Research Article

Serum Levels Of CYP21A2, CXCL10, NF-Kb P105, And IP-10 In Patients With Cytomegalovirus-Associated Kidney Disease And Recurrent Miscarriage

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Abstract

Background: Chronic HCMV infection is associated with kidney disease and miscarriage. Biomarkers including CYP21A2, CXCL10, NFKB105, and IP-10 may play roles in disease pathogenesis, but limited data exist in Iraqi patients. **Materials and Methods:** A case-control study included 100 participants (75 HCMV patients: 17 males with kidney disease, 58 females with miscarriage; 25 healthy controls). Blood samples were collected from three Baghdad hospitals (December 2025-March 2026). Biomarker levels were measured and analyzed using ANOVA and t-tests ($P \leq 0.01$).**Results:** CYP21A2 was significantly higher in patients (4.78 ± 0.37) than controls (2.36 ± 0.23) ($P \leq 0.01$). Significant differences were observed among groups: CYP21A2 (kidney: 5.34 ± 1.43, abortion: 4.61 ± 0.25, controls: 2.36 ± 0.23); CXCL10 (kidney: 144.87 ± 50.81, abortion: 10.84 ± 0.62, controls: 13.09 ± 1.59); NFKB105 (kidney: 1452.03 ± 593.07, abortion: 1452.03 ± 260.83, controls: 467.43 ± 21.76); IP10 (kidney: 278.31 ± 39.13, abortion: 42.21 ± 3.68, controls: 78.76 ± 3.66). CXCL10 (41.22 ± 13.01 vs 13.09 ± 1.59, $P = 0.03$) and NFKB105 (2043.96 ± 171.88 vs 467.43 ± 21.76, $P \leq 0.01$) were elevated in patients, while IP-10 showed no significant difference ($P = 0.26$).**Conclusion:** Chronic HCMV infection significantly alters CYP21A2, CXCL10, and NFKB105 levels, with distinct patterns between male kidney patients and women with miscarriage. These biomarkers may indicate disease severity. Further validation studies are needed.

Keywords: Cyp21A2, Cytokines complications, Cytomegalovirus (CMV).

Introduction

Cytomegalovirus (CMV) is a common virus belonging to the herpesvirus family. Most infections in healthy adults cause no symptoms or only mild illness. However, CMV infection during pregnancy is important because it can be transmitted to the fetus and may lead to adverse pregnancy outcomes [1]. Cytomegalovirus (CMV) is a member of the herpesvirus family that establishes lifelong latent infection after primary exposure. In healthy individuals, CMV infection is usually asymptomatic or causes a mild mononucleosis-like illness. However, CMV can cause significant kidney-related complications, particularly in immunocompromised patients such as kidney transplant recipients, patients with HIV/AIDS, and those receiving immunosuppressive therapy [2]. CMV is an important cause of morbidity in patients with kidney disease, especially kidney transplant recipients. It may cause direct kidney infection (CMV nephritis), acute kidney injury, CMV syndrome, and possibly even graft malfunction and rejection. Early detection and viral burden surveillance, followed by early antiviral therapy, are crucial for improving patient outcomes and maintaining renal function [3]. CMV infection can result in kidney failure through immune-mediated damage, direct kidney infection, and transplant complications. CMV is a rare cause of kidney impairment in healthy individuals, but it is a significant cause in immunocompromised individuals. Early diagnosis, laboratory confirmation, and antiviral drug therapy are essential for preserving renal function and improving outcomes [4]. It has the potential to induce CMV syndrome, acute kidney injury, direct kidney infection (CMV nephritis), and may contribute to graft malfunction and rejection. To improve patient outcomes and preserve renal function, it is essential to detect and monitor viral burden early, followed by early treatment with antiviral medications [3]. Kidney failure can be caused by CMV infection through direct infection of the kidneys, immune-mediated injury, and transplant complications. CMV is a rare cause of kidney impairment in healthy individuals, but it is a significant cause in immunocompromised individuals. Early diagnosis, laboratory confirmation, and antiviral drug therapy are essential for preserving renal function and improving outcomes [4]. The NF-κB–IFN–CXCL10 inflammatory signaling pathway in CMV disease severity during pregnancy and renal disease provides a mechanistic link between innate antiviral immunity and tissue damage. Endocrine variables (e.g., cortisol pathways involving CYP21A2) may influence this response, but are not main determinants [5]. Decreased CYP21A2 activity may result in reduced cortisol levels, thereby attenuating the physiological repression of NF-κB signaling [6]. During CMV infection, this may result in augmented NF-κB-driven CXCL10 (IP-

10) responses, thereby worsening inflammatory damage to organs such as the placenta and kidney [7]. However, CYP21A2 does not cause CMV infection or its basic pathophysiology, but may operate as a host-response regulator of inflammatory severity [8]. CXCL10, also known as Interferon-gamma-inducible protein-10 (IP-10), is a chemokine secreted by a variety of cells, including immune cells, endothelial cells, and epithelial cells, in response to inflammatory stimuli such as interferon-γ (IFN-γ) [9]. It mainly binds to the CXCR3 receptor and attracts activated T lymphocytes, natural killer (NK) cells and other immune cells to the sites of inflammation [10].

Materials and Methods

A total of 100 whole blood samples were taken from Ibn Al-Baladi Hospital, Al-Alwia Teaching Hospital and Al-Shaheed Al-Sadr Hospital in the period December 2025 to March 2026. Each sample was divided into two parts: the first was used as whole blood for molecular analysis, and the second was centrifuged at high speed to extract serum for immunological testing.

The case-control study included 100 participants, divided into two groups: 75 patients diagnosed with chronic human cytomegalovirus (HCMV) infection (17 males and 58 females) and 25 healthy individuals as the control group (10 males and 15 females). The clinical diagnosis of chronic HCMV infection was made by the specialist physicians based on the patients' clinical symptoms, medical history, and laboratory findings. Serum levels of CYP21A2, CXCL10 (IP-10), and nuclear factor kappa B p105 (NF-κB p105) were evaluated by enzyme-linked immunosorbent assay (ELISA).

Statistical--analysis

Statistical analysis was done via mean±SE. One-way analysis of variance (ANOVA) was used to compare groups and a p-value of < 0.05 was considered statistically significant.

Ethical--approval

Written informed consent was obtained from all subjects before to the trial. The study was approved by the Medical Ethics Committee on April 24, 2026 (Approval No. 244).

Results-and-Discussion

The age distribution of the participants showed that 37 cases (45.3%) were in the age range of 13–27 years as compared with 15 controls (60%) and 41 cases (54.7%) were older than 27 years as compared with 10 controls (40%). There was no statistically significant difference in age between the-groups-(P=.2).

In terms of sex distribution, there were 8 men (10.7%) compared to 10 controls (40%) and 67 females (89.3%) compared to 15 controls (60%). There was a statistically significant difference between patients and controls according to sex (P = 0.01).

In addition, blood pressure status was evaluated among the cases and it was found that 64 (85.3%) of the participants had normal blood pressure and 11 (14.7%) had raised blood pressure. Also, 69 patients (92%) had normal blood glucose levels and only 6 (8%) had increased blood glucose levels (Table 1).

Table 1: Demographic picture among Patients groups

Properties		Abortion(n=58)		Kidney dis (n=17)		Control (n=25)		P-value
		N	%	N	%	N	%	
Age range (years)	13-27	26	44.8	8	47.1	15	60	0.44
	>27	32	55.2	9	52.9	10	40	
Sexes	Male	0	0.0	11	64.7	10	40	0.01
	Female	58	100.0	6	35.3	15	60	
Blood pressure	Normal	49	84.5	12	70.6	25	100	0.01
	High	9	15.5	5	29.4	0	0	
Blood sugar	Normal	52	89.7	14	82.4	25	100	0.01
	High	6	10.3	3	17.6	0	0	

This indicates that age was reasonably similar across the two groups and unlikely to have played a large confounding role in the observed outcomes. The absence of correlation may suggest that the illness being researched affects people of diverse ages without a significant age-related predilection in the population analyzed. The distribution of age did not significantly influence the occurrence of the disease as observed in other research where participants came from similar demographic backgrounds. Results consistent with current research [11] have been reported by Appleby (2023). The over-representation of females can be attributed to biological factors such as hormonal influences, genetic predisposition, differences in immune responses, and sex-specific physiological traits. Furthermore, this aligns with Sharma et al. (2025), who described social and behavioral factors, such as healthcare-seeking behavior and access to medical facilities, as influencing the likelihood of diagnosis and enrolment in clinical research. The large sex imbalance underscores the need to take sex into account as a potential risk factor and/or effect modification when evaluating the study results [12]. The prevalence of normal blood pressure may be attributed to the generally good cardiovascular condition of the participants or the absence of significant cardiovascular comorbidities in most of the subjects. The clinical significance of the discovery that hypertension is a recognized risk factor for numerous adverse health outcomes, such as cardiovascular disease, stroke, and renal failure, cannot be exaggerated. Specifically, approximately one-sixth of the participants had elevated blood pressure. Therefore, monitoring blood pressure in affected individuals may lead to early detection and management of cardiovascular risk. Also, Goorani et al. (2025) indicated that hypertension (HTN) is a common cardiovascular disease among adult populations around the world, with 30–40% of the population being affected, and characterized by a long-term increase in systemic arterial blood pressure. These findings were in line with the literature. This results in a large disease burden and considerably raises the risk of cardiovascular issues and death [13]. In 92% of cases, the blood glucose tests were normal, and in 8 % increased. This suggests that abnormal glucose metabolism was not a common finding in the study group. The low incidence of elevated blood glucose indicates that the study population had no main characteristics of diabetes mellitus or impaired glucose regulation. However, it should be mentioned that there were some participants with high glucose levels, as hyperglycemia is related to the development of metabolic disorders, systemic inflammation and consequent damage to organs. Early detection and treatment of elevated glucose levels can avoid diabetes and its complications. The fact that some persons had high glucose levels is relevant since hyperglycemia is associated with metabolic problems, systemic inflammatory reactions, and persistent damage to key organs [14] (Tian et al., 2025). The demographic and clinical parameters of the study population were not significantly associated with age and case-control status. There was a significant association with sex, with females over-represented in the case group. Furthermore, most of the individuals had normal values of blood pressure and blood glucose, indicating a decent overall metabolic and cardiovascular profile. The data acquired are important for the evaluation of the results of this research and could propose certain demographic and clinical elements that would be necessary to investigate further in future works. As per the results of Senitan et al. (2026), the results of the present investigation showed that most of the people had normal blood pressure and blood glucose levels indicating a satisfactory cardiovascular and metabolic status in general. This information could be useful in interpreting the study results and could help suggest demographic and clinical characteristics that should be addressed in future research [15].

Table 2. Distribution of cases by disease type in male patients. Renal failure with kidney transplantation was in 6 patients (8%). Kidney failure alone was in 4 patients (5.3%). Kidney failure with dialysis and genetic disease was in 7 individuals (9.3%).

In female patients with CMV infection, the distribution according to the number of prior abortions was: 18 patients (24%) had 1 abortion, 15 patients (20%) had 2 abortions, 17 patients (22.7%) had 3 abortions and 8 patients (10.7%) had 4 abortions.

Monitoring of blood pressure in affected patients may help in early detection and control of cardiovascular risk. Hypertension is also frequent in the adult population worldwide, as revealed by Goorani et al. (2025). Hypertension is a cardiovascular disease characterized by a sustained elevation in systemic arterial blood pressure. 30–40 % of the population suffers from hypertension. These findings were in line with previous findings. This results in a large disease burden and considerably raises the risk of cardiovascular issues and death [13]. In 92% of cases, the blood glucose tests were normal, and in 8% they were increased. This suggests that abnormal glucose metabolism was not a common finding in the study group. The low incidence of elevated blood glucose indicates that the study population had no main characteristics of diabetes mellitus or impaired glucose regulation. However, some participants had high glucose levels, as hyperglycemia is associated with the development of metabolic disorders, systemic inflammation, and consequent organ damage. Early detection and

treatment of elevated glucose levels can avoid diabetes and its complications. The fact that some persons had high glucose levels is relevant since hyperglycemia is associated with metabolic problems, systemic inflammatory reactions, and persistent damage to key organs [14] (Tian et al., 2025). The demographic and clinical parameters of the study population were not significantly associated with age or case-control status. There was a significant association with sex, with females over-represented in the case group. Furthermore, most individuals had normal blood pressure and blood glucose values, indicating a decent overall metabolic and cardiovascular profile. The data acquired are important for evaluating the results of this research and could identify certain demographic and clinical elements that would be necessary to investigate further in future work. As per the results of Senitan et al. (2026), the present investigation showed that most people had normal blood pressure and blood glucose levels, indicating a satisfactory cardiovascular and metabolic status in general. This information could be useful in interpreting the study results and could help suggest demographic and clinical characteristics that should be addressed in future research [15].

Table 2. Distribution of cases by disease type in male patients. Six individuals (8%) developed renal failure and underwent kidney transplantation, 4 patients (5.3%) developed renal failure alone, and 7 patients (9.3%) developed renal failure with dialysis and a genetic disorder.

Distribution of female patients with CMV infection by number of previous abortions (n=75) Number of prior abortions n=75 1 24% (n=18) 2 20% (n=15) 3 22.7% (n=17) 4 10.7% (n=8)

Table 2: Prevalence of cases according the type of disease

Condition	N	%
Kidney failure + kidney transplantation	6	8
Kidney failure	4	5.3
Kidney dialysis + genetic problem	7	9.3
1Abortion with CMV infection	18	24
2 Abortions with CMV infection	15	20
3Abortion with CMV infection	17	22.7
4Abortion with CMV infection	8	10.7
Total	75	100

The presence of kidney failure alone in a proportion of patients reflects the burden of chronic renal impairment and its associated health consequences. Vaidya et al. (2026) reported that chronic kidney failure is known to compromise immune function, increase susceptibility to infections, and contribute to multiple systemic complications. In patients with severe renal illness, there are often changes in both innate and adaptive immunity, which may render them more susceptible to opportunistic infections, including viral infections such as cytomegalovirus (CMV) [16].

The subgroup of patients after kidney transplantation is a very important clinical entity. Immunosuppressive medication is frequently given to kidney transplant recipients to prevent graft rejection, which can greatly increase the risk of CMV infection and reactivation. CMV continues to be one of the most frequent viral infections affecting transplant recipients and is associated with unfavorable outcomes such as graft malfunction, higher morbidity, and prolonged hospitalization. So, the finding that 8% of male participants developed kidney failure with kidney transplantation could be a reflection of a population at increased risk for CMV-related problems. Damian et al. (2026) also reported that kidney transplant recipients typically use immunosuppressive drugs to avoid graft rejection, which may enhance their susceptibility to CMV infection and reactivation. CMV is one of the most frequent viral infections in transplant populations and has been associated with poor outcomes, including graft malfunction, increased morbidity, and length of hospital stay [17].

Also, the highest percentage of male patients was represented by individuals with a genetic condition and kidney failure requiring dialysis (9.3%). Patients on dialysis frequently have a compromised immune response due to the impact of uremia, chronic inflammation, and repetitive exposure to invasive medical procedures. The clinical picture can be further complicated by the presence of a genetic abnormality, which increases the risk of infections. This grouping may consequently indicate patients with more complex medical demands and potentially a higher burden of disease. This discovery is consistent with the results of Birlutiu and Birlutiu (2026), who mentioned that patients under dialysis often experience impaired immune function due to uremia, persistent inflammation, and frequent exposure to invasive medical procedures. Their clinical picture may be

further complicated by an underlying genetic illness, and they are at increased risk of infection [18]. The largest proportion of patients reported one abortion, followed closely by those who had three abortions and two abortions. The relatively high rates seen in several abortion categories could suggest a possible association between CMV infection and unfavorable pregnancy outcomes. CMV is known as one of the most important congenital viral infections in the world and has been associated with fetal loss, spontaneous abortion, intrauterine growth retardation, and congenital malformations. Maternal infection may result in placental infection and transmission to the fetus during pregnancy, with adverse pregnancy outcomes. Mocanu et al. (2024) reported CMV as the leading congenital viral infection worldwide, which is linked to fetal loss, spontaneous abortion, growth limitation, and congenital anomalies. Maternal infection can cause placental and fetal infection, which can result in severe pregnancy outcomes [19].

Repeated abortions in a large number of infected women may reflect continued exposure to risk factors linked with CMV infection or the possibility of the contribution of CMV to recurrent pregnancy loss. Although the present data do not show causality, the findings are consistent with earlier publications implicating CMV as a possible contributor in unfavorable reproductive outcomes. Thus, women with repeated abortions may benefit from complete screening and assessment of infectious reasons, including CMV, especially in populations with high seroprevalence. These reports are in agreement with Mamand and Jawad (2026), who concluded that extensive screening for infectious agents, notably CMV, may be beneficial for women with repeated abortions, especially in areas or populations with high CMV seroprevalence [20].

The fact that 10.7% of women having had four previous abortions is clinically important, as recurrent pregnancy loss is associated with considerable physical, psychological, and social effects. Women who have had several miscarriages usually undergo extensive testing to look for infections, genetic problems, hormonal imbalances, immune system problems, or anatomical abnormalities. The presence of CMV infection in these women may require further study to identify its contribution to recurring reproductive failure. Alhasnawy and Al-Essawi reviewed that recurrent abortion, or recurrent pregnancy loss, is a complex reproductive disorder with multiple contributing factors that affects approximately 1–3% of women of reproductive age and remains a major challenge in clinical and public health [21].

The results indicated that the male participants were primarily represented by a variety of chronic renal illnesses, such as kidney transplantation and dialysis-associated diseases, which are associated with a higher risk of contracting CMV due to immune system impairment. A significant number of female patients reported having undergone one or more abortions, which implies a potential correlation between CMV infection and unfavorable reproductive outcomes. In high-risk patient populations, these findings underscore the importance of targeted clinical surveillance, infection screening, and prophylaxis. The results of the current study are consistent with the fact that a significant proportion of female patients underwent one or more abortions, as demonstrated by Hidaka et al. (2025). This suggests that CMV infection may be associated with adverse reproductive outcomes. These data underscore the importance of preventative strategies, specific clinical surveillance, and screening for infectious diseases in high-risk populations [22].

Table 3 shows the expression levels of the studied biomarkers among male patients with CMV-associated diseases and female patients with CMV-related miscarriages compared with healthy controls. The mean level of CYP21A2 was significantly higher in patients (4.776 ± 0.37) than in the control group (2.36 ± 0.23), demonstrating a highly significant difference ($P \leq 0.01$).

Similarly, the mean level of CXCL10 was elevated in patients (41.22 ± 13.01) compared with controls (13.09 ± 1.59), showing a statistically significant difference ($P = 0.03$). In addition, the mean level of NFKB105 was markedly higher in patients (2043.96 ± 171.88) than in healthy controls (467.43 ± 21.76), with a highly significant difference ($P \leq 0.01$).

In contrast, no significant difference was observed in the mean level of IP-10, which was 95.72 ± 21.76 in patients and 78.76 ± 3.66 in controls ($P = 0.26$).

Table 3: The mean levels of studied parameters between cases and controls

Parameters	Group	Mean	SE	T-test	P-value
Cyp21A2 (pg/ml)	Cases	4.776	0.37	5.4	≤0.01
	Control	2.36	0.23		
CXCL10 (pg/ml)	Cases	41.22	13.01	2.14	0.03
	Control	13.09	1.59		

NFKB105 (pg/ml)	Cases	2043.96	171.88	5.78	≤0.01
	Control	467.43	21.76		
IP10 (pg/ml)	Cases	95.72	14.66	1.12	0.26
	Control	78.76	3.66		

CYP21A2 encodes steroid 21-hydroxylase, an enzyme involved in adrenal steroid biosynthesis, particularly the synthesis of cortisol and aldosterone. Increased expression of this gene may reflect activation of endocrine and stress-response mechanisms triggered by chronic infection and inflammation. Viral infections often stimulate the hypothalamic-pituitary-adrenal axis, leading to changes in steroid hormone metabolism aimed at regulating immune responses and limiting excessive inflammation. Wozniak, et al.(2025) revealed that same findings indicate that CYP21A2 gene, which encodes the 21-hydroxylase enzyme, plays a crucial role in adrenal steroid biosynthesis. Nevertheless, the physiological significance of CYP21A2 transcript variability and their tissue-specific expression profiles in domestic animals, such as cattle, and humans, has not been investigated [23]. An adaptive physiological response to CMV-induced immunological activation in patients could be represented by an increased expression of CYP21A2. Additionally, immunological dysregulation and inflammatory disorders have been linked to altered steroid metabolism, which implies that CYP21A2 expression may be a potential indicator of disease activity or the host response to CMV infection.

Hormonal and inflammatory changes that accompany elevated expression of CYP21A2 may also contribute to adverse pregnancy outcomes in women with recurrent losses. Bacila et al. (2025) confirmed that the expression of CYP21A2 could be a biomarker of disease activity or host immunological responses during CMV infection. In females with recurrent miscarriages, increased CYP21A2 expression could be related to hormonal and inflammatory changes [24].

Interferon-γ and inflammatory cytokines stimulate monocytes, endothelial cells, fibroblasts, and other immune cells to create CXCL10. It recruits activated T lymphocytes, natural killer cells and macrophages to areas of infection. High levels of CXCL10 are frequently found during viral infections and are regarded as markers of active immune response. As a pro-inflammatory chemokine, CXCL10 is a key regulator of antiviral host defence, according to Elemam et al. (2022). It binds its receptor, CXCR3, and promotes transportation of activated immune effector cells to sites of infection [25].

The elevated CXCL10 expression in the present study demonstrates that CMV infection produces a robust inflammatory and antiviral immune response. This conclusion is biologically feasible since CMV infection triggers interferon-mediated pathways resulting in upregulation of chemokine synthesis . Previous investigations have revealed higher levels of CXCL10 in patients with active CMV infection, transplant recipients with CMV reactivation and women with unfavourable pregnancy outcomes associated with viral infections. Thus, the observed rise in CXCL10 may be indicative of increased immune cell recruitment and ongoing inflammatory activity associated with CMV pathogenesis . Deroche et al. (2025) shown that the increased expression of CXCL10 during CMV infection is a marker of a strong antiviral and interferon-dependent immune response, which promotes the recruitment and activation of important immune cells such as T cells and NK cells to the site of infection [26].

The NF-κB pathway controls the expression of several genes involved in inflammation, immunological responses, cell survival and antiviral defence. This route is characteristic of numerous viral diseases such as CMV. CMV can directly trigger NF-κB signalling to promote viral replication and persistence and also induces host inflammatory responses. Kesika et al. (2024) further showed that CMV (Cytomegalovirus) has developed a complex and paradoxical connection with the NF-\(\kappa \)B pathway. It depends on this signalling cascade for viral replication and persistence while exploits it to cause host inflammation, which facilitates the virus dissemination and reactivation [27].

Increased expression of NFKB105 in the patient group suggests activation of inflammatory signalling pathways in CMV infection. Activation of NF-κB can lead to the production of cytokines, recruitment of leukocytes and tissue inflammation. Over-activation of the NF-κB pathway has been linked with disease progression and immune dysfunction in chronic renal sickness patients and transplant recipients . Similarly, dysregulated inflammatory signalling may increase the risk of miscarriage and decreased placental function in pregnant women. Thus NFKB105 can be employed as a measure of the inflammatory burden of CMV infection. Savitz et al. (2024) reviewed the detailed pathophysiology of Cytomegalovirus (CMV) and the key role of Nuclear Factor-kappa B (NF-κB) in inflammation. NF-κB is a major transcription factor that is commonly employed and activated in CMV infections [28].The considerable increase in NFKB105 expression in the patient cohort is a powerful marker for

activation of inflammatory signalling pathways in the context of CMV infection. Activation of NF-κB can lead to the production of cytokines, recruitment of leukocytes and tissue inflammation. Over-activation of the NF-κB pathway has been linked with disease progression and immune dysfunction in chronic renal sickness patients and transplant recipients . Similarly, dysregulated inflammatory signalling may increase the risk of miscarriage and decreased placental function in pregnant women. Thus NFKB105 can be employed as a measure of the inflammatory burden of CMV infection. Savitz et al. (2024) reviewed the detailed pathophysiology of Cytomegalovirus (CMV) and the key role of Nuclear Factor-kappa B (NF-κB) in inflammation. NF-κB is a major transcription factor that is frequently employed and activated during CMV infections [28].
Several factors could explain this finding. First, IP-10 expression may vary according to the stage, severity, or duration of CMV infection. Second, differences in host immune status, underlying kidney disease, transplantation history, or reproductive factors may influence IP-10 production. Third, the timing of sample collection relative to infection onset may affect circulating chemokine levels. Therefore, while IP-10 is known to participate in antiviral immune responses, its role in the studied population may be less consistent than that of CXCL10 and NFKB105. The data presented with (Fernández et al. 2024) who stated that because its expression fluctuates based on the infection's stage, patient immune health, and sample timing, IP-10 is generally a less reliable or consistent indicator of antiviral activity in specific populations than CXCL10 or NFKB105 [29].

Table 4 presents the cytokine concentrations among females with CMV infection according to the number of previous abortions. Among women who had experienced one abortion (n = 18), the mean levels of CYP21A2, CXCL10, NFKB105, and IP-10 were 3.93 ± 0.44, 10.71 ± 0.71, 1817.04 ± 523.62, and 46.62 ± 9.75, respectively.

Among women with two abortions (n = 15), the mean levels of CYP21A2, CXCL10, NFKB105, and IP-10 were 4.96 ± 0.49, 11.82 ± 2.01, 761.09 ± 328.05, and 41.57 ± 4.36, respectively.
In women who had experienced three abortions (n = 17), the mean levels of CYP21A2, CXCL10, NFKB105, and IP-10 were 4.76 ± 0.47, 10.43 ± 0.71, 1841.01 ± 557.78, and 39.37 ± 6.07, respectively.
Among women with four abortions (n = 8), the mean levels of CYP21A2, CXCL10, NFKB105, and IP-10 were 5.13 ± 0.74, 10.15 ± 0.60, 1099.66 ± 607.60, and 39.50 ± 4.53, respectively.
No statistically significant differences were observed in the levels of CYP21A2, CXCL10, NFKB105, or IP-10 according to the number of abortions, with P-values of 0.35, 0.82, 0.34, and 0.87, respectively.

Table 4: The mean levels of studied parameters among aborted women with CMV infection

Condition		Cyp21A2	CXCL10	NFKB105	IP10
1st abortion with CMV infection	Mean	3.93	10.71	1817.04	46.62
	N	18	18	18	18
	SE	0.44	0.71	523.62	9.75
3rd abortion with CMV infection	Mean	4.76	10.43	1841.01	39.37
	N	17	17	17	17
	SE	0.47	0.73	557.78	6.07
2nd abortion with CMV infection	Mean	4.96	11.82	761.09	41.57
	N	15	15	15	15
	SE	0.49	2.01	328.05	4.364
4th abortion with CMV infection	Mean	5.13	10.15	1099.66	39.50
	N	8	8	8	8
	SE	0.74	1.44	607.60	4.53
P-value		0.35	0.82	0.34	0.87

CYP21A2 plays an important role in steroid hormone biosynthesis and is involved in the production of glucocorticoids and mineralocorticoids. Increased expression may indicate activation of hormonal pathways in response to physiological stress, inflammation or infection. The slightly higher levels reported in women with many abortions may suggest enhanced endocrine response to repeated reproductive stress. The identical results reported by Wozniak, et al.(2025) suggest that the expression of CYP21A2 is probably induced by the CMV infection itself and not by the number of pregnancy losses. The absence of a significant correlation further indicates that hormonal responses in CMV-infected women might be essentially similar independent of a history of abortion [23].

CXCL10 is an important chemokine of the antiviral immune response and recruitment of inflammatory cells. Elevated CXCL10 expression has been shown in viral infections such as CMV and is involved in the recruitment of activated T lymphocytes and natural killer cells to the site of infection. The comparable CXCL10 levels in all abortion groups imply that CMV-mediated immune activation occurs independently of the number of previous pregnancy losses. This finding might point to viral infection as the main contributor to the CXCL10-mediated inflammatory response, rather than reproductive history. The results of this investigation are consistent with the results of Nikčević et al. (2026). who noted that comparable levels of CXCL10 across all abortion groups suggest CMV-driven immune activation continues regardless of the number of prior pregnancy losses [30]. NFKB105 is a major regulator of inflammatory and immunological responses and has been shown to be activated after CMV infection . All groups demonstrated increased values supporting the importance of NF-κB signalling in CMV pathogenesis. However, the lack of a clear trend with increasing frequency of abortions shows that recurrent pregnancy loss does not directly alter NFKB105 expression in this population. However, CMV-associated inflammatory activation may be the main determinant of biomarker levels. The present results were in agreement with (Liu et al, 2025) who reported no clear association between abortion number and NFKB105 expression, implying that recurrent pregnancy loss is not an independent predictor of NFKB105 expression in this cohort. Whereas, alterations in biomarker levels might be mainly driven by CMV-induced inflammatory-activation,[31].

The high range seen for NFKB105 levels further implies heterogeneity in individual immunological responses to CMV infection. Such differences in factors such as viral load, duration of infection, host genetic background, immunological system, and concurrent medical disorders may contribute to these differences and mask any links with abortion history. As noted by Venturini and Breuer (2025), the changes in NFKB105 levels further reflect the heterogeneity of host immunological responses to CMV infection. Such diversity may be affected by viral load, chronicity of infection, genetic susceptibility, immunological function, and other health problems [32].

IP-10 is an important mediator of antiviral immune responses and is often elevated during viral infections and inflammatory conditions. The relatively similar levels observed across all groups suggest that IP-10 production remains stable regardless of abortion history. This finding may indicate that CMV infection induces a consistent immune response among affected women, irrespective of the number of prior pregnancy losses. These observations were consistent with (Poveda, et al. 2024) who found that IP-10 is a pro-inflammatory chemokine that helps regulate immune responses and cell migration. While it plays an important role in maternal-fetal immune tolerance and gestational processes, medical studies suggest that baseline or induced IP-10 production levels are generally consistent across individuals, irrespective of whether they have experienced previous medical or spontaneous abortions [33].

ANOVA analysis demonstrated significant differences ($P \leq 0.01$) in the levels of the investigated biomarkers among male patients with kidney disease (n = 17), women with abortion (n = 58), and healthy controls (n = 25). The mean level of CYP21A2 was 5.34 ± 1.43 in kidney disease patients and 4.61 ± 0.25 in aborted women, compared with 2.36 ± 0.23 in the healthy control group. Similarly, the mean level of CXCL10 was significantly higher in male kidney disease patients (144.87 ± 50.81) than in aborted women (10.84 ± 0.62) and healthy controls (13.09 ± 1.59). Furthermore, the mean level of NFKB105 was 1452.03 ± 593.07 in kidney disease patients and 1452.03 ± 260.83 in aborted women, both of which were significantly elevated compared with the healthy control group (467.43 ± 21.76). Likewise, the mean level of IP10 was 278.31 ± 39.13 in kidney disease patients and 42.21 ± 3.683 in aborted women, compared with 78.76 ± 3.66 in healthy controls. These differences were statistically significant ($P \leq 0.01$), as shown in Table 6.

Table 6: ANOVA analysis of study parameters between patient groups

Parameters	Groups	N	Mean	SE	ANOVA P-value
Cyp21A2	Kidney diseases	17	5.34	1.43	≤0.01
	Abortion	58	4.61	0.25	
	Control	25	2.36	0.23	
CXCL10	Kidney diseases	17	144.87	50.81	≤0.01
	Abortion	58	10.84	0.62	
	Control	25	13.09	1.59	
	Kidney diseases	17	4063.47	593.07	≤0.01

NFKB105	Abortion	58	1452.03	260.83	
	Control	25	467.43	21.76	
IP10	Kidney diseases	17	278.31	39.13	≤0.01
	Abortion	58	42.21	3.683	
	Control	25	78.76	3.66	

The elevated CYP21A2 levels may reflect the combined effects of CMV infection, renal dysfunction, metabolic stress, and systemic inflammation. Similarly, in women with abortion, elevated CYP21A2 may indicate endocrine and immunological disturbances associated with pregnancy complications. The lower levels in healthy controls support the hypothesis that CYP21A2 upregulation occurs in response to disease-related stress and inflammatory processes. The present findings were in accordance with (Cemerkaite & Lizdeniene, 2024), who reported that increased CYP21A2 expression may be attributable to the combined effects of CMV infection, impaired renal function, metabolic stress, and systemic inflammatory responses. In the same vein, the increased CYP21A2 expression observed in women who have undergone abortion may be indicative of immune disturbances and endocrine dysregulation that contribute to adverse pregnancy outcomes.[35]. The discovery that kidney disease patients exhibited higher CYP21A2 levels than women who had abortions may indicate that individuals with chronic renal impairment experience a greater degree of systemic stress and immune dysregulation [34]. Hirt-Minkowski and Schaub (2024) observed that elevated CXCL10 levels in kidney disease patients may indicate heightened immune activation as a consequence of a combination of renal pathology and CMV infection. Chronic kidney disease is characterized by immune dysfunction and persistent inflammation, which can enhance chemokine production. Additionally, recurrent immune stimulation is frequently observed in transplant recipients and dialysis patients, which may contribute to elevated CXCL10 expression [36].

In 2025, Bilal proposed that the nearly identical mean values observed in kidney disease patients and women with abortion suggest that NF-κB activation may represent a common pathogenic pathway linking CMV infection to both renal complications and deleterious reproductive outcomes. Chronic inflammation, fibrosis, and tissue injury are all exacerbated by NF-κB activation in kidney disease. In pregnancy, the risk of miscarriage may be elevated by the potential impairment of placental function and foetal development due to excessive inflammatory signalling. In CMV-related disease processes, independent of the affected organ system, the central role of NF-κB-mediated inflammation is underscored by these findings [37].

The disparities in immune modulation during pregnancy may be indicated by the relatively low levels of IP-10 observed in women who had experienced abortion. A meticulously managed immunological milieu is essential throughout pregnancy to support foetal development, and alterations in cytokine production may influence pregnancy outcomes. The reduced IP-10 levels reported in miscarriage patients relative to those in kidney disease patients, as elucidated by Ma et al. (2025), suggest that the inflammatory mechanisms involved in miscarriage may differ from those linked to chronic renal illness.It is noteworthy that healthy controls demonstrated elevated levels of IP-10 compared to women who experienced abortion. This discovery may indicate physiological variance, immunological regulation during pregnancy, or differences in sample characteristics. Further work is required to clarify the biological implications of this observation [38].

The inflammatory response was most pronounced in male patients with kidney disease, particularly in terms of CXCL10 and IP-10 levels. This discovery was consistent with the hypothesis of (Li, et al. 2023) that renal involvement may be linked to a larger inflammatory burden and a stronger systemic immune activation. Chronic kidney disease, transplantation, and dialysis are all conditions that have been identified as potentially exacerbating CMV-related inflammation and altering immune function [39].

Furthermore, women who experienced abortion demonstrated significant alterations in biomarkers, notably increased levels of CYP21A2 and NFKB105. This indicates that endocrine dysregulation and inflammatory signalling are significant factors to reproductive problems linked to CMV. Conversely, (Rotundo et al., 2025) posited that the reduced levels of CXCL10 and IP-10 relative to those in kidney disease patients may suggest that the immunological mechanisms implicated in miscarriage are divergent [40].

The results of the ANOVA are clearly indicative that markers of steroid metabolism, chemokine signalling and inflammatory regulation are dramatically altered in CMV associated kidney disease and CMV associated abortion. The patient groups had elevated levels of CYP21A2 and NFKB105 compared to the controls. These data imply that the activation of NF-κB and endocrine-immune interactions are implicated in the pathogenesis of CMV. Dobrer et al. (2024) found that women with renal illness had far higher levels of CXCL10 and IP-10, suggesting a more substantial inflammatory response and immunological activation than women who had

abortions. Together these data support a role for cytokine dysregulation and inflammatory signalling in the aetiology of CMV-associated diseases and suggest these indicators may have relevance in understanding disease processes and monitoring clinical outcomes [41].

There were significant alterations in biomarkers in abortion patients, most notably higher levels of CYP21A2 and NFKB105. This indicates that the primary drivers of CMV-associated reproductive abnormalities are endocrine disruption and inflammatory signalling. However, Rotundo et al. (2025) hypothesised that the decrease of CXCL10 and IP-10 compared to those with kidney sickness would imply various immune pathways involved in miscarriage [40].

ANOVA analysis showed that biomarkers involved in steroid metabolism, chemokine signalling and inflammatory regulation are significantly modified in CMV linked kidney disease and CMV related abortion. The two groups of patients showed higher levels of CYP21A2 and NFKB105 compared to healthy controls, showing that NF-κB activation and endocrine-immune cross-talk are significant in the pathogenesis of CMV. those with renal disease had considerably greater levels of CXCL10 and IP-10, markers of inflammation and immunological activation, than those with abortions (Dobrer et al., 2024). Our results corroborate the importance of cytokine dysregulation and inflammatory signalling in the aetiology of CMV-related illness and highlight the potential utility of these biomarkers in understanding disease processes and predicting clinical outcomes,[41,42].

The ANOVA results provide compelling evidence for significant changes in biomarkers related to steroid metabolism, chemokine signalling and inflammatory regulation in CMV-associated kidney disease and CMV-associated abortion. Both patient groups had increased levels of CYP21A2 and NFKB105 compared to healthy controls, indicating a possible role for NF-κB activation and endocrine-immune interactions in the pathogenesis of CMV. Dobrer et al. (2024) reported that CXCL10 and IP-10 levels were considerably higher in women with renal disease compared to those who had an abortion, suggesting a stronger inflammatory response and immunological activation. These studies imply a role for cytokine dysregulation and inflammatory signalling in the aetiology of CMV-associated diseases and suggest that these markers may be useful in understanding disease processes and monitoring clinical outcomes [41].

There were significant alterations in biomarkers in abortion patients, most notably higher levels of CYP21A2 and NFKB105. This indicates that the primary drivers of CMV-associated reproductive abnormalities are endocrine disruption and inflammatory signalling. However, Rotundo et al. (2025) hypothesised that the decrease of CXCL10 and IP-10 compared to those with kidney sickness would imply various immune pathways involved in miscarriage [40].

ANOVA analysis suggests that biomarkers related to steroid metabolism, chemokine signalling and inflammatory modulation are significantly altered in CMV associated kidney disease and CMV related abortion. Both patient groups showed increased levels of CYP21A2 and NFKB105 compared to healthy controls, suggesting a significant involvement of NF-κB activation and endocrine-immune interaction in the pathogenesis of CMV. Dobrer et al. (2024) discovered that patients with renal disease had significantly higher levels of CXCL10 and IP-10, suggesting a greater inflammatory response and immunological activation compared to women who had abortions. These studies collectively confirm the role of cytokine dysregulation and inflammatory signalling in the aetiology of CMV-related illnesses, and highlight the potential utility of these biomarkers to understand disease mechanisms and track clinical outcomes [41,42,43].

Conclusions

- Significant variations in the levels of CYP21A2, CXCL10, NF-κB p105, and IP-10 were seen in the study's healthy control group, women who had abortions, and patients with renal illness ($P < 0.01$).
- Kidney disease is important: Compared to healthy controls and women who had abortions, patients with kidney disease had significantly higher levels of CXCL10, NF-κB p105, and IP-10, indicating an intense immune and inflammatory response.
- Women who had abortions showed either intermediate or elevated levels of biomarkers, particularly CYP21A2 and NF-κB p105, in comparison to the control group. Miscarriage might be triggered by an imbalance between the immune system and the endocrine system.
- The biomarker levels in the healthy control group were consistently the lowest, suggesting that kidney disease and abortion are associated with elevated levels of inflammatory and CYP21A2-related indicators. Common inflammatory pathways may be at work here, influencing the disease's progression.

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