




# The study of the correlation level of cystatin-c elevation in hemodialysis patients with *Toxoplasma gondii* in Baquba / Diyala

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## Abstract

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**Background:** *Toxoplasma gondii* is the most common infection of protozoa, affecting a wide range of hosts. Toxoplasmosis is usually asymptomatic in immunocompetent persons, but in immunocompromised persons (e.g., patients on dialysis) significant problems, and may progress to a life-threatening infection.

**Objective:** To investigate the correlation level of cystatin-C elevation in hemodialysis patients with *Toxoplasma gondii* in Baquba / Diyala.

**Patients and Methods:** A group of blood samples, consisting of 75 dialysis patients and 50 healthy controls, to totaling 125 were examined for the detection of anti-toxoplasma antibodies and Cystatin-C In Baquba Teaching Hospital from November 2020 to April 2021 using Enzyme-Linked Immunosorbent assay .

**Results:** The total numbers Of the 125 samples examined, were showed that the Mean  $\pm$  SE for cystatin-c in the group of patients was  $2.43 \pm 0.10$  higher compared to the healthy individuals  $2.02 \pm 0.21$ , The results show that correlation coefficient between *Toxoplasma IgG* and Cystatin-c in hemodialysis patients, where it was found that the correlation coefficient between them was 0.34.

**Conclusion:** The level of cystatin-C in hemodialysis patients was higher compared to the control group , and found significant correlation between the rice of Cystatin-C and the presence of toxoplasma IgG in dialysis patients.

**Keywords:** *Toxoplasma gondii*, Hemodialysis, Cystatin-c

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## Introduction

*Toxoplasma gondii* is a parasitic obligate intracellular one-celled eukaryote, (particularly an apicomplexan) that causes toxoplasmosis .*T. gondii* was discovered in 1908 by Louis Mancoand Charles Nicole through working in Tunis. Although Nicole

and Manco initially thinking the organism was a member of the Leishmania, which they described as "Leishmania Gondi," they quickly realized that they had discovered a completely new organism, which they renamed it *Toxoplasma gondii* [1]. *T. gondii*

may infect almost any warm-blooded animals [2] but felids, such as domestic cats, are the only known definitive hosts in which the parasite can reproduce sexually [3]. The *Toxoplasma* parasite can live in the bodies of humans (and other animals) for long periods of time, possibly even a lifetime [4] transmission occurs mainly via drinking of water, of water, or ingestion of vegetables or soil contaminated by oocysts (sporozoites) or uncooked meat containing live tissue cysts (bradyzoites). This disease is classified as food-borne Zoonoses [5]. *Toxoplasma gondii* is an opportunistic protozoan parasite, reactivates with impairing of the immunity and emerges as a life-threatening risk in immune-compromised individuals.

An autoimmune disease is a condition caused by an abnormal immune response to a healthy body part. There are at least 80 different kinds of autoimmune diseases. Almost any part of the body can be involved [6]. Chronic kidney disease (CKD) It is a defect in the structure or function of the kidneys that occurs gradually over months to years, leading to irreversible impairment of kidney function and impairment of immunity system [7]. Hemodialysis this is a method of cleansing the blood of a person whose kidneys are not functioning normally using a dialysis machine. When the kidneys are in a condition of renal failure, this form of dialysis achieves the extracorporeal elimination of waste products such as creatinine and urea, as well as free water from the blood [8]. Cystatin C or cystatin 3 A protein encoded by the CST3 gene. Cystatin C belongs to the type 2 cystatin gene family, has a low molecular weight (about 13.3 kilo daltons), and is

eliminated from the bloodstream via the kidneys' glomerular filtration. Cystatin C levels in the blood are increased as the kidney function and glomerular filtration rate diminish [9]. CST3 is mainly used as a biomarker of kidney function than serum creatinine levels [10].

## Patients and Methods

**Study protocol:** This study was a cross-sectional study that included seventy-five confirmed cases of kidney failure on dialysis at Baquba Teaching Hospital and fifty healthy subjects who visited the hospital for examination and were used to compare result.

### Study population

Inclusion criteria in this study were the research sample is affected persons and control groups. No cases are excluded depending on the blood sampling collected from the dialysis patients and control groups.

### Study design

Blood samples were collected during (November 1, 2020) to (April 30, 2021). from a total of 75 patients and 50 healthy subjects. Three mls of brachial vein blood was drawn from each group. Sera were separated after 5 minutes of centrifugation at 4000 rpm and stored at -20°C until needed. Information was recorded from patients on hemodialysis questionnaire paper.

### Statistical Analysis

To detect the effect of different factors in study parameters, the Statistical Analysis System- SPSS version 22 program was used. To compare percentages, the Chi-square test was used (0.05 and 0.01 probability). T-test, mean and standard deviation was used to represent the comparison of means in this study, and estimate the correlation coefficient  $-r$ .

## Results

The results of cystatin-c are shown in table (1) for the group of hemodialysis patients and the healthy ones, as it was shown that the

Mean  $\pm$  SE for cystatin-c in the group of patients was  $2.43 \pm 0.10$  higher compared to the healthy individuals  $2.02 \pm 0.21$ , and P-value was 0.0433.

**Table (1):** Effect of cystatin-c of function kidney in dialysis patient and healthy

Group	Mean	Standard division	T-test	P-value
Patients	2.43	0.10	0.405	0.0433
Control	2.02	0.21		

The current study shows Table (2) the results of the correlation coefficient between *Toxoplasma* IgG and Cystatin-c in hemodialysis patients, where it was found that the correlation coefficient between them

was 0.34, which indicates a positive and significant correlation of 0.05 between the rise of cystatin C in the blood and the presence of *Toxoplasma* IgG .

**Table (2):** Correlation coefficient between IgG toxoplasma and Cystatin-c in patient haemodialysis

Parameters	Correlation coefficient-r
Cystatin-c & IgG toxoplasma	0.34 *
P-value	0.0498
* (P $\leq$ 0.05)	

## Discussion

*Toxoplasmosis* is one of the infectious causes of morbidity and mortality among hemodialysis patients and immune compromised individuals [11]. *Toxoplasma gondii* is a high priority for hemodialysis patients and people with immune system disorders [12]. Because of their immunodeficiency, hemodialysis patients are at a higher risk of reactivating toxoplasmosis infection. As a result, in these individuals, an early definitive diagnosis is highly recommended [13]. Because hemodialysis patients are at a higher risk of *T. gondii* infection, the goal of this study was conducted to investigate the association between the cystatin-C elevation in hemodialysis patients with *Toxoplasma gondii* in Baquba / Diyala. *Toxoplasmosis*, on the other hand, is mostly found in tropical and subtropical areas [14]. The results of this

study indicate that cystatin-C showed an increase in hemodialysis patients of  $2.43 \pm 0.10$  higher than in healthy people, which was  $2.02 \pm 0.21$ , P value = 0.0433, and this indicates a defect in kidney function in patients, which caused the occurrence of Impaired kidney function. Increase protein in the blood, as a result of a viral or parasitic infection or other diseases that affect the kidneys and impair their functions in purifying the body of toxins and other substances. The estimation of glomerular filtration rate (GFR) is required for the evaluation of renal function patients. Cystatin C serum has been proposed as a new endogenous marker for GFR after the Hojs, *et al* [15] study demonstrated that cystatin C serum is a reliable marker of GFR in patients with mild to moderate renal function impairment and has a higher diagnostic accuracy than creatinine. The study

conducted by Chenami Uyabo in 2006, which summed up that serum cystatin C is more beneficial than serum creatinine in detecting early renal insufficiency, resembled them, as did the study of Hassan H, Al-Saeed, 2020, but the study of Oddoze C, 2001 differed from them. Mussap, M *et al* [16] revelation that serum cystatin C concentration progressively increased as glomerular filtration rate decreased. The overall relationship between mutual Cystatin C and GFR ( $r = 0.84$ ) was significantly stronger than the relationship between serum creatinine and GFR ( $r = 0.65$ ). Because to a decrease in the glomerular filtration rate (GFR) from 120 to 20 mL / min / 1.73 m<sup>2</sup>, cystatin C increased serum than creatinine , which gives a stronger signal than the creatinine signal over the measured GFR range. Serum cystatin C had a significantly higher maximum diagnostic accuracy (90%) than serum creatinine (77%). Study Tian, S *et al* [17] indicates that cystatin C can also be used as an indicator of low molecular weight protein clearance rate with various types of high flux membranes in hemodialysis, especially to detect a slight decrease in glomerular filtration rate. The Kumaresan R and Giri P. A [18] study revealed that, regarding the relationship between cystatin C and creatinine with the measured GFR in this study, the results showed that as the age of a CKD patient increased, the glomerular filtration rate decreased slightly and the cystatin C levels increased significantly. Receptor Run Curve (ROC) analysis indicates that cystatin C (sensitivity: 73.1%) is higher than creatinine (sensitivity: 48.3%) that was similar to the Hojs ,R et al (13) study. The researcher did not find a study

linking IgG of *toxoplasmosis* and cystatin c. The current study was the first study to link them, as the results of this study showed that there is a positive relationship between the rise of cystatin c in the blood and the presence of *IgG toxoplasmosis* in dialysis patients, where the correlation coefficient between them was 0.34 and significant at 0.05, this indicates that the increase in cystatin protein C in the blood indicates the renal dysfunction because propossibility presence of a parasitic infection in immunocompromised persons, including patients with dialysis and other immune diseases.

### Conclusions

The level of Cystatin-C in hemodialysis patients was higher compared to the control group due to dysfunction renal which leads to Cystatin -C accumulation in the blood , and found significant correlation between the rice of Cystatin-C and the presence of toxoplasma IgG in dialysis patients.

### Recommendations

The health authorities of diyala must pay more attention to control of the toxoplasmosis infection, especially in hemodialysis patients.

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**Ethical clearance:** Ethical approval was obtained from the Medicine College / Diyala University ethical committee for this study.

**Conflict of interest:** Nil

## References

[1] Flegr J, Prandota J, Sovičková M, Israili ZH . "Toxoplasmosis – a global threat. Correlation of latent toxoplasmosis with specific disease burden in a set of 88 countries ". PLOSONE, 2014; 9 (3): e90203 .Bibcode:2014PLoSO...990203F.

<https://doi.org/10.1371/journal.pone.0090203>

[2]Dubey, J. P , "General Biology". Toxoplasmosis of Animals and Humans (Second ed.). Boca Raton, London, New York: Taylor and Francis Group. 2010;pp. 1–20.

[3]Knoll, Laura J, Dubey JP, Wilson, Sarah K, Genova , et al. "Intestinal delta-6-desaturase activity determines host range for Toxoplasma sexual reproduction", 2019 ;p 60-77

<https://pubmed.ncbi.nlm.nih.gov/31430281/>

[4] CDC - Toxoplasmosis - Biology". 2015. <https://www.cdc.gov/parasites/toxoplasmosis/biology.html> . [accessed 13 May 2021]

[5]Tenter A M, Heckeroth A R, and Weiss L M. Toxoplasma gondii: From animals to humans. Int. J. Parasitol . 2000 ; 30 (12–13), p1217–1258.

<https://pubmed.ncbi.nlm.nih.gov/11113252>

[6]Fakhri Y, Majidiani H . Autoimmune diseases fact sheet. Office on Women's Health. U.S. Department of Health and Human Services ,2016. 16 July.

[7] Johns Hopkins Medicine , 2017.What is renal failure

<https://www.hopkinsmedicine.org/health/con>

[ditions-and-diseases/end-stage-renal-disease-esrd](https://www.hopkinsmedicine.org/health/conditions-and-diseases/end-stage-renal-disease-esrd) . [accessed 12 March 2021].

[8]Hall YN, Larive B, Painter P. Effects of six versus three times per week hemodialysis on physical performance, health and functioning, Frequent Hemodialysis Network (FHN) randomized trials. Clinical Journal of the American Society of Nephrology. 2012;7(5):782–794.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3338281/>

[9]Shlipak MG, Matsushita K, Ärnlöv J, Inker LA, Katz R, Polkinghorne KR, et al. ,2013. "Cystatin C versus creatinine in determining risk based on kidney function". The New England Journal of Medicine. 369 (10): p 932-943.

[10]Roos JF, Doust J, Tett SE, Kirkpatrick CM , 2007. "Diagnostic accuracy of cystatin C compared to serum creatinine for the estimation of renal dysfunction in adults and children--a meta-analysis". Clinical Biochemistry. 40 (5–6): p383–391.

[11]Mousavi S S B, Faramarzi M. Do we Need to Screen Uremic Patients for Toxoplasmosis before Kidney Transplantation? Shiraz E-Med . 2013;14(4).

[12]Nissapatorn V, Leong, TH, Lee R , Ibrahim J, Yen TS . Seroepidemiology of toxoplasmosis in renal patients. Southeast Asian J Trop Med Public Health. 2011;42(2):237.PMID:21710842

<https://www.thaiscience.info/Journals/Article/TMPH/10689112.pdf>

[13]Saki ,J, Khademvatan ,S, Soltani ,S, Shahbazian, H ,2013. Detection of toxoplasmosis in patients with end-stage renal disease by enzyme-linked immunosorbent assay methods. Parasitol



Res.;112(1):163-168. DOI: 10.1007/s00436-012-3120-6.

[14]Dubey, JP . The history of *Toxoplasma gondii*—the first 100 years. *J Eukaryot* DOI:10.1111/j.1550-7408.2008.00345.x

*Microbiol.* 2008;55(6):467-475 .

[15]Hojs R, Bevc S, Ekart R, Gorenjak M, Puklavec L. Serum cystatin C as an endogenous marker of renal function in patients with mild to moderate impairment of kidney function. *Nephrol Dial Transplant.* 2006 ; Jul;21(7):1855-62. doi: 10.1093/ndt/gfl073.Epub2006Mar8.PMID:16524933.<https://pubmed.ncbi.nlm.nih.gov/16524933/>

[16]Mussap M, Dalla Vestra M, Fioretto P, Saller A, Varagnolo M, Nosadini R, et al. Cystatin C is a more sensitive marker than creatinine for the estimation of GFR in type 2 diabetic patients. *Kidney Int.* 2002 Apr;61(4):1453-61. doi: 10.1046/j.1523-

1755.2002.00253.x. PMID: 11918752.

<https://pubmed.ncbi.nlm.nih.gov/11918752/>

[17]Tian S, Kusano E, Ohara T, Tabei K, Itoh Y, Kawai T, *et al.* Cystatin C measurement and its practical use in patients with various renal diseases. *Clin Nephrol.* 1997 Aug;48(2):104-8. PMID: 9285147.

<https://pubmed.ncbi.nlm.nih.gov/9285147/>

[18]Kumaresan R, Giri PA , 2011 .comparison of serum cystatin C and creatinine with glomerular filtration rate in Indian patients with chronic kidney disease. *Oman Med J.* 2011;26(6):421-425. doi:10.5001/omj.

<https://pubmed.ncbi.nlm.nih.gov/22253951/>

## دراسة ارتباط مستوى ارتفاع السيستاتين-سي لدى مرضى غسيل الكلى المصابين

### بالتوكسوبلازما جوندي في بعقوبة / ديالى

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#### المخلص

**خلفية الدراسة:** التوكسوبلازما جوندي هي العدوى الأكثر شيوعاً للبروتوزوا ، وتؤثر على مجموعة واسعة من العوائل. عادة ما يكون داء المقوسات بدون أعراض في الأشخاص المؤهلين مناعياً ، ولكن في الأشخاص الذين يعانون من نقص المناعة (على سبيل المثال: مرضى غسيل الكلى) يمكن أن تضمن المشاكل الكبيرة ، وقد تتطور إلى عدوى تهدد الحياة.

**اهداف الدراسة:** للتحقق من مستوى ارتباط ارتفاع السيستاتين-سي في مرضى غسيل الكلى مع التوكسوبلازما جوندي في بعقوبة / ديالى.

**المرضى والطرائق:** تم فحص مجموعة من عينات الدم ، تتكون من ٧٥ مريضاً غسيل الكلى و ٥٠ من الضوابط السليمة ، باستخدام مقايصة الممنز المناعي المرتبط بالإنزيم (ELISA) للسيستاتين ، للكشف عن التوكسوبلازما في مستشفى بعقوبة العام من تشرين الثاني ٢٠٢٠ الى نيسان ٢٠٢١.

**النتائج:** أظهر العدد الإجمالي للعينة التي تم فحصها وعددها ١٢٥ عينة أن متوسط  $SE \pm$  للسيستاتين-ج في مجموعة المرضى كان أعلى بمقدار  $٢,٤٣ \pm ٠,١٠$  مقارنة بالأفراد الأصحاء  $٢,٠٢ \pm ٠,٢١$  ، وأظهرت نتائج معامل الارتباط بين توكسوبلازما IgG و السيستاتين-سي في مرضى غسيل الكلى حيث وجد أن معامل الارتباط بينهما  $٠,٣٤$ .

**الاستنتاجات:** مستوى السيستاتين-سي في مرضى غسيل الكلى ارتفع بشكل ملحوظ مقارنة بمجموعة التحكم.

**الكلمات المفتاحية:** التوكسوبلازما جوندي ، غسيل الكلى ، سيستاتين سي

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