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Seroprevalence of Rubella Virus in Chronic Kidney Disease Patients

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Abstract

Relevance. *Rubella virus is commonly associated with a minor infection, however, if transmitted during pregnancy, it can cause serious consequences which includ congenital rubella syndrome (CRS), people with chronic kidney disease (CKD) often have weakened immune systems, making it difficult for them to fight off rubella infection or receive the vaccine. As a result, determining the amount of rubella antibodies in these patients can aid in developing more effective preventative strategies.* ***Aims.*** *The purpose of this study was to assess and compare rubella virus antibody levels (IgM and IgG) in CKD patients and healthy controls.* ***Materials and Methods.*** *A case-control study design was adpted, with 180 CKD patients and 180 apparently healthy persons, serum samples were analyzed for rubella-specific IgM and IgG antibodies by using an enzyme-linked immunosorbent assay (ELISA).* ***Results.*** *Rubella IgM was detected in 81/180 of controls and 65/180 of CKD patients. Rubella IgG was positive in all participants (360/360, 100%). Mean IgG concentration was significantly higher in CKD patients (456.82 ± 144.90 IU/ml) than in controls (169.45 ± 117.52 IU/ml; t = 20.666, p < 0.001).* ***Conclusion.*** *Both CKD patients and controls tested positive for rubella IgG, while CKD patients had a lower IgM positivity rate, patients with chronic renal disease had significantly higher mean IgG titers, which could indicate changed immune regulation or changes in exposure and immunization history. These findings need careful interpretation and additional testing of rubella immunity in patients with chronic kidney disease (CKD).*

Keywords: *Rubella virus, chronic kidney disease, seroprevalence, IgM, IgG, ELISA*

No conflict of interest to declare.

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Серопревалентность вируса краснухи среди пациентов с хронической болезнью почек

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Резюме

Актуальность. *Вирус краснухи обычно ассоциируется с легкой инфекцией, однако, если он передается во время беременности, это может привести к серьезным последствиям, включая синдром врожденной краснухи (CRS). У людей с хронической болезнью почек (ХБП, CKD англ.) часто ослаблена иммунная система, что затрудняет им борьбу с краснухой или делает вакцинацию малоэффективной. Определение количества антител к краснухе у этих пациентов может помочь в разработке более эффективных профилактических стратегий.* ***Цель.*** *Оценить и сравнить уровень антител к вирусу краснухи (IgM и IgG) у пациентов с ХБП и здоровых лиц контрольной группы.* ***Материалы и методы.*** *Был разработан план исследования «случай-контроль», в котором приняли участие 180 пациентов с ХБП и 180 практически здоровых людей, образцы сыворотки крови которых были проанализированы на наличие специфичных к краснухе антител IgM и IgG с помощью иммуноферментного анализа (ELISA).* ***Результаты.*** *IgM к краснухе был обнаружен у 81 из 180 пациентов контрольной группы и у 65 из 180 пациентов с ХБП. IgG к краснухе был выявлены у всех участников (360 из 360, 100%). Средняя концентрация IgG была достоверно выше у пациентов с ХБП (456,82 ± 144,90 МЕ/мл), чем в контрольной группе (169,45 ± 117,52 МЕ/мл; t = 20,666, p < 0,001).* ***Вывод.*** *Как в группе пациентов с ХБП, так и в контрольной группы по результатам теста были определено присутствие IgG краснухи. При этом у пациентов с ХБП при более низком уровне IgM, средние титры IgG были значительно выше, что может указывать как на встречу с вирусом краснухи, так и относительно недавней иммунизацией. Эти данные требуют дополнительного тестирования и тщательной интерпретации иммунитета к краснухе у пациентов с хронической болезнью почек.*

Ключевые слова: *вирус краснухи, хроническая болезнь почек, серопревалентность, IgM, IgG, иммуноферментный анализ*
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Introduction

Rubella, often known as German measles is caused by a single-stranded, enveloped RNA virus belong to Matonaviridae family and Rubivirus genus. Rubella typically causes a minor rash in children and adults. However, contracting rubella while pregnant can cause major birth abnormalities called congenital rubella syndrome (CRS) [1]. The virus is normally transmitted through respiratory droplets, but it can also pass through the placenta, especially during the first trimester of pregnancy [1–4].

A weaker immune system has been linked to an increased risk of contracting rubella, people with weakened immune systems, such as leukemia patients undergoing chemotherapy, may still contract rubella even after being vaccinated. In some circumstances, the infection may cause prolonged viral shedding, high IgM antibody levels, and detectable viral RNA in blood cells, occasionally forcing the suspension of treatment [5]. Vaccine-derived rubella virus (iVDRV) can persist and promote chronic granulomatous inflammation in primary immunodeficiencies (PIDs) due to viral alterations that enhance tissue stability and dispersion [6]. Children and pregnant women with adverse birth outcomes are particularly susceptible, exhibiting confirmed IgM seroprevalence rates between 3% and 12% [7]. Identifying rubella antibodies early on is a key way to stop congenital transmission and its effects.

Chronic kidney disease (CKD) is defined as a deterioration in kidney function lasting at least three months regardless of the underlying etiology. Common indications include albuminuria and a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 [8,9]. 8 to 16% of the world's population has CKD. In affluent countries, diabetes and high blood pressure are the main causes [10]. As kidney function falls, the body's capability to eliminate waste diminishes, resulting to systemic instability, elevated cardiovascular risk, increased vulnerability to infections, and early death [8,9]. The treatment for CKD focuses on detecting it early controlling risk factors such as high blood pressure and proteinuria, and preventing complications such as anemia, metabolic acidosis, and secondary hyperparathyroidism, progressive nephron loss and compensatory hyperfiltration in the remaining nephrons eventually result in irreparable damage; advanced cases typically require dialysis or kidney transplantation for survival [8–10]. Investigating rubella seroprevalence in CKD patients is critical because their altered immune response may affect infection susceptibility and vaccination efficacy. The MMR vaccine is recommended for those with CKD; however, evidence of rubella protection in this population, particularly in Iraq is limited. Local seroprevalence investigations can assist identify at-risk individuals and prescribe preventive measures like timely vaccines, these findings are especially relevant for enhancing national immunization programmes and aligning them with the World Health Organization's guidelines for high-risk populations [11–13]. Therefore, this study aimed to examine the prevalence of rubella virus antibodies (IgM and IgG) among persons with chronic renal disease compared with seemingly healthy controls.

Materials and methods

A case-control study was done on serum samples from 180 chronic kidney disease (CKD) patients admitted to the Dialysis Center at Al-Imamain Al-Kadhimain Medical City in Baghdad, Iraq, and 180 serum samples from individuals considered to be apparently health as the control group. A healthy group was included to determine whether chronic kidney disease was associated with a defective immune response to Rubella compared to individuals with normal renal function.

The study included adult patients with chronic kidney disease aged ≥18 years, excluding child patients. The control group consisted of adults who appeared healthy, excluding children, those with kidney problems, those with chronic diseases, and pregnant women. Enzyme Linked Immunosorbent Assay (ELISA) was used to measure anti-rubella virus IgM and IgG in all samples. The manufacturer of the kits used in this study is NovaLisa (Germany), reference No: RUBM0400 (Rubella virus IgM) and RUBG0400 (Rubella virus IgG).

Ethical Approval: This study was approved by the Ethics Committee of Ibn Sina Unersity of Medical and Pharmaceutical Sciences under approval number ISU6.2.25.

Statistical Analysis

Data description, analysis, and presentation were performed using the Statistical Package for the Social Sciences (SPSS, Version 26; Chicago, Illinois, USA). Statistical analyses were conducted in two main steps. First, the Shapiro Wilk test was used to assess the normality of quantitative variables. Second, based on the distribution of the data, appropriate statistical tests were applied. For normally distributed variables, the independent-samples t-test was used to compare group means, while the chi-square test was used to analyze associations between categorical variables.

A p-value < 0.05 was considered statistically significant for all analyses

Results

In Table 1, it is noted that the percentage of females in the control group (56.2%) is higher than in the patient group (43.8%), while the percentage of males in the patient group (54.2%) is higher than in the control group (45.8%).

The mean of age in the control group was 42.24, and in the patient group, 55.87, as shown in table 2.

Of the 180 individuals in each group, 81 were positive for IgM in the control group and 65 in the patient

Table 1. Sex Distribution Between Control and CKD Patient Groups
Таблица 1. Распределение по полу между Контрольной группой и группами пациентов с ХБП

Sex Пол	Control Контроль (n =180)	Patient Пациенты(n=180)	Total (n=360)	Chi-Square	p-value
Female Женский	82 (56.2%)	64 (43.8%)	146 (40.6%)	3.733	0.053
Male Мужской	98 (45.8%)	116 (54.2%)	214 (59.4%)		

Table 2. Age Distribution Between Control and Patient Groups
Таблица 2. Распределение по возрасту между Контрольной группой и группами пациентов

Group Группа	Mean (years) Среднее значение (в годах)	Std. Deviation Стандартное отклонение	Std. Error of Mean Средняя стандартная ошибка	t-test	p-value
Control Контроль (n = 180)	42.24	16.083	1.199	8.895	<0.001
Patient Пациенты (n = 180)	55.87	12.801	0.954		

group. As for IgG, all samples, whether in the control group or the patient group, were positive, as shown in Tables 3 and 4.

In table 5, it is noted that the mean concentration of IgG in CKD patient groups was higher than in the control group.

Discussion

The rubella virus remains a threat, especially to at-risk groups such individuals with chronic kidney disease (CKD) who have weakened immune systems. ELISA testing of rubella-specific IgG and IgM antibodies is necessary to find out if a group is immune

Table 3. Distribution of Rubella IgM Between Control and CKD Groups
Таблица 3. Распределение IgM краснухи между контрольной группой и группой с ХБП

Status IgM	Control Контроль (n = 180)	Patient Пациент (n =180)	Total Всего (n = 360)	Chi-Square X^2	p-value
Positive	81 (45%)	65 (35.1%)	146 (40.6%)	2.950	0.086
Negative	99 (55%)	115 63.9%)	214 59.4%)		

Table 4: Distribution of Rubella IgG Between Control and CKD Groups
Таблица 4. Распределение IgG к краснухе между контрольной группой и группой с ХБП

Status IgG	Control Контроль (n =180)	Patient Пациенты (n=180)	Total Всего (n = 360)	p-value
Positive	180 (100%)	180 (100%)	360 (100%)	0.001
Negative	0 (0%)	0 (0%)	0 (0%)	

Table 5: Mean Concentration of Rubella IgG (IU/ml) in Control and CKD Groups
Таблица 5. Средняя концентрация IgG краснухи (МЕ/мл) в контрольной группе и группе с ХБП

Group Группа	Mean (IU/ml) Среднее значение	Std. Deviation Стандартное отклонение	Std. Error of Mean Средняя стандартная ошибка	t-test	p-value
Control (n=180)	169.45	117.520358	8.759450	20.666	< 0.001
Patient (n=180)	456.82	144.898447	10.800093		

and to find out if they have recently been infected. People with chronic kidney disease (CKD) may be less likely to respond to vaccines and more likely to get infections. This is why it's important to know how common rubella is in people with CKD in order to make plans for vaccination and infection control. This research not only finds ways to improve care for people with CKD, but it also tells us a lot about their immune systems in terms of measles. The fact that there were more men in the patient group than in the control group might be because the sample was taken at the same time that this group was admitted to the dialysis facility. Poudyal A et al. (2022) and Fu Ruijie et al. (2024) reported similar findings [14,15]. The average age of 55.87 years among patients with chronic kidney disease (CKD) aligns with global trends indicating that CKD predominantly affects middle-aged and older adults. People are more likely to acquire CKD as they get older because they are more likely to have high blood pressure, diabetes, and heart disease. Although many studies show an average age of over 65, an average age of about 56 years may better represent the population's unique demographics and health characteristics, such as earlier onset or different stages of disease. Age significantly impacts chronic kidney disease (CKD), as older adults show a higher prevalence of the condition and display differing rates of progression and outcomes compared to younger patients, with mortality acting as a competing risk factor, people between the ages of 55 and 60 are substantially more likely to have chronic kidney disease (CKD) because that is when they are normally going through a transitional stage. This is because of how they live and other health issues. This age is often documented in CKD cohorts from various regions, indicating that CKD is not solely a condition of the elderly but can also present markedly in middle age [16–19]. Comparable research involving CKD patients in Iraq revealed an average age of almost 55.87 years [20–23], demonstrating that the mean age in this study aligns with existing data on CKD populations in Iraq. The analysis showed no statistically significant relationship between gender or age group and IgG or IgM level, indicating that the immune response against rubella in CKD patients is not influenced by age or gender.

The positive rubella IgM tests in 81 of 180 controls and 65 of 180 chronic kidney disease (CKD) patients likely indicate distinct recent or acute rubella infections or immunological responses between the two groups, rather than an influence of CKD itself. If a person tests positive for rubella IgM, it suggests they have recently been around or infected with the virus. In patients with chronic kidney disease (CKD), immune dysfunction may modify antibody responses, potentially resulting in diminished IgM seropositivity relative to controls if immune activation or infection exposure varies. Studies indicate that seroprotection rates for rubella IgG and IgM can be comparable between CKD patients and controls, but late-stage CKD may decrease antibody titers due to immune compromise. Also, local epidemiology, vaccination status, and exposure history strongly influence IgM prevalence. Thus, the lower IgM positivity in your CKD group could be due to impaired or altered immune responses in CKD or differences in recent exposure rather than CKD protecting from rubella infection [24–26].

The positive rubella IgG results in both the control and CKD groups indicate universal immunity to rubella, this is usually because they have had a natural infection or gotten a shot to protect them from it. Rubella IgG antibodies are made after a person is first exposed to the virus or is immunized against it. They stay in the body for a long time, often their whole lives, and show that the person is protected from getting sick. It is usual for most adult groups to test positive for IgG rubella, and the fact that everyone did is compatible with large-scale vaccination campaigns or earlier virus circulation. Studies have shown that having rubella IgG antibodies helps to tell them apart from having rubella IgM antibodies, which means they were recently infected. IgG alone does not indicate an acute infection; nonetheless, it confirms immunity, which is crucial for assessing an individual's level of protection, particularly in epidemiological and clinical contexts [27,28].

The higher mean rubella IgG level in the chronic kidney disease (CKD) group compared to controls may be due to changes in the immune systems of CKD patients, which can cause unusual rises in antibody levels. Chronic kidney illness is associated with immunological activity and inflammation, perhaps resulting in increased production of IgG and other antibodies. Antigen exposure from illnesses or immunizations can also raise IgG levels. Cross-reactivity and molecular mimicry can raise IgG levels in chronic renal disease patients. Rubella antibodies typically rise in response to viral antigens or as part of an inflammatory immune response. Elevated rubella IgG levels have also been seen in individuals with severe COVID-19, presumably indicating a greater antibody response produced by systemic inflammation. This could happen because, despite being stressed, the immune system becomes more active in producing antibodies during inflammation. Individuals with chronic kidney disease (CKD) frequently have low-grade inflammation and immunological dysregulation, these factors may contribute to increased IgG titers even if overall immunological competence is reduced. As a result, positive rubella IgG responses in CKD patients may indicate both prior viral exposure and ongoing immunological changes, rather than full protection [12,29].

Conclusion

This study discovered that all subjects, both CKD patients and healthy controls, tested positive for rubella IgG, indicating a broad level of immunity, most likely due to previous infection or immunization. However, IgM positive, which typically suggests

a recent infection, was lower among CKD patients. This disparity may be due to the modified immune responses noted in patients with compromised renal function. Additionally, the CKD group exhibited significantly elevated mean IgG titers compared to the healthy group, likely due to the chronic inflammatory condition and immune activation linked to kidney disease.

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