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Prevalence of anti-BK polyomavirus IgG in A Sample of Iraqi renal transplant recipients

Ghufran Hammoodi Abed (MSc)[1], Wisam Mahdi alsaeed (PhD)[2] , Mustafa Rasul Hussein (PhD)[3], Asmaa Baqer Al-Obaidi (PhD)[4], Ahmed Sattar Abood (PhD)[5], Mohammad A H Al-Dabagh (PhD)[6]

[1,2] College of Medicine, Al-Mustansiriya University, Baghdad, Iraq
[3] Baghdad Medical City, Baghdad, Iraq
[4,6] College of Medicine ,Al-Nahrain University, Baghdad, Iraq
[5]College of Education , Al-Iraqia University, Baghdad, Iraq

Abstract

Background: BK virus, a human polyomavirus, causes nephropathy and allograft loss in renal transplant recipients. Although it was discovered in 1971, understanding of the humoral immune response to BKV is limited.
Objective: To serological detection and level estimation of anti-BK-IgG in renal-transplanted recipients and healthy blood donors as control.
Patients and Methods: Serum samples were collected from 106 renal transplant recipient patients and 100 healthy blood donors as control groups, and were analyzed for anti-BK IgG antibodies by using quantitative and qualitative Human BK Virus IgG (BK-IgG) ELISA kit for detection and estimation positivity of BK_IgG and titration.
Results: Out of 206 subjects, 114(55.3%) have a positive result for BK-IgG. seropositivity was detected in 54(50.9%) of 106 RTR patients and 60 (60.0%) in the 100 control group, so there was no significant difference between seropositivity of BKV IgG antibody among the studied groups, p =0.191.
Conclusion: The highly significant differences between seropositivity of BK-IgG with high levels of serum creatinine.
Keywords: Prevalence, Anti-BK IgG antibodies, and Renal transplanted recipients

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Correspondence Address: Ghufran Hammoodi Abed
College of Medicine, Al-Mustansiriya University, Baghdad, Iraq
Email: Ghamoodi2018@gmail.com

Website: https://djm.uodiyala.edu.iq/index.php/djm

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Introduction

According to a recent research, BKV co-evolved with humans, which explains the high prevalence and low morbidity among healthy individuals [1]. Children are protected against BKV infection by maternal antibodies during the first few months of life; but, once these antibodies begin to decline, BKV infection may begin to develop, as indicated by 10 to 30 percent seropositivity in newborns and 65 to 90 percent seropositivity between the ages of 5 and 10 years old [1].

After the first infection in immunocompetent individuals, the BKV may be found in the kidney, in the leukocytes of the peripheral blood, and perhaps in the brain. The initial infection is typically asymptomatic or is characterised by mild nonspecific symptoms [1,2]. Similar to earlier studies, Hirsch *et al*.,[3] found 80%

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seropositivity in a prospective study of patients with kidney transplantation. Fecal-oral, oral and respiratory routes of transmission have been proposed for different human polyomaviruses [4]. Since all viruses can be detected at increased frequencies in blood and lymphoid tissues during host immunosuppression [4]. BKV establishes persistent infections in renal tissue and the virus is shed into the urine. Reactivation of BKV, as reflected by increased viruria, occurs during immunosuppression, soBKV levels correlate with the degree of immunosuppression. Variations in illness severity upon reactivation may be attributable, at least in part, to variances in the tissue tropism and mechanism of viral latency and persistence among members of the same viral family [4,5]. In the first year after receiving a kidney transplant, around two-thirds of patients develop an infection, which increases the risk of complications and even graft rejection. Rejection and graft loss may occur when immunosuppression is too low, whereas infections and cancer can develop when it is too high [6].Aim of this study to determine seropositivity of BK-IgG among renal transplant recipients and healthy blood donors, and its impact on renal function.

Patients and Methods

Study protocol

This Case-control study was carried out from November 2021 to April 2022. Samples were collected at Baghdad's Medical City from the (Centre of Kidney Diseases and Transplantation) and the (Iraqi blood donation centre). This study was conducted in the Medical Research Unit of Al-Nahrain University's College of Medicine. A total of 206 serum samples were collected from (106) renal transplant recipients (RTR) and (100) healthy blood volunteers within the first two years after transplantation.

Study population

Inclusion criteria in this study were all children in the selected schools of aged 7-12 years while exclusion criteria were eye trauma, recent eye surgery, patients who are on systemic, local antibiotic and chemotherapy.

Study design

All serum specimens were analyzed for anti-BK IgG antibodies by using quantitative and qualitative Human BK Virus IgG (BK-IgG) ELISA Kit and according to the manufacturer (ABBKINE, China), the cut of value=66pg/ml that was mentioned in the leaflet of BKIgG ELISA kit for detection and estimation positivity of BK_IgG and titration. A microplate has been pre-coated with an antigen. The wells are filled with standards or test samples, incubated, and then rinsed. Anti-human IgG antibody conjugated with HRP is then added and incubated. The plate is cleaned once more, and then the chromogen solution is added, which is catalyzed by HRP to produce a blue hue following incubation. The addition of a stop solution produces a yellow color change at 450 nm that is proportionate to the quantity of analyte bound.

Statistical Analysis

The Statistical Analysis System- SPSS version 28 program was used. To compare percentages, the Chi-square test was used (0.05 and 0.01 probability).

Results

Serum samples from all the 206 subjects enrolled in the study were analyzed for anti-

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BK IgG antibodies by ELISA and according to the manufacturer, the cut of value=66pg/ml that was mentioned in the leaflet of BKV-IgG ELISA kit, the mean of anti-BK-IgG titer was 74.135±75.858 table [1].

Table (1): Mean of anti-BK titer in this study

	N	Mean	Std. Deviation
Anti-BKV Titer	206	74.135	57.858

Table (2) demonstrate the positive result for BK-IgG was 114/206 (55.3%). Seropositivity was detected in 54(47.4%) of 106 RTR patients and 60 (52.6%) in the 100 control group, so there was no significant difference in seropositivity of BKV IgG antibody among the studied groups, p-value =0.191.

Table (2): Seroprevalence of BKV in RTR and control groups

			Study Groups		Total
			Patients	Control	
Seropositivity	Positive	Count	54	60	114
		% of Seropositivity	47.4%	52.6%	100.0%
		% patient-control	50.9%	60.0%	55.3%
	Negative	Count	52	40	92
		% of Seropositivity	56.5%	43.5%	100.0%
		% patient-control	49.1%	40.0%	44.7%
Total		Count	106	100	206
		% Seropositivity	51.5%	48.5%	100.0%
		% patient-control	100.0%	100.0%	100.0%
Chi-sequare test			0.191		

The patients' group was subdivided according to serum creatinine into two subgroups the first one equal to or less than 1.3mg/dl and the second more than 1.3mg/dl. After the distribution of these subgroups according to seropositivity was carried out, the finding showed seropositive BK-IgG were 27 (38.0%) in the first subgroup and 27(77.1%) in the second one, with highly significant differences (p-value ≤0.000) as shown in Table (3).

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Table (3): Distribution of seropositive BKV-IgG according to serum creatinine

			Seropositivity		Total
			Positive	Negative	
Serum Creatinine	≤1.3	Count	27	44	71
		% within Serum Creatinine	38.0%	62.0%	100.0%
		% within Seropositivity	50.0%	84.6%	67.0%
	>1.3	Count	27	8	35
		% within Serum Creatinine	77.1%	22.9%	100.0%
		% within Seropositivity	50.0%	15.4%	33.0%
Total		Count	54	52	106
		% within Serum Creatinine	50.9%	49.1%	100.0%
		% within Seropositivity	100.0%	100.0%	100.0%
Chi-square test			0.000		

Discussion

Based on serological studies, BKV is picked up during infancy, and prevalence rate either stays the same or goes down with age [6]. In children less than 10 years of age, primary BKV transmission seems to occur effectively, with IgG seroprevalence reaching at least 90% by early adolescence [3]. Moreover, in adult population seroprevalence rates of 65-90%. The overall IgG seroprevalence of BKV is approximately 82%.Importantly, high antibody levels correlated with higher BKV-specific CD4 T-cell activity [3,4]. The primary infections caused by BKV have not yet been adequately defined.

BKV can remain active throughout an individual's lifetime, and the cells of the proximal renal tubule and mononuclear blood cells may serve as tissue sanctuaries for the virus. In this study, BKV-IgG was investigated in serum of both RTRs and control using ELISA and showed out of 206 subjects frequencies of 114(55.3%) have a positive result for IgG which included 54 out of 106 (47.4%) cases of RTR have a positive IgG, while in the control group 60 out of 100 (52.6%) were positive for this antibody so there was no significant difference between seropositivity of BKV IgG antibody among the studied groups, p-value =0.191. Pre-transplantation BKV seroprevalence in kidney transplant patients ranged from 80 – 88%, according to the findings of Hogan et al. and Gardner et al., whereas post-transplantation rates varied from 18 - 44 percent (7&8). Recipients' seropositive rates drop due to BKV replication early after transplantation and after chemotherapy for rejection, when immunosuppression is high and immune control is low.

However, the relative contributions of the humoral, cellular, and innate immunecompartments to immune control are not well understood [9]. The presence of BKV-specific antibodies that prevent the progression of BKV infection has not been demonstrated, despite the fact that 60%-80% of recipients are BKV-seropositive before transplantation. However, a graduated protective effect of recipient BKV-specific antibody titer has been hypothesised to exist. Children who test negative for BKV seropositivity are more likely to develop

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BKV viruria and nephropathy [10].Shah [11] found that seropositive donors and seronegative recipients were both 43% more likely to develop a BKV infection that could be defined by its antibody response.

According to Bohl *et al.* [12], BKV viruria was 50% more likely to be acquired by donors and recipients who tested positive for antibodies to the virus. Both sets of researchers found that 10% of seronegative donors and recipients contracted BKV throughout the course of their research.

In our finding result, there were no significant differences of seronegative BK-IgG in recipients groups was56.5% whereas in control groups 43.5% Consequently of this, Although BKV-specific antibodies may aid in the immune response, they may also signal the possibility of the virus becoming active again.By decreasing the levels of immune suppressants, BKV-specific IgG antibody titers rise, BKV-specific cellular immunity is developed, viremia is cleared, and graft function is maintained [13]. There does not appear to be much of an effect from the prevalence of BKV antibody. According to our research, the explanation provided by Chen et al. supports the hypothesis that there is a correlation between a positive serology for BK-IgG and elevated levels of serum creatinine. individuals with BKV nephropathy who had high BKV antibody titers but inadequate cytotoxic T cell responses had persistent viremia and elevated creatinine levels. Even though these individuals had healthy cytotoxic T cell responses, this was nonetheless the case [14]. Repeated BKV viremia was linked to a low frequency of IFN-producing cells, as found by Comoli *et al.*[15], despite repeatedly increased BKV antibody titers. This was the case even when BKV antibody titers had been high for a long time.

In contrast, a high cytotoxic T cell response but modest antibody titers resulted in viremia clearing and creatinine levels returning to normal in the recipients. And BKV nephropathy has already affected these patients [7, 14, 15].

Conclusions

The highly significant association between seropositivity of BK-IgG with high levels of serum creatinine

Recommendations

Genotyping of BKV in Iraqi RTRs to find out which genotype is most prevalent in Iraq.
A larger sample size including all transplantation centers in Baghdad, to estimate the prevalence of BKV in RTRs by qRT-PCR.

Source of funding: The current study was funded by our charges with no any other funding sources elsewhere.

Ethical clearance: For this study, the Medicine College / Al-Mustansiriya University ethical committee provided approval.

Conflict of interest: Nil

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انتشار فيروس التورامي المتعدد المضاد ل(BK IgG) في عينة من متلقي زراعة الكلى العراقيين

غفران حمودي عبد[١] ، أ.د. وسام مهدي السعيدي[٢]، د. مصطفى رسول حسين[٣] ، أ.د. أسماء باقر العبيدي[٤]
م.د. احمد ستار عبود[٥] ،أ.م.د. محمد عبدالجبار الدباغ[٦]

الملخص

خلفية الدراسة: فيروس التورامي المتعدد البشري (BKV) BK يسبب اعتلال الكلية (BKN) وفقدان allograft في متلقي زرع الكلى. على الرغم من اكتشافه في عام ١٩٧١ إلا أن فهم الاستجابة المناعية الخلطية ل BKV محدود.
اهداف الدراسة: هو واحد من التقارير الأولى عن الكشف المصلي وتقدير مستوى مضاد BK-IgG في المتلقين المزروعين في الكلى والأشخاص الأصحاء كمراقبة.
المرضى والطرائق: تم جمع عينات المصل من ١٠٦ مرضى متلقين لزراعة الكلى و ١٠٠ مجموعة أصحاء ضابطة ، وتم تحليلها بحثا عن الأجسام المضادة ل BK IgG باستخدام مجموعة ELISA لفيروس التورامي البشري (BK-IgG) الكمية والنوعية للكشف عن إيجابية BK_IgG والمعايرة بالتحليل الحجمي.
النتائج: من بين ٢٠٦ عينات، حصل ١١٤ (٥٥,٣٪) على نتيجة إيجابية ل BK-IgG. تم الكشف عن الإيجابية المصلية في ٥٤ (٥٠,٩٪) من ١٠٦ مرضى RTR و ٦٠ (٦٠,٠٪) في ١٠٠المجموعة الضابطة لذلك لم يكن هناك فرق كبير بين الإيجابية المصلية للأجسام المضادة BKV IgG بين المجموعات المدروسة.
الاستنتاجات: الارتباط الوثيق بين الإيجابية المصلية ل BK-IgG مع مستويات عالية من الكرياتينين في الدم.
الكلمات المفتاحية: الانتشار ،الأجسام المضادة لـ BK IgG ،زراعة الكلى
البريد الالكتروني: Ghamoodi2018@gmail.com
تاريخ استلام البحث: ١٦ آب ٢٠٢٢
تاريخ قبول البحث: ٢٧ أيلول ٢٠٢٢

[١،٢] كلية الطب – الجامعة المستنصرية - بغداد - العراق
[٣] مدينة الطب - بغداد – العراق
[٤،٦] كلية الطب – جامعة النهرين – بغداد – العراق
[٥] كلية التربية – الجامعة العراقية – بغداد - العراق