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ORIGINAL ARTICLE

Detection of Parvovirus B19 in Patients with End Stage Renal Disease

Rana Ali Ibrahim [1,*] and Israa Hashim Saadoon [1]

[1]*Department of Medical Microbiology, College of Medicine, Tikrit University, Tikrit, IRAQ*

[*]*Corresponding author email: Rana.firas.m@gmail.com*

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ABSTRACT

Background: Dialysis patients are more vulnerable to viral infections, including Human Parvovirus B19, which is the only human pathogenic parvovirus. It is highly erythrotropic and preferentially replicates in erythroid progenitor cells. Parvovirus B19 is associated with kidney disease in three settings: Acute glomerulopathy, anaemia in end-stage renal disease, and kidney transplantation. This study aimed to detect parvovirus B19 infection among individuals undergoing dialysis.

Methods: A case-control study was carried out in Kirkuk from April 4 to November 11, 2023. This involved patients with chronic renal failure admitted to Kirkuk Teaching Hospital/Haemodialysis Center. A questionnaire was used to collect clinical data such as age, gender, body mass index, and medical history. Molecular detection of parvovirus B19 was done using Real-time PCR.

Results: The study involved a predominance of male patients (75%) compared to females (25%). Most patients were 60 years or older (45%). In terms of Body mass index, the majority fell into the 20-25 range. Patients with chronic renal failure frequently reported hypertension (60%), followed by diabetes mellitus (28.33%), and cardiovascular disease (11.66%). Results highlighted a significant increase in Parvovirus B19 infection rates with prolonged dialysis, and RT-PCR detected Parvovirus B19 in 18.3% of patients.

Conclusion: Parvovirus B19 was detected in end-stage renal disease and could significantly contribute to the development and progression of the disease.

Key words: Haemodialysis; Human parvovirus B19; Real time PCR; End stage renal disease.

INTRODUCTION

Chronic kidney disease (CKD) is increasingly recognized as a significant global public health issue due to its high prevalence, substantial complication rates, elevated healthcare costs, and poor patient outcomes. Over 850 million people across the globe are affected by some form of CKD, which is nearly double the number of individuals living with diabetes mellitus and 20 times more than those diagnosed with cancer [1]. Patients with CKD are more likely to develop various issues, including anaemia, metabolic acidosis (poor acid excretion by the kidneys), and cardiovascular disease (CVD), which complicate patient treatment [2].

The postulated role of parvovirus B19 infection is based on the temporal relationship between viral infection and renal failure. Patients on dialysis may be more susceptible to both acute and chronic anaemia following parvoviral infection. Factors that predispose this population to the consequences of parvovirus B19 infection include poor immunological response, insufficient erythropoietin production, and likely lower erythrocyte survival [3].

Parvovirus B19 is a single-stranded DNA virus that belongs to the family Parvoviridae, subfamily Parvovirinae, and genus Erythrovirus. The Parvovirus B19V genome encodes three proteins: NS1, a nonstructural protein, and VP1 and VP2, which are viral capsid proteins. Parvovirus B19 infection is associated with various clinical signs. Parvovirus B19-related conditions include erythema infectiosum, typically in children, aplastic crises, especially in individuals with underlying hemolytic conditions, hydrops fetalis during pregnancy, arthralgia, and arthritis [4].

The virus has been linked to acute glomerulopathy as well as anaemia in those with end-stage renal disease and kidney transplant (KT) recipients. Parvovirus B19 has also been identified as a potential cause of renal damage. Several instances of glomerulonephritis (GN) following a primo-infection with parvovirus B19 have been documented. It can cause a range of symptoms, from mild febrile illness to life-threatening medical problems. The virus is usually spread through respiratory droplets; recurrent blood transfusions and immunosuppression are also risk factors for parvovirus B19 infection. When infection is suspected, patients should be tested for Parvovirus B19 infection using polymerase chain reaction (PCR) rather than IgG and IgM antibody-based serology [5].

MATERIAL AND METHODS

A case-control study was conducted in Kirkuk City from April 4 to November 11, 2023, involving 60 patients with chronic renal failure admitted to the Kirkuk Teaching Hospital/Hemodialysis Center and 30 healthy individuals serving as a control group. A questionnaire was used to collect clinical data such as age, gender, body mass index (BMI), and medical history; patients who tested positive for hepatitis were excluded. Two milliliters of venous whole blood were drawn from all participants into 2% EDTA-Na2 anticoagulant tubes. DNA extraction from whole blood was performed using the nucleic acid extraction kit from New England Biolabs (NEB, England) following the manufacturer's instructions. The parvovirus B19 DNA was amplified using primers NS1 F (5´ - GTTCAGCAGAATCAATTTGTCG - 3´) and NS1 R (3´ - AGAAAAGGGATTAGAAGCTCC - 3´).

Five microliters of extracted DNA were added to an amplification mixture containing 12.5µof Taq 2X master mix, 1µL of Forward Primer, 1µof Reverse Primer, and nuclease-free water, making a total volume of 25 µ. The thermocycling conditions for polyomavirus BK included an initial denaturation of 1 minute at 95 °C followed by 35 amplification cycles consisting of denaturation for 15 seconds at 95 °C, annealing for 30 seconds at 52 °C, and a final extension cycle of 50 seconds at 72 °C.

The statistical analysis was conducted using Chi-square tests and T-tests. The interpretation criteria for T-tests were as follows:

- **P-value** ≤ 0.01: Highly Significant (**HS**)
- $0.01 <$ **P**-value ≤ 0.05: Significant **(S)**.
- **P-value** > 0.05: Non-significant (**NS**)

RESULTS

The current data demonstrated that 45 (75%) of the patients involved in the study were male, while 15 (25%) were female. Conversely, the control group was predominantly male, which was statistically non-significant.

The study revealed that most patients were in the age group of 60 years or older, with 27 (45%) in this group, followed by 18 (30%) between the ages of 51 and 60, and 5 (8.35%) in the 41-50 age group. The lowest representation was in the age group of 20 years or younger, with 2 (3.33%). In the control group, the 31-40 age group comprised 10 (33.33%), while the lowest age group was also 20 years or younger, containing 2 (6.66%). The results were statistically non-significant.

Regarding Body Mass Index (BMI), the results from the cur-

Table 1. Demographic data Distribution Among Patients and Control Group

Category	Group	Patients		Control		P value
		No.	%	No.	%	
Sex	Male	45	75.00	21	70.00	0.61
	Female	15	25.00	9	30.00	
Age Group (Years)	≤ 20	2	3.33	2	6.66	0.48
	21-30	4	6.66	4	13.33	
	31-40	4	6.66	10	33.33	
	41-50	5	8.35	7	23.33	
	51-60	18	30.00	3	10.00	
	≥ 60	27	45.00	4	13.33	
Body Mass Index	< 20	6	10.00	2	6.66	0.78
	20-25	27	45.00	20	66.66	
	26-30	20	33.33	7	23.33	
	> 30	7	11.67	1	3.33	

rent study indicated that most patients had a BMI between 20 and 25, accounting for about 45%. Patients with a BMI between 26 and 30 represented the second-highest rate at 33.33%, while the lowest proportion of patients had a BMI below 20. In the control group, the BMI between 20 and 25 accounted for about 66.66%, whereas those with a BMI greater than 30 had the lowest proportion at 3.33%. However, the results were statistically non-significant, as indicated in Table 1.

Regarding comorbidities, the results showed that patients with chronic renal failure were most likely to complain of hypertension at 36 (60%), followed by diabetes mellitus at 17 (28.33%), and 7 (11.66%) were diagnosed with cardiovascular disease, as demonstrated in Figure 1.

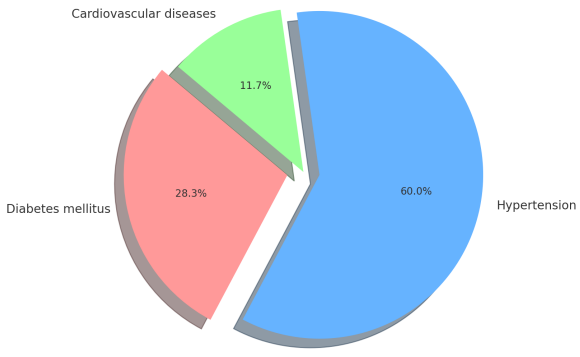

Figure 1. Distribution of comorbidity factors among patients with chronic renal failure

Figure 2 shows the relationship between the duration of dialysis and the percentage of patients infected with Parvovirus B19. The infection rate increases significantly with longer dialysis durations, with the highest rate observed in patients undergoing dialysis for more than three years.

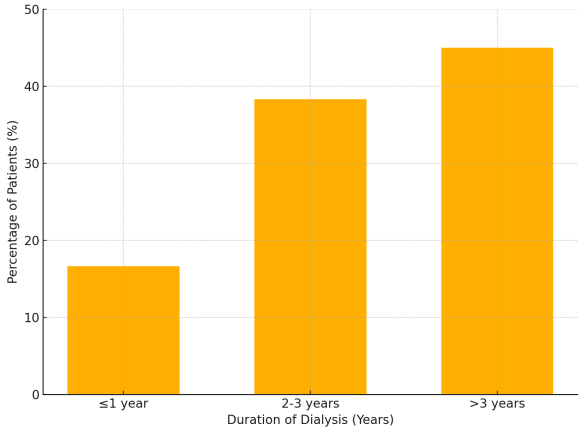

Figure 2. Relationship between the duration of dialysis and the percentage of patients infected with Parvovirus B19.

The current data indicates that parvovirus B19 was detected in 11 (18.3%) of the patients using RT-PCR. Furthermore, Figure 3 shows the real-time curves of parvovirus B19 DNA detection.

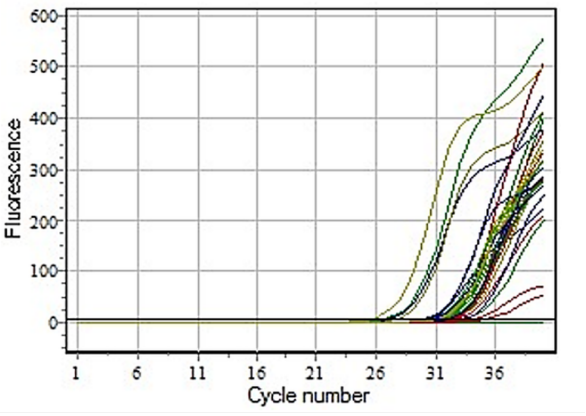

Figure 3. Real time curves of parvovirusB19 DNA detection

DISCUSSION

End-stage renal disease is the final stage of CKD, characterized by irreversible loss of kidney function requiring dialysis or kidney transplantation for survival. It is a major global health concern, with an increasing prevalence due to the rising burden of diabetes mellitus, hypertension, and other chronic conditions. ESRD significantly impacts patients' quality of life, leading to complications such as anaemia, cardiovascular disease, bone mineral disorders, and an increased risk of infections [6].

The current study revealed that the highest rate of patients with ESRD were males (75%), which is consistent with studies conducted in the Southern provinces of Iraq [7], as well as a study in Sulaimani City that indicated the prevalence of ESRD was higher among males compared to females apart from Halabja and Kalar, in which the prevalence was higher among females. This could be due to lifestyle differences between both genders, such as dietary protein intake, salt consumption, and smoking [8].

The present study showed that the majority of patients were in the age group of 60 years and older (45%) which is comparable to the previous study has shown that the risk of CKD increases significantly in people over the age of 65. The rising prevalence of CKD among individuals over the age of 65 is linked to a higher incidence of co-morbid conditions, such as cardiovascular disease, diabetes mellitus, and hypertension [9]. The current findings indicate that the majority of patients had a Body Mass Index (BMI) within the range of 20-25 (45%). This observation aligns with previous studies. For instance, Han et al. reported that the mean BMI of 67 haemodialysis patients was 21.2 ± 2.6 kg/m² [10].

Another study by Agarwal found that among 368 hemodialysis patients, 33% had a normal BMI (18.5-25 kg/m²), 30% were overweight (25-30 kg/m²), and 33% were obese (BMI >30 kg/m²) [11]. Consequently, these studies suggest that a significant proportion of patients undergoing hemodialysis have a BMI within or below the normal range.

The current data indicates that parvovirus B19 was detected in 18.3% of the patients. The precise impact and significance of Parvovirus B19 infection in patients with CKD remains unknown. Nevertheless, there are numerous reasons to suspect that parvovirus could be a substantial pathogen in these populations. Anaemia is a predictable outcome of chronic renal insufficiency and is a common complication of parvovirus B19 infection. In CKD patients, anaemia results from factors such as inadequate erythropoietin production and reduced red blood cell lifespan. Parvovirus B19 can exacerbate anaemia by infecting erythroid progenitor cells, leading to pure red cell aplasia.[12]. Furthermore, individuals suffering from renal failure and undergoing dialysis experience disturbances in their immune system as a result of the immunosuppressive effects of uremia, inadequate synthesis of erythropoietin, and a substantial reduction in the lifespan of red blood cells. This makes them more susceptible to infections, including parvovirus B19 [13], this finding aligns with a previous study that investigated the frequency of human parvovirus B19 in individuals with ESRD undergoing haemodialysis at Suez Canal University Hospital in Ismailia City, Egypt. Parvovirus B19 viremia was detected in 15% of patients with HD, but none of the control patients had positive results for viremia [14]. As well as in the study conducted in Iran, which detected parvovirus B19 DNA in 10% (5/50) of CKD patients [15], in contrast with the Alves et al study [16] who surveyed 120 dialyzed patients and showed that the overall parvovirus B19 DNA was found in 10 (8.3%) of patients. The differences in study setting, population characteristics, laboratory methodologies, and infection control measures may explain why our findings do not align with those of Alves et al. Further comparative studies with standardized methodologies are needed to clarify the true burden of parvovirus B19 infection in haemodialysis patients across different regions.

CONCLUSION

Parvovirus B19 was detected in 18.3% of patients with end-stage renal disease. This emphasizes the need for routine screening, especially in dialysis patients with refractory anaemia. Their compromised immune function and frequent blood transfusions increase their susceptibility. This highlights the importance of targeted diagnostic and management approaches to minimize potential complications.

ETHICAL DECLARATIONS

- ### Ethics Approval and Consent to Participate

  The study protocol, subject information, and permission form underwent assessment and approval by a local ethics committee in Kirkuk Health Directorate, as per document number 1161, dated 02/05/2023.

- ### Consent for Publication

  Non.

- **Availability of Data and Material**

  The datasets are available from the corresponding author upon reasonable request.

- **Competing Interests**

  The authors declare that there is no conflict of interest.

- **Funding**

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- **Authors' Contributions**

  All authors contributed significantly, directly, and intellectually to the work and consented to its publication.

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