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Investigation into Parvovirus B19 Antibodies in Serum Samples Sent with Pre-diagnosis of Arthritis-Arthralgia

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ABSTRACT

Objectives: Parvovirus B19 belonging to the Erythrovirus genus is a single-stranded DNA virus in the family Parvoviridae. The present study aims to determine parvovirus B19 seropositivity in serum samples sent with pre-diagnosis of arthritis/arthralgia and to evaluate the age dispersion retrospectively.

Methods: Parvovirus B19 IgM and IgG tests were investigated in serum samples with pre-diagnosis of arthritis/arthralgia sent to Virology Laboratory between January 2017 and February 2019 retrospectively. In serum samples of the patients, parvovirus B19 IgM and IgG tests were investigated using the enzyme immunoassay method.

Results: Sixty-one patients with pre-diagnosis of arthritis/arthralgia were included in this study. The mean age of the patients was 45.2±17.8 years. Parvovirus B19 IgG and IgM positivity rates were 40 (65.6%) and 2 (3.3%), respectively. Parvovirus B19 IgG positivity was highest at the ages over 50 years and lowest at the ages under 30 years (p=0.362). Parvovirus B19 IgG seropositivity was the highest in females with a rate of 72.0% (p=0.241).

Conclusion: As a result, parvovirus B19 IgG and IgM positivity rates in the patient group with pre-diagnosis of arthritis/arthralgia were 65.6% and 3.3%, respectively, in our study. As the parvovirus B19 seropositivity rate was found high when compared to the general population studies, latent parvovirus B19 infection should be investigated in synovial tissue in patients with chronical arthritis and arthralgia complaints.

Keywords: Arthritis, arthralgia, enzyme immunoassay, Human Parvovirus B19

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INTRODUCTION

Parvovirus B19 belonging to the *Erythrovirus* genus is a single-stranded DNA virus in the family *Parvoviridae* and was accidentally discovered in 1974. Parvovirus B19 was firstly associated with transient aplastic crisis in 1981, and then, its role in the etiology of erythema infectiosum, hydrops fetalis, chronic aplastic anemia, and finally, arthritis in 1985 was revealed.[1–3] While parvovirus B19 is transmitted through the respiratory tract, it is also transmitted by vertical transmission from mother to fetus, bone marrow and organ transplantation and blood transfusion.[4] Seroprevalence of globally common parvovirus B19 infection increases by age and serological evidence of previous infection in 15% of pre-school children, 50% of teenagers and about 85% of the adults is reported.[5, 6] Incidence of the infection varies seasonally and it is more common in winter and spring months in mild climates.[7] Most of the infections are observed in children and adults are at risk in household.[8] Parvovirus B19 is associated with erythema infectiosum and arthralgia in children, fetal death during pregnancy, transient aplastic crisis in patients with hematologic disorder and persistent infection in immunosuppressed people.[9] Parvovirus B19 infection is also associated with a number of autoimmune diseases, such as rheumatologic, neurologic, neuromuscular, cardiovascular, hematologic, nephrologi-

cal and metabolic diseases.[10]

Occurrence of arthritis after specific antibody formation reveals that immune complexes may have a role on the development of parvovirus.[11, 12] In addition, acute symptomatic parvovirus B19 infection is related to broad proinflammatory cytokine secretion. DNA of parvovirus B19 can be detected in the synovial fluid and tissues of the inflamed joint.[1] Arthropathy and arthritis are more common in women and adults and there can only be one clinic symptom of the infection.[13, 14] The incidence of arthritis maybe 8% in children and 50-80% in adults.[2, 11] While oligoarthritis affecting major asymmetric joints is the most common in children, polyarticular and symmetrical involvement are seen in adults.[15] Arthritis lasts one to three weeks and generally limits itself. Approximately 20% of the cases tend to become chronic.[16] In parvovirus-associated arthritis cases, autoantibodies, such as rheumatoid factor, antinuclear antibody and extractable nuclear antigen, may be detected in low titers. Arthritis can be treated with nonsteroidal anti-inflammatory drugs. Also, severe parvovirus arthritis cases positively responding to intravenous immunoglobulin are reported.[17]

While anti-parvovirus B19 IgG antibodies are the evidence of previous Parvovirus B19 infection, parvovirus B19 IgM antibodies can be detected within two months from the acute period and remain positive for more than six months. The most sensitive test for the diagnosis is the detection of viral DNA. Parvovirus B19 DNA of the patients with chronical Parvovirus B19 arthropathy can be detected without any pathological change in their synovium.[10, 18]

Studies related to the rates of parvovirus B19 seropositivity in patient groups with specific complaints are quite limited in our country. This study aims to determine the rates of parvovirus B19 seropositivity in serum samples sent to the virology laboratory with pre-diagnosis of arthritis/arthralgia and to evaluate the age dispersion retrospectively.

METHOD

This study was planned to be a retrospective study. Parvovirus B19 IgM and IgG tests were investigated in serum samples with pre-diagnosis of arthritis/arthralgia sent to Virology Laboratory of the University of Health Sciences, Ankara Gülhane Training and Research Hospital between January 2017 and February 2019 with parvovirus B19 IgM capture and IgG indirect ELISA principle and with VirClia EIA/CLIA device (Vircell, Granada, Spain) using enzyme immunoassay (EIA) test kits (Vircell S.L, Granada, Spain). Interpretation of the results was evaluated using the antibody index (sample RLU/calibrator RLU) in accordance with the recommendations of the manufacturer. Samples with index values under 0.9 were accepted as negative, samples with index values between 0.9-1.1 as vague and samples with values over 1.1 as positive.

This study was performed with the approval of the Non-Interventional Clinical Research Ethical Committee of the University of Health Sciences Ankara Gülhane Training and Research Hospital (Reference number: 2019/19/102).

Statistical Analysis

Based on the data collected in this study, SPSS 25 software (SPSS Inc, Chicago, IL, USA) was used for statistical evaluation. Continuous data were given as mean and standard deviation, while categorical data were given as counts and percentages. Compliance of the variables with the normal distribution was assessed by visual methods (histogram and probability graphs) and Kolmogorov-Smirnov test. Variables were compared by Student T-test and qualitative variables were compared by Pearson Chi-Square or Fisher exact tests. The results with p-value under 0.05 were accepted statistically significant.

RESULTS

In this study, parvovirus B19 IgM/IgG antibodies with pre-diagnosis of arthritis/arthralgia were investigated in 61 pa-

Table 1. Parvovirus B19 IgM and IgG positivity rates in patients with pre-diagnosis of arthritis- arthralgia according to age groups

Age group (years)	Parvovirus B19		Parvovirus B19		p*
	IgM negative n (%)	IgM positive n (%)	IgG negative n (%)	IgG positive n (%)	
≤30	14 (23.7)	0.0	7 (33.3)	7 (17.5)	
31-50	25 (42.4)	0.0	8 (38.1)	17 (42.5)	0.362
>50	20 (33.9)	2 (100.0)	6 (28.6)	16 (40.0)	
Total	59 (100.0)	2 (100.0)	21 (100.0)	40 (100.0)	

*Pearson ki-kare.

tients 32 (52.5%) males and 29 (47.5%) females. Their mean age was 45.2±17.8 years. Mean age were 40.1±18.9 years in males and 50.7±14.8 in females (p=0.022). While the parvovirus B19 IgG positivity rate was 40 (65.6%) and parvovirus B19 IgM positivity was two (3.3%) (Table 1). No statistically significant difference between genders of parvovirus B19 IgG positive patients was found concerning mean age (Figure 1) (p=0.101). Parvovirus B19 IgM seropositivity was the highest in males with a rate of 6.0%, and IgG seropositivity was the highest in females with a rate of 72.0% (Figure 2 and 3) (p=0.173 and p=0.244 respectively).

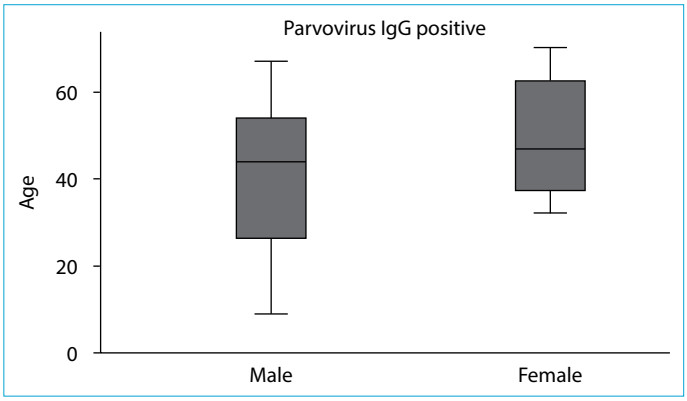

Figure 1. Mean age of Parvovirus B19 IgG positive male and female patients.

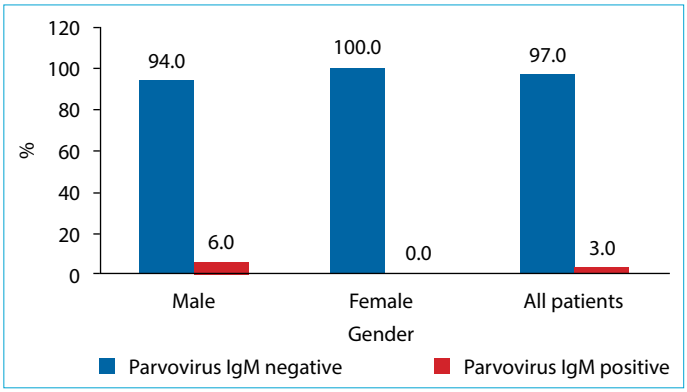

Figure 2. Parvovirus B19 IgM positivity rates in males and females.

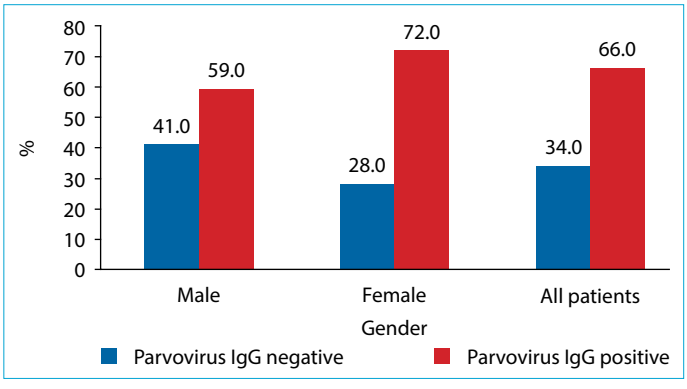

Figure 3. Parvovirus B19 IgG positivity rates in males and females.

DISCUSSION

Human parvovirus B19 is associated with erythema infectiosum, which is a childhood disease and various symptoms mimicking autoimmune disease. While arthritis is an acute and transient condition, the persistency of the virus was revealed in synovial tissues of the patients with chronic arthritis.[19, 20] This virus mainly affects children. Arthritis/arthralgia develops in approximately 8% of the teenagers and 60% of the adults affected by parvovirus.[21] Detection of viral DNA by molecular techniques and EIA and Radioimmunoassay methods detecting specific parvovirus B19 IgM and IgG antibodies are commonly used in the diagnosis of parvovirus B19 infection.[22]

The incidence and seroprevalence of parvovirus B19 infection in blood donors represent the general population. While seropositivity is 40-60% over 20 years of age, it increases the rate of 85% after 70 years of age.[23] It is reported that parvovirus B19 IgG seropositivity rates vary between 6% and 82.3% in different regions of the world.[24]

Parvovirus B19 prevalence slightly differs in Europe. Higher prevalence is observed in Finland, one of the Scandinavian countries, when compared to other European countries.[25] There is a limited number of parvovirus B19 seroprevalence studies in our country. In Mersin, Buyukkose et al. found anti-parvovirus B19 IgG positivity at a rate of 81.3% in 75 patients with fibromyalgia and 64% in the healthy control group of 75 people and the difference was statistically significant.[26] In Konya, Turkdagi et al. found in a study including child and adult patients that parvovirus B19 seropositivity was 28.9% in general population, 20.7% (the lowest rate) in the age group of 0-17 and 53.8% (the highest rate) over 60 years of age.[27] In Erzurum, Aktas et al. found in the general population that parvovirus IgG was 27.8%, IgM was 8.5% and IgM and IgG seropositivity together was 2.5%.[28] In Ankara, Goral et al. found in blood donors that parvovirus B19 IgG seropositivity was 58.9% and IgM seropositivity was 3.92%.[29] In this study, parvovirus B19 IgG positivity was 66% and IgM positivity was 3% in patients with prediagnosis of arthritis/arthralgia. Having found a high rate may be related to including a specific patient group with specific pre-diagnosis, such as arthritis/arthralgia, associated with parvovirus B19 in this study.

In most of the studies, evaluating seropositivity according to the age groups, it was reported that seroprevalence increased by age and this increase was found statistically significant.[30–32] In this study, parvovirus B19 IgG antibody seropositivity was 50% under the age of 30 and 73% over the age of 50. However, the difference was not statistically significant.

In our study, parvovirus B19 IgM seropositivity in the patient group included in the study was 3%. Low rates of IgM seropositivity were consistent with the ones in other similar studies.[28, 29] Parvovirus B19 IgM prevalence in the general population is generally under 2%. However, the rate may be higher, depending on the duration of the outbreak cycle. Most of the infections are seen in spring in mild climates. Outbreaks regularly occur at intervals of a few years.[33]

As a result, in our study, parvovirus B19 IgM and IgG seropositivity in the patient group with pre-diagnosis of arthritis/arthralgia were 3% and 66%, respectively. Since the parvovirus B19 seropositivity rate was high when compared with the studies on the general population, latent parvovirus B19 infection should be investigated in patients with chronic arthritis and arthralgia complaints.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Ethics Committee Approval: This study was approved by the Local Ethics Committee with the protocol number of 2019/19/102 was in accordance with the ethical standards established in the Declaration of Helsinki (03/26/2019).

Authorship Contributions: Concept – H.T.A., A.B.; Design – H.T.A., A.B.; Supervision – H.T.A., A.B.; Materials – H.T.A.; Data collection &/or processing – H.T.A., A.B.; Analysis and/or interpretation – H.T.A., A.B.; Literature search – H.T.A.; Writing – H.T.A., A.B.; Critical review –M.G., M.T.Y.

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