P*: Probability.		

Table 3 : Serum Levels of IL-10 in O.T. and A.T. patients groups.

IL-10 (pg/ml)	O.T. (No. = 25)	A.T. (No. = 25)
Mean ± S.E.	264.65 ± 19.8	156.82 ± 16.3
P-value	< 0.001** HS	
- (**) Highly Significant increase *P* < 0.01 compare to control. - S.E: Standard Error, No: Number, *P*: Probability.		

De-la-Torre et al., (2014) found that the response of TH2 was elevated in OT patients, mainly characterized by higher levels of the suppressive cytokine IL-10. Meira et al., (2014) explained that The deviation to a Th2 immune response, which includes the production of anti-inflammatory cytokines such as IL-10, may facilitate the survival of the parasite, resulting in tissue immune destruction. IL-10 production in T. gondii-infected brains may contribute to the persistence of parasites by downregulating the intracerebral immune response, which lends trust to the concept that IL-10 is central to the induction of the permissive state observed in the eyes of South American OT patients (de-la-Torre et al., 2014). These data, also, The deviation to a Th2 immune response, including the production of anti-inflammatory cytokines such as IL-10, TGF-, and IL-4, could explain the parasite's ability to survive. This is necessary to sustain immune balance in the eye and prevent tissue immune destruction (Neyer et al., 1997; Gaddi and Yap, 2007) , IL-10 production in T. gondii-infected brains may contribute to parasite persistence by suppressing the intracerebral immune response.

Marino Ana et al., (2020) found that no difference was found in serum levels of IL-10 when *T. gondii*-infected patients when compared to healthy (disagree with data

of table 10). Matowicka-Karna et al., (2009) found that They found the level of IL-10 to be five times higher in toxoplasmosis than in healthy controls and explained that IL-10 plays a crucial role in the inflammatory response during T. gondii infection (agree with data of table 1), since where it inhibits the cellular-type immune response (IL-12, TNF-α) and inflammatory response (IL-6) (Nickdel et al., 2004; Wilson et al., 2005). Immunosuppression induced by IL-10 during T. gondii invasion is helpful for both the host and the parasite (Lang et al., 2007).

IL-10 counteracts the harmful consequences of the inflammatory response based on the increased production of TNF-, IFN-, and NO that is associated with intestinal proliferation of T. gondii (Liesenfeld, 1999). IL-10 can deactivate macrophages, induce IFN- production by T. gondii, and enhance intracellular parasite survival. Immunosuppression induced by IL-10 during T. gondii invasion is advantageous for both the host and the parasite. (Liesenfeld ,1999).

Dawson et al.(2018) demonstrated in their studied ,Patients with uveitis have elevated IL-10 levels and low to undetectable IL-6 levels, whereas patients with lymphoma have an IL-10-to-IL-6 ratio of less than 1.

Sijssens et al.(2007) demonstrated in their studied that a High IL-10 levels are primarily associated with active infectious uveitis and are regarded as crucial in the early stages of infection, and also found that high IL-10 levels are associated with active infectious uveitis and are regarded as crucial in the early stages of infection. Wang, and Tao (2021) detected significantly increased levels of IL-10 in Uveitis patients compared with normal eyes.

In uveitis, IL-10, a primary immunomodulatory cytokine, possesses significant anti-angiogenic and anti-inflammatory properties in ocular tissues (Owlia et al.,2012). IL-10 serves a crucial role in the balance between immune pathology

development and protective immunity. Patients with OT were found to have higher levels of IL-10 than healthy controls (Ongkosuwito et al.,1998).

Extraction of genomic DNA

Nano drop results indicated that the extracted genomic DNA purity (1.7-1.9) and, was variable in concentration (10.2 – 56.3 µg/ml). Agarose gel electrophoresis was used following Nano drop to confirm the integrity of extracted DNA, bands visualized under UV light, as shown in figure (1).

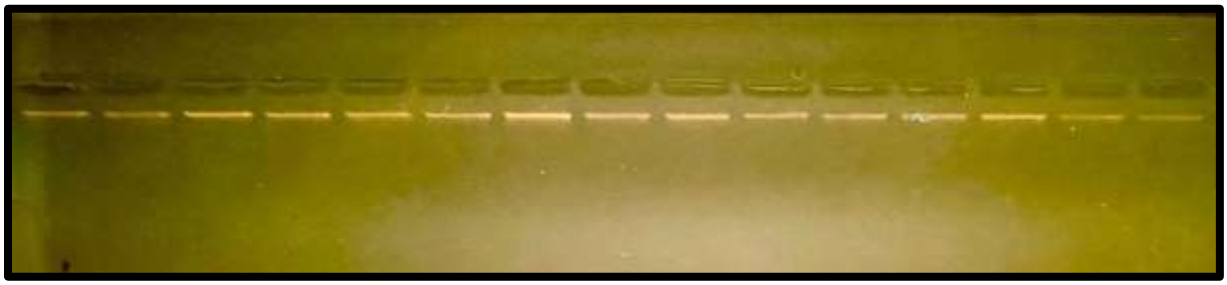

Fig. (1): Genomic DNA bands extracted from human blood samples.

IL-10 gene Amplification Results by Using HRM :

Genetic polymorphisms of *IL-10* (-1082, rs1800896 A>G, located on 2KB Upstream Variant in gene promoter, chr1) were determined in OT and AT patients and apparently healthy control by the HRM real-time PCR method, the sizes of fragmented specific amplicons as A allele, and G allele. Figure (2) depicts the thermocycler output from the HRM analysis process for the amplification of DNA.

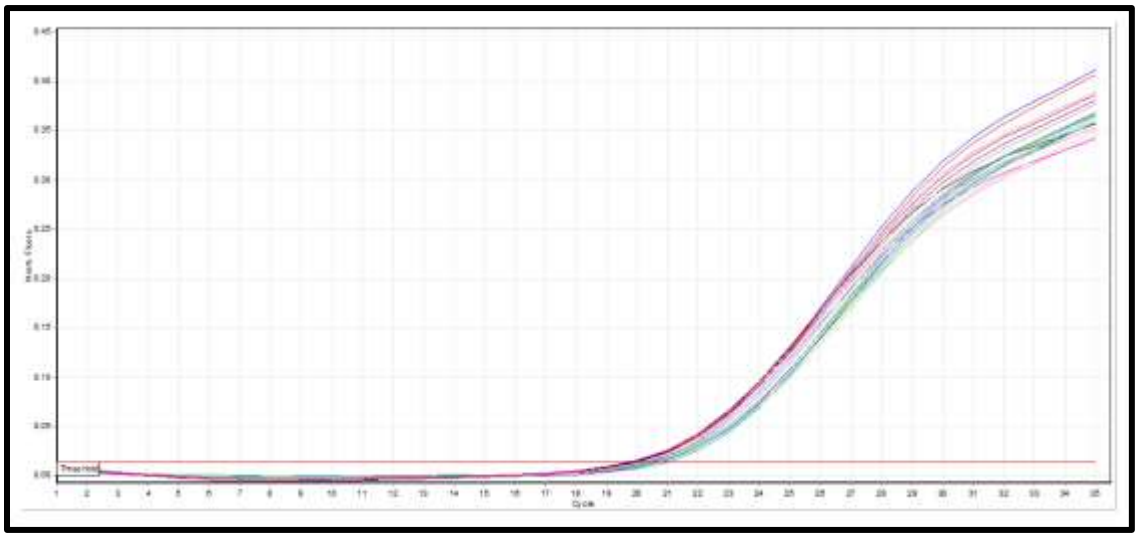

Fig. (2): Amplification of DNA, the picture was taken directly from HRM analysis software.

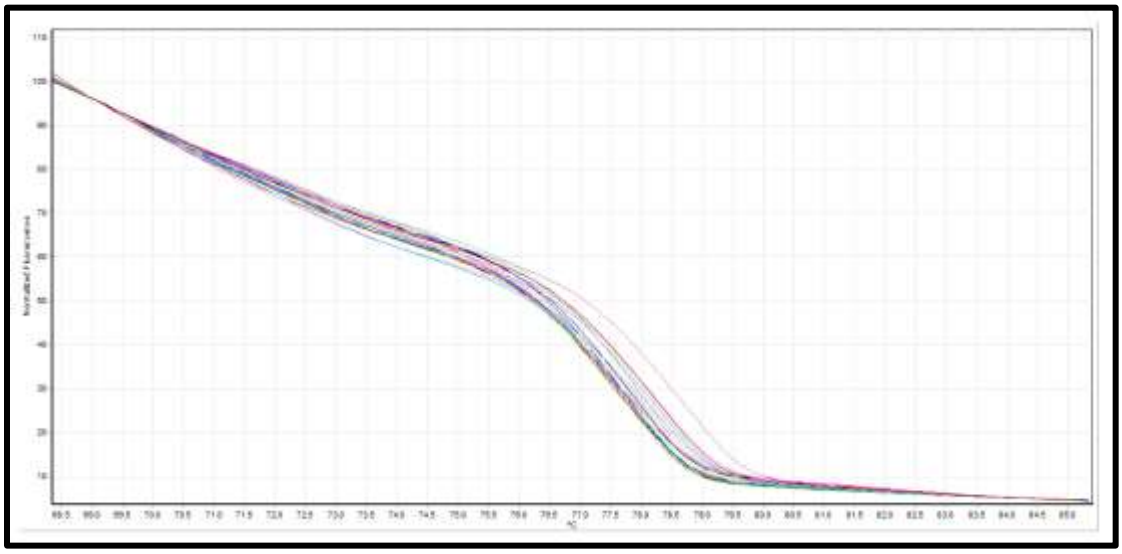

Fig. (3): Amplification of DNA, the picture was taken directly from HRM analysis software.

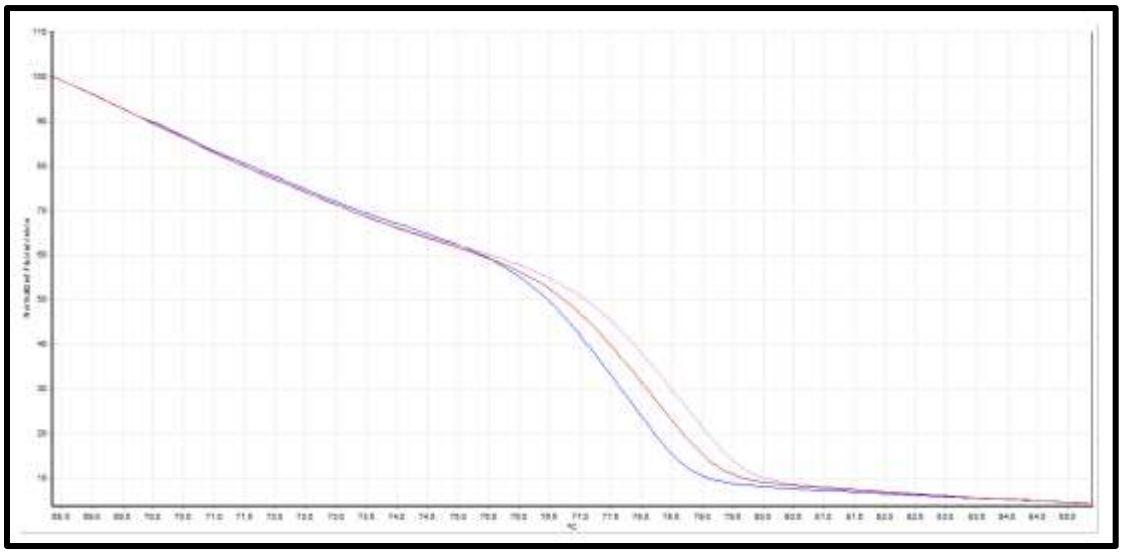

Fig. (4): shows the genotype result for SNP rs187084, where figure (A) represents the HRM result, while figure (B) represents the wild, heterozygous and mutant genotypes.

Distribution of *IL-10* genotypes and alleles

The present study included genetic analysis of *IL-10* polymorphism for patients and healthy control in the table (4). The homozygous genotype TT (the wild type) was low frequent in OT and AT groups, 16% and 28% while in control was higher incidence 60 % in control. The frequency of heterozygous genotype TC was 28 %, 52 % and 30 in each of OT, AT and control groups, respectively. The frequency of homozygous CC genotype (mutant type) was 56% and 20 % in OT and AT patients and control group was 10 %. The mutant genotype CC was the higher incidence in OT group ($\chi^2 = 6.32$, $P = 0.042$), carrier genotype TC was the higher incidence in AT group ($\chi^2 = 4.16$, $P = 0.125$), while wild genotype TT was the higher incidence in control group.

The frequency of T allele (dominant allele) was 30 %, 54 % and 75% in OT, AT patients and control group respectively, G allele (recessive allele) was 70%, 46 % and 25% in asthmatic patients and 18.33 % in OT, AT patients and control group respectively. The mutant C allele was higher incidence in OT group ($\chi^2 =$

8.0, P = 0.004), while T allele was higher incidence in each of AT patients (χ^2 = 0.076, P = 0.78) and control groups (χ^2 = 15.0, P = 0.001).

Table 4: Genotypes of *IL-10* and allele frequency in patients and control groups.

Group	OT Patients (No. = 25)		AT Patients (No. = 25)		Control (No. = 30)	
***IL-10* Genotypes**	**No.**	**%**			**No.**	**%**
TT	**4**	**16**	**7**	**28**	**18**	**60**
TC	**7**	**28**	**13**	**52**	**9**	**30**
CC	**14**	**56**	**5**	**20**	**3**	**10**
Total	**25**	**100**	**25**	**100**	**30**	**100**
χ^2	**6.320**		**4.160**		**11.400**	
***P*-value**	**0.042***		**0.125 NS**		**0.003****	
T	**15**	**30**	**27**	**54**	**45**	**75**
C	**35**	**70**	**23**	**46**	**15**	**25**
Total	**50**	**100**	**50**	**100**	**60**	**100**
χ^2	**8.00**		**0.076**		**15.00**	
***P*-value**	**0.004****		**0.78 NS**		**0.001****	

χ^2: Chi-square, No: Number, *P*: Probability, **: Significant at < 0.01
***: Significant at < 0.05 NS: Non-significant**

the current study showed no deviation from HWE in the OT and AT patients group (χ^2= 2.78, P=0.09 and χ^2= 0.0545, P=0.2), there were non-significant differences in the observed and expected genotypes frequencies, indicating agreement with the equilibrium and the three genotypes (TT, TC, CC) with both alleles (T and C) are fixed between generations, as shown in table (5).

Table 5 : Observed and expected frequencies of genotypes and alleles of the *IL-10* using Hardy-Weinberg equilibrium in patients groups.

Studied Groups	Genotypes	TT	TC	CC	χ^2 *P*-value	T	C

OT Patients (No.=25)	**Observed**	**No.**	**4**	**7**	**14**	**2.78 (0.09 NS)**	**0.3**	**0.7**
		%	**16**	**28**	**56**			
	Expected	**No.**	**2.25**	**10.5**	**12.25**			
		%	**9**	**42**	**49**			
AT Patients (No.=25)	**Observed**	**No.**	**7**	**13**	**5**	**0.0545 (0.2 NS)**	**0.54**	**0.46**
		%	**28**	**52**	**20**			
	Expected	**No.**	**7.29**	**12.42**	**5.29**			
		%	**29.16**	**49.68**	**21.16**			
- χ^2: Chi-square, No: Number, *P*: Probability, NS: Non-significant								

The odds ratio (OR) is the odds of an event in an experimental group relative to that in a control group. The relative risk (RR) is the risk of the event in an experimental group relative to that in a control group. An RR or OR of 1.00 indicates that the risk is comparable in the two groups. A value greater than 1.00 indicates increased risk; a value lower than 1.00 indicates decreased risk. The 95% confidence intervals and statistical significance should accompany values for RR and OR. (Andrade, 2015).

Table (6) showed odds ratios (OR) and p-value of TT, TC, and CC genotypes and both alleles T and C. the results showed that TT genotype was the protective genotype with OR < 1 with significant difference in OT and AT groups compare to control (OR= 0.127, CI = 0.0348-0.4636, *P*=0.001; OR= 0.25, CI = 0.0831-0.8093, *P*=0.02, respectively). TC genotype was the protective genotype with OR < 1 with non-significant difference in OT group compare to control (OR= 0.9075, CI = 0.2813-2.9275, *P*=0.87) while TC was etiologic OR > 1 in AT

patients with non-significant difference compare to control (OR= 2.52, CI = 0.8356-7.6471, *P*=0.1). CC genotype was the etiologic genotype with OR > 1 with significant difference in OT group compare to control (OR= 11.45, CI = 2.7397-47.89, *P*=0.008), also in AT group with non significant difference compare to control (OR= 2.25, CI = 0.4805-10.5349, *P*=0.3).

According to T and C alleles, the results showed that C allele was the etiologic allele in OT group (with significant difference $P < 0.001$) compare to protective T allele (OR= 7.0, CI = 3.0188-16.2314), also C allele was the etiologic allele in OT group (with significant difference $P = 0.022$) compare to protective T allele (OR= 2.55, CI = 1.1406-5.7258), these results suggesting that it is CC genotype (C allele) may associated with the development of OT and AT diseases.

Table 6 : The Statistical evaluations of *IL-10* SNP between patients and control.

***IL-10* Genotypes**	**OT Patients**	**Control**	**Odd Ratio (OR)**	**Relative Risk (RR)**	**Confidence intervals**	***P*-value**
TT	**4**	**18**	**0.127**	**0.2667**	**0.0348-0.4636**	**0.001****
TC	**7**	**9**	**0.9074**	**0.933**	**0.2813-2.9275**	**0.87 NS**
CC	**14**	**3**	**11.45**	**5.60**	**2.7397-47.89**	**0.008****
Allele Distribution						
T	**15**	**45**	**0.1429**	**0.40**	**0.0616-0.3313**	**< 0.001****
C	**35**	**15**	**7.00**	**2.80**	**3.0188-16.2314**	
***IL-10* Genotypes**	**AT Patients**	**Control**	**Odd Ratio (OR)**	**Relative Risk (RR)**	**Confidence intervals**	***P*-value**
TT	**7**	**18**	**0.25**	**0.467**	**0.0831-0.8093**	**0.02***
TC	**13**	**9**	**2.52**	**1.733**	**0.8356-7.6471**	**0.10 NS**

CC	**5**	**3**	**2.25**	**2.00**	**0.4805-10.5349**	**0.30 NS**
Allele Distribution						
T	**27**	**45**	**0.3913**	**0.72**	**0.1746-0.8767**	**0.022***
C	**23**	**15**	**2.55**	**1.84**	**1.1406-5.7258**	
-N.S.: Non Significant, P: Probability, *: Significant at < 0.05, **: Significant at < 0.01						

A study by Araujo et al., (2023) on ocular toxoplasmosis (OT), showed that the genotypes and alleles of the rs1800896 polymorphisms (–1082 G > A) of the IL10 gene variants were not associated with the occurrence of OT, in contrast to the findings of the current study and other studies. In the population from southeastern Brazil, Cordeiro et al., (2008) concluded that association was found between the A allele (rs1800896) and the presence of OT. In Colombian patients, Naranjo-Galvis et al., (2018) concluded that IL-10 gene promoter (-1082G/A) was significantly more prevalent in OT patient than in controls, they showed that individual homozygous for the -1082G allele have higher circulating IL-10 levels, a higher expression levels of IL-10 mRNA, and higher levels of production of IL-10 following *in vitro* stimulation (Galley et al., 2003; Suarez et al., 2003). Indeed, The presence of the G allele at position -1082 correlates with increased IL-10 protein production in vitro and in the pleural fluid of tuberculosis patients. (Turner et al., 1997; Liang et al., 2011; Meenakshi et al., 2013). These studies indicate that carriers of the -1082G allele are at a high risk for the progression of OT because the -1082G allele may suppress the immune response by increasing IL-10 expression. (Naranjo-Galvis et al., 2018). Yousefi et al., (2019) in their study on Hepatitis disease they showed that the A allele at position –1082 is connected with a lower level of production of IL-10.

Differences in methodology, sample size, and patient selection could contribute to the observed discrepancies between studies. Additionally, additional factors that are difficult to control in the context of toxoplasmosis, such as infection duration, may also influence ocular disease and serve as a bias. Furthermore, as the allelic frequency of cytokine genes can vary between populations based on regional differences (Ness et al., 2004; Yao et al., 2018).

In a study by Jung et al., (2019) on autoimmune uveitis they showed that IL-10 -1082 A (T) allele with OR < 1 (OR = 0.91) which deal with current results that showed that T allele was the protective allele, but none of their genotype-result suggested a significant association, They found that the -1082 A/G polymorphisms of IL-10 were not associated with autoimmune uveitis based on a meta-analysis. Also, Li et al., (2020) their data indicated that In the general population, there was no relationship between the -1082A>G polymorphism and Behcet's disease risk (OR of genotypes and alleles > 1).

In Another study on different disease, Hepatitis B Virus, Mahavar et al., (2021) demonstrating a significant association with IL-10-1082 polymorphisms in the GG (CC) genotype (P = 0.03), but no association with other genotypes, they found that IL-10-1082 GG was associated with a reduced risk of chronic hepatitis B infection (OR: 2.33). In a study by Datta et al., (2020) on cancer of cervical, they discovered Only the GG genotype was associated with an increased incidence of cervical cancer.

In a study by Abbood et al., (2023) on SARS-COV-2 variants, they showed that the COVID-19 mortality rate was associated with rs1800896 GG and AG genotypes in the Delta and Omicron variants, but there was no association with the Alpha variant. While Rizvi et al., (2022) concluded that In their population, the IL-

10 rs1800896 polymorphism was not found to increase the risk of COVID-19 severity.

Serum Level of IL-10 according to genotypes

The results in table (7) represent IL-10 serum levels in three genotypes of three groups. In OT patients, there was non-significant difference (P=0.445) between mean of serum levels of IL-10 of three genotypes (244.96 pg/ml in TT genotype, 306.13 pg/ml in TC and 249.53 pg/ml in CC). In AT patients, also non-significant difference (P=0.148) was noticed between mean of serum levels of IL-10 of three genotypes (108.23 pg/ml in TT genotype, 168.27 pg/ml in TC and 195.10 pg/ml in CC), as well as, in control group there was non-significant difference (P=0.211) was noticed between mean of serum levels of IL-10 of three genotypes (123.99 pg/ml in TT genotype, 133.40 pg/ml in TC and 93.60 pg/ml in CC), the current study suggests that may be there is no effect of genotype on IL-10 serum levels.

Table 7 : The comparison of serum level of IL-10 pg/ml according to genotypes in patients and control groups.

Group	OT Patients No. = 25		AT Patients No. = 25		Control No. = 30	
	Serum level of IL-10 pg /ml		Serum level of IL-10 pg /ml		Serum level of IL-10 pg /ml	
IL-10 Genotypes	(No.)	Mean ± S.E.	(No.)	Mean ± S.E.	(No.)	Mean ± S.E.
TT	4	244.96 ± 22.93	7	108.23 ± 10.15	18	123.99 ± 6.32
TC	7	306.13 ± 34.28	13	168.27 ± 28.01	9	133.40 ± 15.22

CC	**14**	**249.53 ± 30.0**	**5**	**195.10 ± 19.85**	**3**	**93.60 ± 5.74**
***P*-value**	**0.445 NS**		**0.148 NS**		**0.211 NS**	
LSD was used to compare between means (According to Genotypes). **No: Number, S.E.: Standard Error *P*: Probability, N.S.: Non-Significant.**						

Conclusion

According to CC genotype (mutant allels) may be reduce the level of IL-10 in Iraqi patients that infected with ocular toxoplasmosis , depending on table (7) this may be due to the recurance infection of the eye.

References

- Abbood, S. J. A., Anvari, E., & Fateh, A. (2023). Association between interleukin-10 gene polymorphisms (rs1800871, rs1800872, and rs1800896) and severity of infection in different SARS-CoV-2 variants. *Human Genomics*, *17*(1), 1-9.
- ADEGBEHINGBE, S. A. (2020). *SEROPREVALENCE OF OCULAR TOXOPLASMOSIS IN THE MAJOR REFERRAL EYE CENTRE IN AKURE, ONDO STATE* (Doctoral dissertation, FEDERAL UNIVERSITY OF TECHNOLOGY, AKURE).
- Andrade, C. (2015). Understanding relative risk, odds ratio, and related terms: as simple as it can get. *The Journal of clinical psychiatry*, *76*(7), e857-e861.
- Araujo, W.M.R., Ayo, C.M., Previato, M., de Faria Jr, G.M., Frederico, F.B., Siqueira, R.C., de Almeida Jr, G.C., Pereira-Chioccola, V.L., De Mattos, L.C. and Brandão, C.C. (2023). Role of interleukin 1β and

interleukin 10 variants on ocular toxoplasmosis in Brazilian individuals. *Frontiers in Ophthalmology*, *3*, 1-

- Cordeiro, C. A., Moreira, P. R., Andrade, M. S., Dutra, W. O., Campos, W. R., Oréfice, F., & Teixeira, A. L. (2008). Interleukin-10 gene polymorphism (− 1082G/A) is associated with toxoplasmic retinochoroiditis. *Investigative ophthalmology & visual science*, *49*(5), 1979-1982
- Datta, A., Zahora, F.T., Aziz, M.A., Uddin, M.S., Ferdous, M., Millat, M.S., Sarwar, M.S., Barek, M.A., Jafrin, S., Nahar, S. and Islam, M.S. (2020). Association study of IL10 gene polymorphisms (rs1800872 and rs1800896) with cervical cancer in the Bangladeshi women. *International Immunopharmacology*, *89*, 1-8.
- Dawson, A. C., Williams, K. A., Appukuttan, B., & Smith, J. R. (2018). Emerging diagnostic tests for vitreoretinal lymphoma: a review. *Clinical & Experimental Ophthalmology*, *46*(8), 945-954.
- De-la-Torre, A., Pfaff, A. W., Grigg, M. E., Villard, O., Candolfi, E., & Gomez-Marin, J. E. (2014). Ocular cytokinome is linked to clinical characteristics in ocular toxoplasmosis. *Cytokine*, *68*(1), 23-31
- Fehrmann, R. S., Jansen, R. C., Veldink, J. H., Westra, H. J., Arends, D., Bonder, M. J., ... & Franke, L. (2011). Trans-eQTLs reveal that independent genetic variants associated with a complex phenotype converge on intermediate genes, with a major role for the HLA. *PLoS genetics*, *7*(8), e1002197.
- Galley, H. F., Lowe, P. R., Carmichael, R. L., & Webster, N. R. (2003). Genotype and interleukin-10 responses after cardiopulmonary bypass. *British journal of anaesthesia*, *91*(3), 424-426.

- Jung, J., Song, G., Kim, J. H., & Choi, S. (2019). The associations between interleukin 10 polymorphisms and susceptibility to autoimmune uveitis–a meta-analysis. *Central European Journal of Immunology*, *44*(3), 246-252.
- Lang, C., Groß, U., & Lüder, C. G. (2007). Subversion of innate and adaptive immune responses by Toxoplasma gondii. *Parasitology research*, *100*, 191-203.
- Li, X. F., Huang, Z. Z., Hu, Y. Y., Niu, Y. M., & Cai, J. W. (2020). Association between Interleukin-10 Gene Polymorphisms and Behcet's Disease Susceptibility: Evidence from a Meta-Analysis. *Journal of Immunology Research*, *2020*, 1-17.
- Liesenfeld, O. (1999). Immune responses to Toxoplasma gondii in the gut. *Immunobiology*, *201*(2), 229-239.
- Mahavar, N., Naseri, M., Sarab, G.A., Fereidouni, M., Ziaee, M., Naghizadeh, M.S., Tane, A. and Mahdavi, R. (2021). IL-10-1082 A/G (RS1800896) polymorphism is effective in clearing hepatitis B virus infection. *Jundishapur Journal of Microbiology*, *14*(4), 1-6.
- Marino Ana, P. M. P., Dos Santos, L. I., Henriques, P. M., Roffe, E., Vasconcelos-Santos, D. V., Sher, A., ... & Antonelli, L. R. (2020). Circulating inflammatory mediators as biomarkers of ocular toxoplasmosis in acute and in chronic infection. *Journal of Leucocyte Biology*, *108*(4), 1253-1264.
- Meenakshi, P., Ramya, S., Shruthi, T., Lavanya, J., Mohammed, H.H., Mohammed, S.A., Vijayalakshmi, V. and Sumanlatha, G. (2013). Association of IL-1β+ 3954 C/T and IL-10-1082 G/A cytokine gene

polymorphisms with susceptibility to tuberculosis. *Scandinavian journal of immunology*, *78*(1), 92-97.

- Meira, C.S., Pereira-Chioccola, V.L., Vidal, J.E., de Mattos, C.C.B., Motoie, G., Costa-Silva, T.A., Gava, R., Frederico, F.B., de Mattos, L.C. and Toxoplasma Groups. (2014). Cerebral and ocular toxoplasmosis related with IFN-γ, TNF-α, and IL-10 levels. *Frontiers in microbiology*, *5*, p.492.
- Naranjo-Galvis, C. A., de-la-Torre, A., Mantilla-Muriel, L. E., Beltrán-Angarita, L., Elcoroaristizabal-Martín, X., McLeod, R., ... & Sepúlveda-Arias, J. C. (2018). Genetic polymorphisms in cytokine genes in Colombian patients with ocular toxoplasmosis. *Infection and immunity*, *86*(4), e00597-17.
- Naranjo-Galvis, C.A., de-la-Torre, A., Mantilla-Muriel, L.E., Beltrán-Angarita, L., Elcoroaristizabal-Martín, X., McLeod, R., Alliey-Rodriguez, N., Begeman, I.J., López de Mesa, C., Gómez-Marín, J.E. and Sepúlveda-Arias, J.C. (2018). Genetic polymorphisms in cytokine genes in Colombian patients with ocular toxoplasmosis. *Infection and immunity*, *86*(4), 10-1128.
- Ness, R. B., Haggerty, C. L., Harger, G., & Ferrell, R. (2004). Differential distribution of allelic variants in cytokine genes among African Americans and White Americans. *American journal of epidemiology*, *160*(11), 1033-1038.
- Neyer, L. E., Grunig, G., Fort, M., Remington, J. S., Rennick, D., & Hunter, C. A. (1997). Role of interleukin-10 in regulation of T-cell-dependent and T-cell-independent mechanisms of resistance to Toxoplasma gondii. *Infection and immunity*, *65*(5), 1675-1682.

- Owlia, P., Ghazanfari, T., Ghasemi, H., & Shahmirzady, R. (2012). Roles of IL-10 in ocular inflammations: A Review. *Ocular Immunology & Inflammation*, *6*(20).
- Rizvi, S., Rizvi, S. M., Raza, S. T., Abbas, M., Fatima, K., Zaidi, Z. H., & Mahdi, F. (2022). Implication of single nucleotide polymorphisms in Interleukin-10 gene (rs1800896 and rs1800872) with severity of COVID-19. *Egyptian Journal of Medical Human Genetics*, *23*(1), 1-8.
- Saadh, M. J., Mustafa, M. A., Batoo, K. M., Chandra, S., Kaur, M., Hussain, S., ... & Su, G. (2024). Performances of nanotubes and nanocages as anodes in Na-ion battery, K-ion battery, and Mg-ion battery. Ionics, 1-8.
- Saeij, J. P. J., Coller, S., Boyle, J. P., Jerome, M. E., White, M. W., & Boothroyd, J. C. (2007). Toxoplasma co-opts host gene expression by injection of a polymorphic kinase homologue. *Nature*, *445*(7125), 324-327
- Santos, D. K. C., Mustafa, M. A., Bansal, P., Kaur, H., Deorari, M., Altalbawy, F. M., ... & Zhang, L. (2024). Investigation of ORR and OER Mechanisms by Co-and Fe-doped Silicon Nanocages (Si48 and Si60) and Co-and Fe-doped Silicon Nanotubes (SiNT (5, 0) and SiNT (6, 0)) as Acceptable Catalysts. Silicon, 1-13.
- Sijssens, K. M., Rijkers, G. T., Rothova, A., Stilma, J. S., Schellekens, P. A., & de Boer, J. H. (2007). Cytokines, chemokines and soluble adhesion molecules in aqueous humor of children with uveitis. *Experimental eye research*, *85*(4), 443-449.
- Suarez, A., Castro, P., Alonso, R., Mozo, L., Gutierrez, C. (2003). Inter individual variations in constitutive interleukin-10 messenger RNA and protein levels and their association with genetic polymorphisms. Transplantation, 75, 711–717.

- Taha, W. A., Shakir, O. M., Meri, M. A., & Mustafa, M. A. (2023, December). Study of some biochemical indicators levels in the people infected by Toxoplasma gondii. In AIP Conference Proceedings (Vol. 2977, No. 1). AIP Publishing.
- Turner, D., Williams, D. M., Sankaran, D., Lazarus, M., Sinnott, P. J., & Hutchinson, I. V. (1997). An investigation of polymorphism in the interleukin-10 gene promoter. *European journal of immunogenetics*, *24*(1), 1-8.
- Valluru, D., Mustafa, M. A., Jasim, H. Y., Srikanth, K., RajaRao, M. V. L. N., & Sreedhar, P. S. S. (2023, March). An Efficient Class Room Teaching Learning Method Using Augmented Reality. In 2023 9th International Conference on Advanced Computing and Communication Systems (ICACCS) (Vol. 1, pp. 300-303). IEEE.
- Valverde, V., Ortiz, D. T. C., Mustafa, M. A., Kumar, A., Kaur, I., Karim, M. M., ... & Lasisi, A. (2024). Design gas sensor based on transition metal doped graphene like nanosheets: A quantum chemical study. Diamond and Related Materials, 110895.
- Wang, H., & Tao, Y. (2021). Relationship between the higher inflammatory cytokines level in the aqueous humor of Fuchs uveitis syndrome and the presence of cataract. *BMC ophthalmology*, *21*, 1-9.
- Wilson, E. H., Wille-Reece, U., Dzierszinski, F., & Hunter, C. A. (2005). A critical role for IL-10 in limiting inflammation during toxoplasmic encephalitis. *Journal of neuroimmunology*, *165*(1-2), 63-74.
- Yao, S., Hong, C.C., Ruiz-Narváez, E.A., Evans, S.S., Zhu, Q., Schaefer, B.A., Yan, L., Coignet, M.V., Lunetta, K.L., Sucheston-Campbell, L.E. and Lee, K. (2018). Genetic ancestry and population differences in levels of inflammatory cytokines in women: role for evolutionary selection and environmental factors. *PLoS genetics*, *14*(6), 1-17.

- Yousefi, A., Bidoki, A.Z., Shafioyoun, A., Sadr, M., Varzaneh, F.N., Shabani, M., Motamed, F., Farahmand, F., Khodadad, A., Fallahi, G. and Najafi, M. (2019). Association of IL-10 and TGF-beta cytokine gene polymorphisms with autoimmune hepatitis. *Clinics and Research in Hepatology and Gastroenterology*, *43*(1), 45-50.