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Circulating miR-146a and pro-inflammatory cytokines in women with toxoplasmosis in Iraq, Baghdad

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Abstract

Toxoplasmosis is a prevalent parasitic infection caused by intracellular parasite T. gondii that can affect immune responses to variable levels. MicroRNAs (miRNAs) are a cluster of small non-coding RNAs that have a crucial regulatory function of immune response manifested by dynamic changes in the expression level of miRNA during different immune responses. The objective of this study is to assess the expression of miR-146a and its correlation with the levels of pro-inflammatory cytokines TNF- α, IFN-γ, and IL-12 among women who were acutely and chronically infected with toxoplasmosis. This study was conducted on 55 female patients with positive results for toxoplasmosis as diagnosed by the ELISA technique. They were assigned to 20 women diagnosed with acute toxoplasmosis, and 35 women diagnosed with chronic toxoplasmosis. The control group included 35 healthy women. A significant upregulation in the expression levels of miRNA 146a was observed in patients with acute and chronic infections compared to the control group. However, women with acute toxoplasmosis showed significantly higher levels of miRNA146a expression in comparison to those with chronic Toxoplasmosis. Moreover, patients with acute toxoplasmosis showed a significant increase in the levels of TNF-α, IFN-γ, and IL-12 in comparison to those with chronic infection, and non-infected women. MiR-146a plays a more significant role in the activation of innate immune response (acute response) against toxoplasmosis so that manipulation of its expression could be utilized to monitor the disease severity that aids in the treatment of acute infectious diseases. However, future research is required to evaluate the precise role of miRNAs in both acute and chronic infections..

Introduction:

Toxoplasmosis is a widely spreading infection affecting about 30% of the population worldwide, caused by an intracellular parasite known as *Toxoplasma gondii* [1, 2]. The disease can be transmitted by Ingestion of Infected Meat from animals harboring *T. gondii* tissue cysts, by Ingesting food or water contaminated with cat feces, or by exposure to contaminated environmental samples (such as soil or litter boxes), or rarely blood Transfusion or organ transplantation [2]. Acute infection in individuals with intact immune systems is often asymptomatic or shows flu-like symptoms associated with the conversion of the parasite's infective form tachyzoites into dormant bradyzoites within tissue cysts [3]. Therefore, the

infection is latent and maintained inside the host throughout life. However, in immunocompromised individuals such as those diagnosed with HIV, cancer, or organ transplantation, severe toxoplasmosis may develop because of possible reactivation of bradyzoites into tachyzoites that disseminate to affect different sites of the body producing severe health problems or even death [4]. The pathophysiology of *T. gondii* is distinct, and its efficacy likely stems from its capacity to control the immunological response of the host [5]. Where the human immune response against *T. gondii* infection is complex, including both natural and acquired responses that are demonstrated by early production of cytokines which are critical for the host to control parasite replication, succeeding by activation of T-helper type 1 (Th1) to get rid of or at least control the infection [6]. However, the resistance to *T. gondii* mediated by a Th1 cell-mediated immune response relies on generating IL-12 and IFN-γ [7, 8].

MicroRNAs represent a group of small non-coding RNA, typically ranging from 18 to 22 nucleotides in length [9, 10]. Increased evidence indicated that miRNAs display a crucial role in several immunomodulatory processes within the immune system, including T cell activation and differentiation, as well as cytokine synthesis [11]. Moreover, dysregulation of miRNAs has been reported in a variety of illnesses and inflammatory disorders, suggesting the possible relation between endogenous regulation of host miRNA to infectious diseases that result in either resistance to or liability to infections [12]. In this regard, later studies emphasize the impact of miRNAs in inflammation and immunological response, which shed light on the exciting prospects of miRNAs as diagnostic, therapeutic, and prognostic agents [13].

It has been suggested that the expression profile of miRNAs in host cells may be altered abnormally at various stages of *T.gondii*, infection (acute and/or chronic), and the specific strain of the parasite, which may permit the use of miRNAs to monitor disease severity and to better understand its etiology [14]. Accordingly, there is a great interest in studying how dysregulation of miR-146a affects toxoplasmosis and what clinical implications it might have [15]. As miRNA-146a is considered to have a significant role in immunomodulation and the inflammatory process [16]. Where changes in its production are thought to be critical in determining the parasite load, the development of infection, and its subsequent outcome. Therefore, this study aimed to assess the expression of miRNA146a in females diagnosed to have either acute or chronic toxoplasmosis and to examine the possible influence on the immunological response of these individuals by measuring selected pro-inflammatory cytokines.

Methods

Patients and clinical samples

This study was performed on 90 nonpregnant females attending Ibn-Albalady Hospital, AL-Madain Hospital, and Kamal AL-Sammaraii hospitals in Baghdad, Iraq during the period between September 2022 to June 2023. They are in the age range 18-47 years, they were allocated into three groups; the control group included 35 healthy women and seronegative for toxoplasmosis infection. The second group included 20 women who appeared to be IgM positive and proved to have acute Toxoplasmosis. At the same time, the third group included

35 females diagnosed with chronic Toxoplasmosis. Serum samples were collected from all participants; each sample was centrifuged at 3000rpm and kept at -20^{o}c until analysis.

ELISA for *T. gondii* IgG and IgM antibodies

The basis of the ELISA used to identify *T. gondii* (IgG and IgM) was the two-site sandwich enzyme immunological assay. For both IgG and IgM antibodies, a sample was determined to be positive if the OD value was above 1.1 and negative if it was 0.9 or lower. The assays were performed using kits provided by Calbiotech Inc., USA, catalog numbers TX024M for IgM and TX022G for IgG, under the kit manufacturer's instructions.

Serum concentrations of TNF-a, IL-12, and IFN-γ were measured by enzyme-linked immunoassay (MyBiosource, USA).

Determination of serum levels of mature miR-146

A. RNA isolation

RNA was isolated from serum samples using a TRIZOL reagent (Invitrogen, United States). In summary, 1 ml of TRIZOL reagent was added to 250 µl of serum supernatant following the guidelines. Chloroform was introduced into the mixture and left for 5 minutes at room temperature. Subsequently, the mixture was subjected to centrifugation at 12,000 g and a temperature of 4°C for 15 min. The higher aqueous phase moved to a new reagent tube and a volume of ethanol equal to 1.5 times its volume was added. The RNA extraction process involved the utilization of 30 microliters of nuclease-free water.

B. Quantification of miRNA in serum samples

Quantification was performed using the Qubit 4.0 fluorimeter platform, renowned for its superior selectivity towards miRNA as compared to other RNA types. The assay shows high accuracy in assessing initial sample concentrations ranging from 10 pg/L to 100 ng/L. The experiment, when performed at room temperature, can sustain stable signals for a period of up to 3 hrs. Also, the Qubit 4.0 test shows resilience against common impurities like salts, free nucleotides, solvents, detergents, or proteins, without suffering any detrimental effects.

C. Quantitative PCR (qPCR)

A high-capacity cDNA Kit (ProtoScript® II First Strand cDNA Synthesis Kit, NEW ENGLAND BIOLABS) was used to reverse transcribe the RNA.

D. RNA reverse transcription

In this study, we used the reverse transcription technique with the ProtoScript® II First Strand cDNA Synthesis Kit to evaluate the expression of PCR target genes. Using oligo-dT primers, the ubiquitous tag sequence on the 5' end of these oligo-dT primers allowed for the subsequent amplification of mature miRNA during the real-time PCR step, except for the template RNA. It was then, combined and added to PCR tubes. The template RNA was put into each tube, and then, following quick centrifugation, the lines were put into a thermal cycler. The reverse transcriptase enzyme was deactivated by incubating for 5 min at 95°C after 60 min at 37°C.

Primer preparation

The amplification of miRNA genes was conducted using specialized primers, as indicated in Table 1. MacroGen® supplied these primers in a lyophilized state. The lyophilized

primers were reconstituted in distilled water to produce a stock RNA solution with a final concentration of 100 pmol. Afterward, a functional solution of the primers at a concentration of 10 pmol/µl was created by mixing 10 µl of the primer stock solution with 90 µl of deionized distilled water.

Table 1: The name, and sequence of primers used in this study

No.	Name of Primer	Sequence	Ref.
1	miR-146RT	GTCGTATCCAGTGCGTGTCGTGGAGTCGGCAATTGCACTG GATACGACAACCCA	[17]
2	MiRNA-146 forward	GGGTGAGAACTGAATTCCA	[17]
3	MiRNA-146 Reverse	CAGTGCGTGTCGTGGAGT	[17]
4	U6 Forward	GAGAAGATTAGCATGGCCCCT	[18]
5	U6 Reverse	ATATGGAACGCTTCACGAATTTGC	[18]

A. Detection of miRNA by RT-qPCR

SYBR-Green reagents were used for the RT-qPCR measurement of mRNA levels. Following 40 cycles of denaturation at 94°C for 20 seconds, annealing at 60°C for 1 minute, and extension at 72°C for 30 seconds, the amplification conditions were established as follows: The second step of the methodology involved choosing and processing cDNA samples. Every sample was run through two different PCR tubes, one for miRNA-146a and the other for U6 snRNA, the study's housekeeping gene. Specific ingredients were carefully combined to create the reaction mix components and their respective quantities.

B. Data analysis: comparative CT method ($\Delta\Delta C_T$)

The miRNA expression level was quantified using the CT technique. The expression level of each miRNA was calculated by subtracting its CT value from the average CT value of reference genes within a certain sample set for each sample. The reference gene employed was U6 snRNA. The fold change in relative expression for each candidate miRNA within each group was computed using the equation $2^{-\Delta\Delta CT}$. The ΔC_T for each miRNA in each sample was calculated as follows: $\Delta C_{Tsample} = C_{TtargetmiRNA} - C_{TU6snRNA}$. Then, $\Delta\Delta C_T$ was calculated as follows: $\Delta\Delta C_T = (C_{TmiRNA} - C_{TU6snRNA})_{\text{patients}} - (C_{TmiRNA} - C_{TU6snRNA})_{\text{controls}}$.

C. Ethical considerations

The present study was conducted in adherence to the authorized process and rules set out by the institutional scientific committee of Al-Mustansiriyah University, namely within the College of Science, Department of Biology. The ethical permission form utilized in this investigation was received from the research office affiliated with the Ministry of Health in Baghdad, Iraq. The form was applied to all individuals included in the study, and it was assigned the reference number BCSMU/0422/00026Z.

Statistical analysis

The statistical analysis was performed using GraphPad Prism 8 software. The statistical significance of differences across groups was assessed using an unpaired t-test and analysis of variance (ANOVA) in this study. Statistical significance was determined by using p-values less

than 0.05. The quantification of relative miRNA levels was performed using the 2-ΔΔCT method.

Results and discussion

Concentration of TNF-α

The infected groups had significantly higher levels of TNF-α in their serum than the healthy control women (P≤0.001), showing that TNF-α levels were significantly higher across all groups.

Table 2: The concentration of TNF- α (Pg/mL) in serum of women infected with Toxoplasmosis according to study groups.

Groups	Mean	Std. Error of Mean
Control	21.77800 [a]	0.847008
Acute infection	154.59152 [b]	11.672196
Chronic infection	92.79945 [c]	6.259374
P Value	0.001 **	

Different superscript letters (a, b, c) indicated significant differences compared to the control group.

Concentration of IL-12

The serum concentration of IL-12 in the infected groups and the control group, increased significantly (P≤0.001) among different groups, as shown in Table 3.

Table 3: The serum concentration of IL-12 (Pg/ml) in women infected with Toxoplasmosis according to study groups.

Groups	Mean	Std. Error of Mean
Control	70.82789 a	2.392964
Acute infection	615.52462 b	27.097054
Chronic infection	311.75455 c	5.932487
P Value	0.001 **	

Different superscript letters (a, b, c) indicated A significant difference compared to the control group

Serum concentration of IFN- γ

The serum concentration of IFN-γ in infected groups showed higher levels in the acute group when compared with the chronic group and control group; this increase was highly significant (P≤0.001) among different groups, as shown in Table 4.

Table 4: The serum concentration of IFN- γ (Pg/mL) of women infected with Toxoplasmosis according to study groups.

Groups	Mean	Std. Error of Mean
Control	53.15721 [a]	7.175717
Acute infection	400.98219 [b]	28.614580
Chronic infection	198.72584 [c]	11.761862
P Value	0.001 **	

Different superscript letters (a, b, c) indicated a significant difference compared to the control group

MiR-146a Expression

In this study, the molecular experiment of miR-146a expression was performed to detect the amplification plots of the target miRNA-146a and U6 (reference gene). The Ct values were used to quantify real-time RT-PCR data that are inversely associated with the amount of starting template and calculate the melting temperature curve, as shown in Figure 1.

(a) (b)

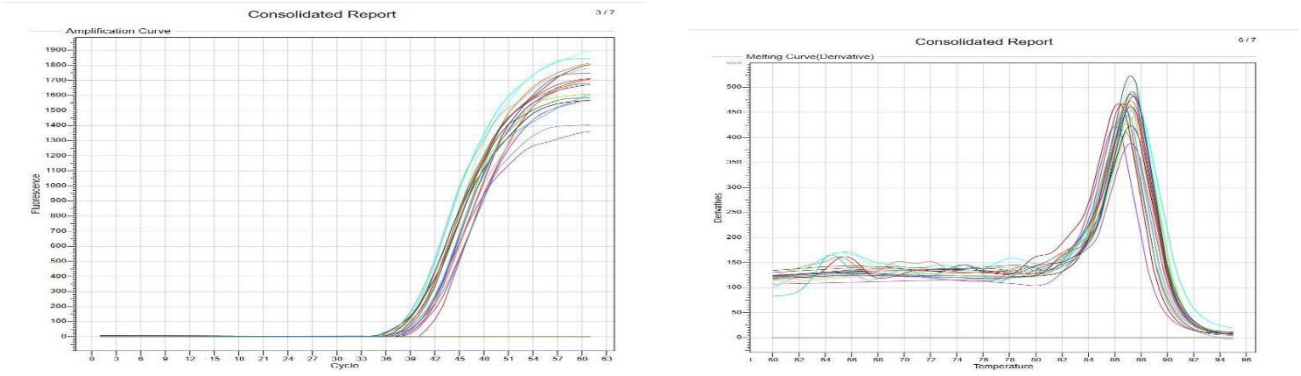

Figure (1): miR-146a expression obtained by Real Time-PCR (a): Amplification plots. (b) Melting Curve.

The Ct value of miRNA-146a in the acute group was 36.085 ng/µL and in the chronic group, it was 38.2912 ng/µL, while in the control group, it was 33.84 ng/µL. The levels of miRNA-146a estimate revealed an increase in the acute patient group when compared with healthy controls, and this increase was a highly significant increase ($p \leq 0.05$). On the other hand, there were no significant differences between the chronic and healthy control groups.

Table 5: Fold of MiR146a expression for patients and the control groups.

Groups	Means Ct of miR-146a	Means Ct of U6	ΔCt (Means Ct of miR-146a	$2^{-\Delta Ct}$	experimental group/ Control group	Fold of gene expression
Control	33.84	22.482	11.358	0.000380	0.000380/0.000380	1.00 [a]
Acute infection	36.085	25.89625	10.18875	0.000856	0.000856/0.000380	2.2489 [b]

Chronic infection	38.29125	27.87875	10.4125	0.000733	0.000733/0.000380	1.9258 [a]
P value	----	----	----	----	-----	0.0052 **

Different superscript letters (a, b) indicated significant differences ($p \leq 0.05$) compared to the control group.

The correlation between miRNA-146a and immunological parameters.

Analysis of the correlation coefficient was conducted to show the relationship between miRNA-146a with the investigated immunological parameters of this study TNF-α, IL-12, and IFN-γ for women infected with Toxoplasmosis.

The obtained data presented in Table (6) shows that miRNA-146a displayed a significant positive correlation with TNF-α, while a non-significant correlation was obtained with other inflammatory cytokines such as IL-12 and IFN- γ.

Concerning miRNA-146a, the results of this study showed a non-significant correlation with both IL-12 and IFN-γ. These results could be attributed to the small number of samples studied, as well as the possibility of the presence of variable strains of Toxoplasma sp., mostly in chronic cases according to the duration of infection that may vary from months to years. This is besides other factors such as unannounced abortions or taking some medications, in addition to possible hormonal changes due to menstruation and/or unannounced lactation.

Table (6): correlation between miRNA-146a and immunological parameters.

		IL-12	**TNF-a**	**IFN- γ**	**Fold miR-146a**
IL-12	Pearson Correlation	1	.873**	.900**	.273
	Sig. (2-tailed)		.000	.000	.230
TNF-α	Pearson Correlation	.873**	1	.836**	.550**
	Sig. (2-tailed)	.000		.000	.009
IFN-γ	Pearson Correlation	.900**	.836**	1	-.077
	Sig. (2-tailed)	.000	.000		.739
Fold miR-146a	Pearson Correlation	.273	.550**	-.077	1
	Sig. (2-tailed)	.230	.009	.739	

There is an increasing amount of data suggesting that cytokines, which are non-antigen-specific mediators secreted by cells, have protective or regulatory functions. Furthermore, it has been observed that these cytokines can exert their biological effects even at low doses [19]. The beginning of immunization for *T.gondii* is mostly driven by type-1 inflammatory cytokines, including TNF-α and IL-12 [20, 21]. According to reports, certain pro-inflammatory cytokines, such as TNF-α and IFN-γ, can activate CD8 T-cytotoxic cells. When these cells are

activated, they change into major cytotoxic effector cells that kill tachyzoite-infected cells. This process serves to restrict the spread of the parasite during the acute infection phase and hinders the formation of cysts during the chronic infection phase [22]. Interferon-gamma (IFN-γ) is well recognized as the primary cytokine produced by T cells (specifically CD4+ and CD8+) and natural killer (NK) cells, playing a crucial role in the immune response against both the acute and chronic stages of *T. gondii* infection [23, 24]. A previous experimental study demonstrated that the neutralization of INF-γ through the use of antibodies in vivo renders mice vulnerable to both primary infection (acute infection) and reactivation of the ME49 strain parasite in chronic infection. This finding highlights the crucial role of INF-γ in effectively eliminating the infectious pathogen. Broadly speaking, immunity against toxoplasmosis is mostly mediated by T cells. The establishment of a symbiotic relationship between *T. gondii* and its host is dependent on the involvement of many inflammatory cytokines, including IFN-γ, TNF-α, and IL-12 [25]. This immune response triggers the transformation of the parasite into bradyzoites and restricts its spread inside the host's tissues [26]. Nevertheless, *T. gondii* infection must have a strict dependence on IFN-γ in the initial phase of the disease to regulate the replication of tachyzoites. Furthermore, during the chronic stage of the infection, IFN-γ is necessary to sustain latency and prevent the reactivation of the infection [27]. Dogruman-Al et al. (2011) conducted a study that showed the dependence of Toxoplasma infection on the equilibrium of signals originating from pro-inflammatory (IL-12, IFN-γ, and TNF-α) and anti-inflammatory cytokines, which inhibit parasite multiplication and regulate the inflammatory response [28]. El-Sayed et al. (2016) earlier in vivo experimental study demonstrated that mice infected with the cyst of the ME49 non-virulent strain of *T. gondii* had increased blood levels of TNF [29]. These studies are in agreement with our study in the increment of proinflammatory cytokines during toxoplasmosis infection. In a different study, Moradi et al. (2023) demonstrated that male mice with a persistent *T. gondii* infection displayed a notable upregulation in the genetic manifestation of pro-inflammatory cytokines, with a focus on TNF-. A big rise in TNF-α was seen in this study. This might be because immune cells were activated, which stopped the parasite from spreading and stopped cysts from forming. These mechanisms are believed to be protective against chronic toxoplasmosis [30]. Based on our findings, it was discovered that women diagnosed with toxoplasmosis displayed IL-12 levels above those of the control group without infection. This occurrence might be closely linked to the development of host resistance in parasitic infections. (IFN) synthesis is crucial for Th1 cell-mediated immunity because this cascade only happens after the release of (IL-12). The stimulation of IL-12 is recognized as a significant elicit in initiating the Th1 cell-mediated immune response, which eventually has a significant influence on designing host defense against *T. gondii*.

The immune system is crucial in protecting against both acute & chronic forms of toxoplasmosis. Results obtained from a study by Alkhanak et al. (2015) demonstrated that regardless of gender, the IL-12 levels were significantly elevated in subjects with chronic infection. [31].

Besides, results from a research study showed that in Al-Qadisiyah/ Iraq, women who experienced abortions and contracted acute/chronic toxoplasmosis displayed an increase in concentrations of IL-12 in their blood, as opposed to healthy control women [32]. In the specific situation of Bangladesh, a correlation between the activation of IL-12 and chronic

Toxoplasmosis has been recognized by Ashraf et al. (2023). This correlation is substantiated by the thought of significantly increased levels of IL-12 in both male and female cohorts, as compared to a control group comprising of control individuals [33].

Al-Kuraishi *et al*. (2023) showed an independent examination revealing a significant elevated in IL-12 expression between toxoplasmosis-infected pregnant women from Iraq in comprise to healthy, non-infected pregnant females [34]. In addition, the study directed by Ivanova et al. (2019) illustrates that IL-12 plays a significant role in augmenting the cytotoxicity of immune cells, T cells & natural killer cells, during the immune response to infections. Hence, this result shows that IL-12 has the possible to fight *T. gondii* infection might be because it helps make immune cell killing more effective [35].

In a recent study, human cells were employed to examine the production of IL-12 by peripheral blood monocytes and dendritic cells. The study revealed that the production of IL-12 occurred exclusively following the phagocytosis of live tachyzoites. This finding explains the detected increase in the acute group compared to the control group [36]. Furthermore, there have been reports, indicating that the dense granule protein (GRA15) of *T. gondii* can induce pro-inflammatory cytokines. The GRA15 protein is transported to the membrane of the parasitophorous vacuole, where it initiates the activation of the NFκB signaling pathway, regardless of the presence of MyD88. So, the activation of IL-12 is facilitated. However, it should be noted that GRA15 derived from Type I parasite strains does not exhibit this particular action [37]. Subsequent evidence has demonstrated that interferon-gamma (IFN-γ) functions as an inducer of guanylate binding proteins (GBP), which accumulate on the surface of the intracellular stage of *T. gondii*. The fact that GBP builds up suggests that IFN-γ controls the parasite's too rapid growth inside the host mouse since not having GBP can kill the parasite [38]. The intracellular virus *T. gondii* has demonstrated significant adaptation in its ability to counteract the host immune response through its interference with the NF-κβ signaling pathway [39, 40]. On the other hand, it has been seen that when *T. gondii* infects cells, the expression of iNOS, a protein that is also activated by interferon (IFN), goes up. While the absence of inducible nitric oxide synthase (iNOS) in mice does not impact the initial management of *T. gondii* infection, it is noteworthy that animals without iNOS are more vulnerable during the latter stages of infection. This heightened susceptibility ultimately leads to mortality, mostly owing to the escalated parasite load in the brain [41]. The findings of the current study align with prior research, which also observed elevated levels of IFN-γ in individuals with asymptomatic toxoplasmosis compared to healthy individuals. Therefore, this means that toxoplasmosis starts a strong type-1 cytokine response, especially IFN-γ, in the early stages of infection by turning on T cells and natural killer cells [42, 43]. The findings demonstrate a considerable upregulation of miRNA-146a expression in the serum of individuals afflicted with both acute and chronic toxoplasmosis. This heightened expression has garnered attention in several studies since it has been consistently shown that miR-146a is markedly elevated during parasite infections. A recent case-control study conducted in Iran found a heightened expression of miR-146a in 20 patients diagnosed with hydatid cysts, as compared to a control group of 20 healthy individuals [44]. Another study conducted independently found a notable increase in the expression of miR-146a in individuals infected with *Leishmania donovani* [45]. Still, some research shows that this microRNA (miRNA) is very important for stopping the production of pro-inflammatory cytokines, which in turn

changes how strong the inflammatory response is [46]. Furthermore, the study conducted by He et al. (2016) indicated that the up-regulation of miR-146a could serve as a substantial protective factor for the host during the acute stage of schistosomiasis infection. Moreover, this regulatory molecule is essential in facilitating the transition from acute to chronic infection [47]. According to Ballinas-Verdugo et al. (2021), it has been proposed that both acute and chronic infections caused by *T*. *cruzi* may elicit an inflammatory response because of the upregulation of miR-146a and these results are consistent with our research in the increment the pro-inflammatory cytokines during the infection [48]. Furthermore, another study has demonstrated that Toxoplasma alters the miRNA profile of the host cell through a mechanism that requires the presence of viable parasites capable of invading and replicating [49]. MiR-146a plays a pivotal role in the control of immune cell proliferation. Its functionality extends to acting as a miRNA with the potential to target NF-κB signaling mediators, including IRAK1 and TRAF6. Through this action, it inhibits pro-inflammatory responses, such as TNF-α, suppresses Th1 and Th17 cells, and activates regulatory T lymphocytes (Tregs) [50]. The importance of TRAF6 lies in its role in activating the pro-inflammatory cytokine IL-12 within macrophages. This demonstrates the critical nature of controlling *T. gondii* infection [51]. Activation of TRAF6 is also necessary for the fusion of vacuoles and lysosomes, a critical process in *T. gondii* infection [52]. It has also been observed that the expression of miRNA can be affected by different strains of parasites. Studies have shown that infection with the second type strain leads to an increase in the expression of miR146a. In contrast, mice chronically infected with the type III mouse strain showed reduced levels of miR-146a in their brains. Thus, the results show a clear basis for the observed increase in expression in our study.

Conclusion

This study revealed a significantly higher expression of miR-146a among women with acute and chronic toxoplasmosis, compared to a control group consisting of healthy women. Moreover, increased levels of TNF-a, IFN-gamma, and IL-12 were observed in the blood samples of infected women. The potential involvement of elevated miR-146a levels in the pathogenesis of toxoplasmosis arises from its ability to stimulate the production of pro-inflammatory cytokines by dendritic cells (DCs) and CD4-T cells. In this particular context, it has been proven that miR-146, considered an immune regulator, can influence the stages of *T. gondii*, especially in its early stages. Based on these results, further investigation is warranted regarding the impact of host miRNAs on parasite infections. This will enhance our comprehension of the interaction between parasites and hosts. This knowledge possesses the capacity to generate valuable insights regarding the future utilization of miRNAs in the diagnostic and therapeutic treatment of toxoplasmosis.

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الحامض الرايبوزي النووي الدقيق 146 والسايتوكينات المعززة للالتهاب لدى النساء المصابات بداء المقوسات في العراق/ بغداد

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الخلاصة:
داء المقوسات هو عدوى طفيلية منتشرة يسببها طفيل T. gondii داخل الخلايا ويمكن أن يؤثر على الاستجابات المناعية بمستويات مختلفة. MicroRNA s (miRNAs) عبارة عن مجموعة من RNAs الصغيرة غير المشفرة التي لها وظيفة تنظيمية حاسمة للاستجابة المناعية التي تتجلى في التغيرات الديناميكية في مستوى التعبير عن miRNA أثناء الاستجابات المناعية المختلفة. هدفت هذه الدراسة إلى دراسة تعبير miR-146a وارتباطه بمستويات السيتوكينات المسببة للالتهابات TNF- α و IFN-γ و IL-12 بين النساء اللاتي أصيبن بعدوى حادة ومزمنة بداء المقوسات. أجريت هذه الدراسة على 55 مريضة وكانت نتائج تشخيص داء المقوسات إيجابية لديهم بواسطة تقنية ELISA. تم توزيعهم على 20 امرأة تم تشخيص إصابتهن بداء المقوسات الحاد، و35 امرأة تم تشخيص إصابتهن بداء المقوسات المزمن. وتضمنت المجموعة الضابطة 35 امرأة سليمة. وقد لوحظ وجود تنظيم كبير في مستويات التعبير عن miRNA 146a في المرضى الذين يعانون من الالتهابات الحادة والمزمنة مقارنة بالمجموعة الضابطة. ومع ذلك، أظهرت النساء المصابات بداء المقوسات الحاد مستويات أعلى بكثير من تعبير miRNA146a مقارنة بأولئك المصابين بداء المقوسات المزمن. علاوة على ذلك، أظهر المرضى الذين يعانون من داء المقوسات الحاد زيادة كبيرة في مستويات TNF-α وIFN-γ وIL-12 مقارنة بالمصابين بالعدوى المزمنة والنساء غير المصابات. يلعب miR-146a دورًا أعلى أهمية في تنشيط الاستجابة المناعية الفطرية (الاستجابة الحادة) ضد داء المقوسات بحيث يمكن استخدام التلاعب في تعبيره لمراقبة شدة المرض الذي يساعد في علاج الأمراض المعدية الحادة. ومع ذلك، هناك حاجة إلى أبحاث مستقبلية لتقييم الدور الدقيق للmiRNAs في كل من الالتهابات الحادة والمزمنة.