Correlation between parvovirus B19 infections and cardiovascular disease in Najaf Governorate patients

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Abstract
Introduction: The term parvovirus is based on the Latin name for tiny, parvus. It is small-sized, without an enveloped icosahedral human parvovirus. While B19V has been diagnosed and involved in a greater number of clinical conditions including diverse organs and tissues that are primarily neurological and rheumatologic in origins such as encephalopathy, meningitis, and epilepsy, it has also been identified as a significant cardio tropic virus, causing acute myocarditis and probably contributing to the development of severe cardiomyopathies. Cardiovascular disease (CVD) is an umbrella term for a number of linked pathologies, commonly defined as coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease, rheumatic and congenital heart diseases and venous thromboembolism. Aim of study: Study association between parvovirus B19 infections and cardiovascular disease Methodology: This study (cross-sectional study) included 200 individuals with cardiovascular disorders from January 2022 and May 2022 that were clinically diagnosed by cardiology specialists. The patients ranged in age from (1 to 80) years old, with 58 females and 142 males among the 200 cases.The serum samples of patients were obtained for screening of the presence of PV B19 Ag, PV B19_ IgM and IgG antibodies by ELISA using commercial kits (SUNLONG_CHINA). Results: Immunological techniques were applied to determine immunological indicators including the antigens of parvo B19, Anti- parvo B19 IgM & Anti- parvo B19 IgG. Results in age groups differ among parvo B19 Ags compared to Anti- parvo B19 IgM.Significant results for Anti-PV B19 IgM values and PV B19 Ag were present among age group patients with a p-Value equal to 0.03. The study also displays a considerable result for Anti- PV B19 IgG values and Anti- PV B19 IgM was present among age groups patients with a p-Value equal to 0.002. Association of CVD and study markers showed no significant difference between IgG and IgM in cardiovascular disease types with a p-Value equal to 0.481. Conclusions: A significant number of cardiovascular disorders patients are infected with parvovirus B19. As many patients had an increase in both their parvovirus B19 IgG and IgM levels at the same time, activation of parvovirus B19 infection may be the reason for cardiovascular disorders or the progression of pre-existing conditions.
Keyword: Parvovirus B19, cardiovascular diseases, Anti- PV B19 IgM, Anti- PV B19 IgG, Najaf Governorate.

1. Introduction

Parvovirus B19, also known as primate erythroparvovirus 1, is a virus. (1) or, less frequently, erythrovirus B19, (2) is the first and, up to 2005, the unique identified human virus in the genus Erythroparvovirus of the Parvoviridae family; it has a diameter of just 23–26 nm. (3). Due to the absence of a lipid membrane makes it resistant to physical destruction via heating or cleaning agents (4). B19V infection can cause a wide range of clinical signs based on the patient's old age , hematological, and immunological state of them (5). The virus's host extent is quite narrow. The principal targeting cells for successful B19V infections in life are individual erythroid precursors cells presenting the blood type P Ag for their predominant receptor on the cell surface. However, the virus also can invade endothelium cells via another entrance method (6). Parvovirus B19 (B19V) has often being connected to the development of myocarditis and so its progress to dilated cardiomyopathy. The precise role of B19V prevalence and loads stays unknown, as this virus has also been detected in healthy patients' hearts.(7)
There is no information available to us about the relationship in these cases in Iraq.
Cardiovascular disease (CVD) is the leading cause of mortality in the world, according to the World Health Organization representing 32% of all deaths globally which the majority of this in the form of CHD and cerebrovascular accident. Diseases affecting the cardiovascular and vascular systems that supply the heart, brain, and other essential organs are all included in CVD. (8) (9) (10). There are several causes of cardiovascular illness, but atherosclerosis and/or hypertension are the most prevalent. (11).
In recent years, an increasing number of studies have been published establishing a link between PVB19 and several different clinical ailments, including arthritis, myocarditis, other vasculitic, hepatic, and neurological conditions. A rising number of studies

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imply a link between infection with PVB19 and acute and chronic heart problems. ISH tests provided the first indications of a potential etiopathogenetic role for PVB19 infection in the development of heart dysfunctions. In individuals with acute inflammatory cardiomyopathy, radioactive ISH revealed viral genomes in endothelial cells (ECs) of the myocardium, particularly in the venular compartment and small arteries and arterioles, but not in cardiac myocytes or other myocardial tissue components. (12)

2. Subject and Methods

Patients: This study (cross-sectional study) included 200 individuals with cardiovascular disorders that were clinically diagnosed by cardiology specialists. The patients ranged in age from(1 to 80) years old, with 58 females and 142 males among the 200 cases. The " A Heart-Opening Unit " of the "Educational Hospital of Al-Sader " in Iraqi city of Najaf, registered these people as CVD patients. The study's goals and objectives were explained to all groups, and they all accepted. Name, age, gender, smoking, diabetes, and blood pressure were some of the descriptive factors for all patients.

Included criteria: Myocardial infraction, Heart failure, Congestive Heart Failure, Ischemic heart disease, Rheumatic heart disease, Angina: Stable Angina and Unstable Angina, Structural heart disease

Excluded.criteria: Congenital Cardiac problems, Cardiac arrhythmia, Valvular Heart trouble, Cardiac Arrhythmia, Covid-19 patients, Patients who had HCV or HBV.

Approval of the Ethical Committee: The Ethical Committee of the Kufa Medical College gave its approval to the study protocols.

Samples collection and store: Each patient had samples of blood were taken by drawing 4 milliliters of vein blood in to the test tubes and then put in gel tube for biochemical analysis and then were centrifuged at 3000 rpm for 10 minutes to obtain serum, the serum samples were divided into 1.5 ml Eppendorf tubes and preserved in the freezer at -20 C until the time of the immunological examinations.. (PVB19 IgM , PV B19 IgG, PVB19 Ag)

Serological technique (ELISA): The serum samples of patients were obtained for screening of the presence of PV B19 Ag, PV B19_ IgM and IgG antibodies by ELISA using commercial kits (SUNLONG_CHINA).

3. Statistical Analysis

The Chi-square test and a P-value of less than 0.05 were used to calculate the statistical importance of the results. It depends on SPSS 24.

4. Results

Distribution of immunological parameters for Anti- parvo B19 IgM seropositivity and parvo B19 Ags seropositivity in age groups

Immunological techniques were applied to determine immunological indicators including the antigens of parvo B19, Anti- parvo B19 IgM & Anti-parvo B19 IgG. Results in age groups differ among parvo B19 Ags compared to Anti- parvo B19 IgM, where there was appeared in age group(<20) four cases(5.1%) positive for parvo B19 Ags and seven cases(8.1%) positive for Anti- parvo B19 IgM, age group(20-39) one cases(1.3%) positive for parvo B19 Ags and three cases(3.5%) positive for Anti- parvo B19 IgM, age group(40-59) forty-one cases (52.6%)positive for parvo B19 Ags and forty-four cases(51.2%) positive for Anti- parvo B19 IgM and age group(60-79) thirty-two cases (37.2%) positive for parvo B19 Ags and thirty-two cases(41%) positive for Anti- parvo B19 IgM . For more details, see table (1). Table 1 demonstrates that significant results for Anti-PV B19 IgM values and PV B19Ag were present among age-group patients with a p-Value equal to 0.03.

B19 Ags seropositivity in age groups

Table(1) Distribution of immunological parameters according to Anti-PV B19 IgM seropositivity and parvo

Age groups years	Parvo B19 -Ags–ve	Parvo B19 –Ags+ve	Anti-PV B19 IgM–ve	Anti-PV B19 IgM+ve	*p*-value
<20	23(18.9%)	4(5.1%)	20(17.5%)	7(8.1%)	0.03
20-39	8(6.6%)	1(1.3%)	6(5.3%)	3(3.5%)	
40-59	59(48.4%)	41(52.6%)	56(49.1%)	44(51.2%)	
60-79	32(26.2%)	32(41.0%)	32(28.1%)	32(37.2%)	
Total	122(100.0%)	78(100.0%)	114(100.0%)	86(100.0%)	
X^2 = 17.879 , df= 9 , *p*-value ≤ 0.05					

Distribution of immunological parameters according to Anti-PV B19 IgG seropositivity and parvo B19 Ags seropositivity in age groups

Also, the results in age groups differ among parvo B19 Ags compared to Anti- parvo B19 IgG., where there was appeared in age group(<20) four cases(5.1%) positive for parvo B19 Ags and eleven cases (7.6%) positive for Anti- parvo B19 IgG, age group(20-39) one cases (1.3%)positive for parvo B19 Ags and three cases(2.1%) positive for Anti- parvo B19 IgG, age group(40-59) forty-one (52.6%)cases positive for parvo B19 Ags and seventy-five cases (52.1%)positive for Anti- parvo B19 IgG and age group(60-79) thirty-two (41.0%) cases positive for parvo B19 Ags and fifty five(85.9%) cases positive for Anti- parvo B19 IgM . more details shown in table (2). A significant result was found in table 2 for Anti-PV B19 IgG and PV B19Ag were present among age groups patients with p-Value equal to 0.0001.

B19 Ags seropositivity in age groups

Table (2) Distribution of immunological parameters according to Anti-PV B19 IgM seropositivity and parvo

Age groups years	Parvo B19 -Ags– ve	Parvo B19 -Ags +ve	Anti-PV B19 IgG– ve	Anti-PV B19 IgG +ve	No. of cases	*p*-value
<20	23(18.9%)	4(5.1%)	16(28.5%)	11(7.6%)	27 (13 %)	
20-39	8(6.6%)	1(1.3%)	6(10.7%)	3(2.1%)	9 (4 %)	
40-59	59(48.4%)	41(52.6%)	25(44.6%)	75(52.1%)	100 (50 %)	
60-79	32(26.2%)	32(41.0%)	9(16.1%)	55(85.9%)	64 (32%)	0.0001
total	122	78	56	144	200	
X^2= 17.8, *p*-value ≤ 0.05(significant) , df= 9						

Distribution of immunological parameters according to Anti-PV B19 IgM seropositivity and Anti-PV B19 IgG seropositivity in age groups

Furthermore, the results in age groups differ between anti-parvo B19 IgM and anti-parvo B19 IgG, where there was in age group (20) 7 cases(8.1%) were positive for anti-parvo B19 IgM and 11 cases(7.6%) positive for anti-parvo B19 IgG, age group(20-39) 3 positive cases (3.5%) for anti-parvo B19 IgM and 3 positive cases (2.1%) for anti-parvo B19 IgG, age group(40-59) 44 positive cases(51.2%) for anti-parvo B19 IgM and 75 positive cases (52.1%) for anti-parvo B19 IgG and age group(60-79) 32 positive cases (37.2%) for anti-parvo B19 IgM and 55 positive cases (38.2%) for anti-parvo B19 IgG. More details are presented in table (3). Table 3 also displays a significant result for Anti- PV B19 IgG values, and Anti- PV B19 IgM was present among all age groups of patients with a p-value equal to 0.002.

Table (3) Distribution of immunological parameters according to Anti-PV B19 IgM seropositivity and Anti-PV B19 IgG seropositivity in age groups

Age groups years	Anti-PV B19 IgG–ve	Anti-PV B19 IgG+ve	Anti-PV B19 IgM–ve	Anti-PV B19 IgM+ve	*p*-value
<20	16(28.5%)	11(7.6%)	20(17.5%)	7(8.1%)	
20-39	6(10.7%)	3(2.1%)	6(5.3%)	3(3.5%)	
40-59	25(44.6%)	75(52.1%)	56(49.1%)	44(51.2%)	0.002
60-79	9(16.1%)	55(38.2%)	32(28.1%)	32(37.2%)	
total	56	144	114	86	
X2 = 25.916 , df= 6 , *p*-Value≤ 0.05					

Distribution of immunological parameters according to Anti-PV B19 IgM seropositivity and Anti-PV B19 IgG seropositivity according to sex

The total of 142 males with Parvo virus were 64 patients with Anti-PV B19 IgM positive results (74.4%) and 105 patients with Anti-PV B19 IgG positive results (72.9%). While for females, the results were out of a total number of 58 patients, 22 patients with Anti-PV B19 IgM positive results (25.6%), and 39 patients with Anti-PV B19 IgG positive results (27.1%). Figure 1 also demonstrates that no significant results for Anti- PV B19 IgG values and Anti- PV B19 IgM were present among sex groups patients with *p*-Value equal to 0.59.

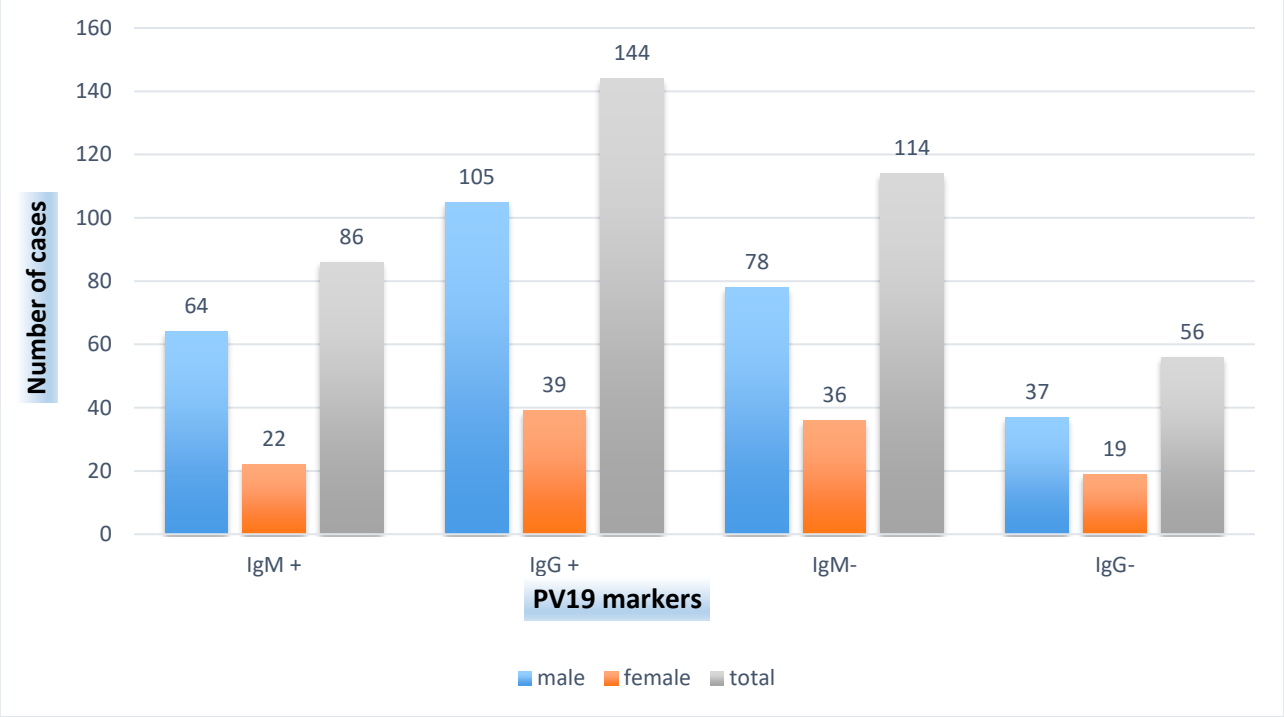

Figure (1) Distribution of Anti-PV B19 IgM seropositivity and Anti-PV B19 IgG seropositivity according to sex. p-Value=0.59(not significant)

Correlations between types of cardiovascular disease and markers of research

In the study, immunological biomarkers from four different types of cardiovascular disease were measured, consisting of 200 participants: 147 ISH cases, 4 HF cases, and 5 cases of cardiomyopathy with 44 cases of structural heart diseases. The research found that there were a total instance with positive Anti-PV B19 IgG were 144, including 111 cases (77.1%) of ischemic heart disease, 2 cases (1.4%) of heart failure, and 4 cases (2.8%) of cardiomyopathy with 27(18.7%) of structural heart disease.

Anti-PV B19 IgM positivity had been documented in 86 case, among these were 68 cases (79.1%) of ischemic heart disease, 1 case of HF (1.1%), and 17 cases (19.8%) with structural heart disease. Association of CVD and study markers were showed no significant difference between IgG with IgM in cardiovascular diseases types with a *p*-Value equal to 0.481.

Table 4: Relationship between types of cardiovascular disease and markers of research

CVD Study markers	Ischemic heart disease (IHD)	Heart failure (H F)	Myocardio-pathy (MCP)	Sructural heart disease (SHD)	Total	P value
IgG+ve	111(77.1%)	2(1.4%)	4(2.8%)	27(18.7%)	144	0.481*
IgM+ve	68 (79.1%)	1 (1.1%)	0 (0.0%)	17 (19.8%)	86	

5. Discussion of Results

Immunological indicators like the human Parvovirus B19 antigen, Anti-Parvovirus B19 IgM and Anti-Parvovirus B19 IgG,were measured utilising immunological methods.

As shown in table (1) in this study ,the human Parvovirus B19 Ags was found to be positive in 78 cases (39%) with the highest levels in age group(40-59) and age group(60-79) with approximately 41(52.6%) and 32 (41%) respectively among the age groups, with only 4 cases in age group(<20) and one case in age group(20-39) . In a study done in Japan by K.Nabae et al .,(2014) (13) showed that the peak proportion of positive Parvovirus Ags was among those aged 30–39 years followed by 40–49 years, and this agrees with my study in part because the high Parvovirus antigen percentage was in age group(40-59) ,but disagrees in that the lowest Parvovirus Ags percentage was among (20–39)years. Atbee et al.,(2020) (14) showd that determination of Parvovirus B19V IgG and IgM antibodies usually adequate to be aware of the progression of parvoviral infections in a serum sample.An IgM test that is positive with or without a positive IgG indicates a recent infection , while An IgG test that is positive with or without a positive IgM indicates a previous infection. Parvovirus B19 IgM antibodies (extant/recently infection) that appear around 10 days post infection and last for about 3 months as reported by Adamson-Small et al.,(2014) (15) were found in 86 (43%) of the cases. Acute infections were observed in people of all ages; However, the age group with the highest IgM seropositivity was in age group(40-59) (51.2%), followed by age group age group(60-79) (37.2%), with a consistent drop by decresing age to 8.1% in the age group age group(<20) and younger cases.

However, 3.5% of acute infections had been indeed observed in the age group of 20–39 yrs. That may be interpreted by direct get in touch to young children due to familial environments, which likely enhances viral transmission hazard. These findings significantly differ from previous results reported in Croatia by T.Vilibic-Cavlek et al., (2021) (16) that showed that acute Parvovirus B19 infections were more prevalent within that youngest group of people(11.1%) and adolescents (8.9%), with a continuing reduction by age to 1.2% within those aged 50-59 yrs and elderly. Table 1 also indicates that significant outcomes regarding Anti-Parvovirus B19 IgM values and Parvovirus B19 Ags were present among age groups patients with p-Value equal to 0.03. Parvovirus B19 IgG antibodies were determined within 144 (72%) of cases. And, as shown in table (4.11), the highest levels were observed in age group(40-59) at approximately 75 (52.1%), followed by 55 (38.2%) in age group(60-79) and decreasing levels to approximately 3 (2.1%), 11 (7.6%) in age group(20-39) and age group(<20) , respectively, and that meant the lowest levels were observed in age group(20-39) . These data are in contradiction with previous results reported by Stewart et al .,(2011) (G. C. Stewart et al., 2011) showing the seropositive rate of Parvovirus B19 IgG in children aged <15 years is 30% to 50% and increases to >90% in elderly patients.

It was found in our study that the maximum levels of anti-Parvovirus B19 IgG among age groups were observed in age group (40-59) of adults aged between 40 and 59 years, about 52.1%, whereas Röhrer, C et al . (2008) (18) found that the highest levels were observed in adults aged between 60 and 69 years. Also, it was found that the lowest levels of anti-Parvovirus B19 were observed in age group(20-39) of young adults between 20 and 39 years old (2.1%). This is in good agreement with a previous study by Röhrer, C et al . (2008) (18), which found the lowest levels at about 1.6% in young adults (18–39) years. Röhrer, C et al . (2008) (18)found that the relatively decreased seroprevalence we observed in the elderly (>70 years) could be attributed to a decrease in individual IgG titers. This hypothesis is confirmed by the finding that the proportion of serum samples with borderline IgG titres rose with age, rising from 1% in young individuals to over 10% in the elderly.

Research by Abraham et al.,(2002) (19) observed a rise in the antibody index, which reflects the age-related rise in particular IgG in a given serum sample. Therefore, it can be concluded that elevated IgG levels in adults do not represent antibodies that persisted after a childhood infection but rather an immune response that was boosted after being exposed to the virus again. We could hypothesise that the population's exposure to PVB 19 leads to infections that start early in life, with repeated exposure at a later age leading to an increase in antibody levels. A study done by Anderson et al.,(1986) (20) reported that with the IgM ELISA, they determined Parvovirus B19 IgM by more 85% of clinical aplastic crisis cases and 5th disease as well as minimal than 2% of controls. The prevalence of Parvovirus B19- IgG Abs are age-related increase. They also observed that Immunoglobulin G for parvovirus B19 were present in around 2 percrnt of children under 5 yrs old with 49 percent of people over 20 yrs old. The Parvovirus B19 Ab ELISAs are sensitive and specific assays to determine Parvovirus B19 infections.

The research showed there were 144 patients (72%) with positive(+ve) Anti- Parvovirus B19 IgG, divided into 111 cases (77.1%) of IHD, 2 cases (1.4%) of HF, 4 cases (2.8%) of MCP and 27 cases (18.7%) of SHD. This result consistent with previous study done by Paszek et al.,(2019) (21) that found Parvovirus B19 IgG antibodies were positive in (82.9%) of patients. The study done by (22) reported the sero-positive ratio of anti-Parvovirus B19 IgG in CAD patients to be 1.5- to 2.7-fold more frequent than in healthy subjects, a finding pointing to either a greater vulnerability to Parvovirus B19 infection in CAD patients or an elevated cardiovascular risk linked with Parvovirus B19 seropositivity .They also found that Significantly greater IgG positivity was found in 64/90(71%) CAD indiviuals.

Liu et al.,(2009) (22) also explained that chronic Parvovirus B19 infection could result in a sustained elevation of circulating cytokines, which could

promote a systemic inflammatory state favourable to atherogenesis. Thus, Parvovirus probably in a direct way penetrated and latently remained in the cells of the coronary artery wall. The endothelial tropism of Parvovirus B19 is most likely caused by attaching Blood group P antigen to its own receptor displayed in endothelial and vascular smooth muscle cells. The results done by Paszek et al.,(2019) (21) showed that patients positive for anti–Parvovirus B19 antibodies had a larger atherosclerotic burden measured by the Gensini score and were more likely to have suffered from a myocardial infarction than seronegative patients. Stewart et al.,(2011) (17) reported that Viral persistence might describe a phase following acute infection but prior to immune clearance. It has been proposed that viral persistence is one indicator of immunotherapy failure in idiopathic cardiomyopathy. Results from Liu et al.,(2009) (22) demonstrated a a sero-epidemiological and histo-pathological correlation of chronic Parvovirus B19 infection along with CAD, indicating here that Parvovirus B19 infections might play a part in the development of cardiac atherosclerosis.

Kühl et al.,(2003) (23) reported that virus genomes can be found in 71% of patients with normal coronary anatomy, clinically mimicking acute myocardial infarction. In addition to EVs and ADVs, Parvovirus B19 was the most frequent pathogen. Anti-Parvovirus B19 IgM positive was found in 86 patients (43%), with 68 cases (79.1%) having ISH, 1 case (1.1%) having HF, and 17 cases (19.8%) having SHD. Our results are in line with previous results by Escher et al.,(2008) (24) reported that specific Anti-Parvovirus B19 IgM antibodies indicating acute or recent infections were only detectable in AMC patients, but not in healthy controls nor in DCM patients. The lack of Parvovirus B19-specific IgM in patients with clinically suspected DCM is consistent with the fact that anti-Parvovirus B19V IgM response is likely to be detectable in early, but not in late infection stages, and might be helpful to differentiate the acuity of the myocardial Parvovirus B19V infection while they found Anti-Parvovirus B19 specific IgGs were detectable in DCM (27.5%) patients, and less frequently, in AMC patients (6.0%). Anti- Parvovirus B19V-specific IgGs are found preferentially in patients with prolonged Parvovirus B19V viremia and persistent infections in other diseases ,and indicate an altered course of viral infection contributing to tissue and cell destruction by apoptosis and direct cytotoxic effects.

6. Conclusion

A significant number of cardiovascular disorders patients are infected with parvovirus B19. As many patients had an increase in both their parvovirus B19 IgG and IgM levels at the same time, activation of parvovirus B19 infection may be the reason for cardiovascular disorders or the progression of pre-existing conditions.The absence of parvovirus B19 antigen does not rule out parvovirus B19 infection because a small percentage of individuals still have positive IgG levels, which may suggest a history of infection. There is no link between parvovirus B19 infection and certain types of cardiovascular disease. The most common cardiovascular type in the study was ischemic heart disease.

References

1. Mariathasan S, Newton K, Monack DM, Vucic D, French DM, Lee WP, et al. Differential activation of the inflammasome by caspase-1 adaptors ASC and Ipaf. Nature. 2004;430(6996):213–8.
2. Broz P, Dixit VM. Inflammasomes: Mechanism of assembly, regulation and signalling. Nat Rev Immunol [Internet]. 2016;16(7):407–20. Available from: http://dx.doi.org/10.1038/nri.2016.58
3. Martinon F, Burns K, Tschopp J. The inflammasome: a molecular platform triggering activation of inflammatory caspases and processing of proIL-β. Mol Cell. 2002;10(2):417–26.
4. Servey JT, Reamy B V., Hodge J. Clinical presentations of parvovirus B19 infection. Am Fam Physician. 2007;75(3).
5. Bouraddane M, Warda K, Zouhair S. Parvovirus B19 and Pregnant Women: A Bibliographic Review. Open J Obstet Gynecol. 2021;11(11):1543–64.
6. Matz B, Kupfer B, Kallies R, Külshammer M, Flötenmeyer M, Kreil TR, et al. Secondary structure of DNA released from purified capsids of human parvovirus B19 under moderate denaturing conditions. J Gen Virol. 2019;100(5):812–27.
7. Verdonschot J, Hazebroek M, Merken J, Debing Y, Dennert R, Brunner-La Rocca HP, et al. Relevance of cardiac parvovirus B19 in myocarditis and dilated cardiomyopathy: review of the literature. Eur J Heart Fail. 2016;18(12):1430–41.
8. Gaziano T, Reddy KS, Paccaud F, Horton S. Chapter 33 Cardiovascular Disease. 2020;(Cvd).
9. Gundugurti P, Bhattacharyya R, Koneru A. Management of psychiatric disorders in patients with cardiovascular diseases. Indian J Psychiatry. 2022;64(8):S355–65.
10. Stewart J, Manmathan G, Wilkinson P. Primary prevention of cardiovascular disease: A review of contemporary guidance and literature. JRSM Cardiovasc Dis. 2017;6:204800401668721.
11. Sniehotta FF, Araújo-Soares V, Brown J, Kelly MP, Michie S, West R. Complex systems and individual-level approaches to population health: a false dichotomy? Lancet Public Heal [Internet]. 2017;2(9):e396–7. Available from: http://dx.doi.org/10.1016/S2468-2667(17)30167-6
12. Bock C-T. Parvovirus B19: a new emerging pathogenic agent of inflammatory cardiomyopathy. Chronic Viral Inflamm Cardiomyopathy. 2006;83–97.
13. Nabae K, Satoh H, Nishiura H, Tanaka-Taya K, Okabe N, Oishi K, et al. Estimating the risk of parvovirus B19 infection in blood donors and pregnant women in Japan. PLoS One. 2014;9(3):7–

11.
14. Atbee MAKA, Hmudi HAMA, Salait SKAA. Molecular detection of human parvovirus B19 in patients with hemoglobinopathies in Basrah Province-Iraq. Int J Pharm Res. 2020;12(2):2257–63.
15. Adamson-Small LA, Ignatovich I V., Laemmerhirt MG, Hobbs JA. Persistent parvovirus B19 infection in non-erythroid tissues: Possible role in the inflammatory and disease process. Virus Res [Internet]. 2014;190:8–16. Available from: http://dx.doi.org/10.1016/j.virusres.2014.06.017
16. Vilibic-Cavlek T, Tabain I, Kolaric B, Mihulja K, Blazevic L, Bogdanic M, et al. Parvovirus b19 in croatia: A large-scale seroprevalence study. Med. 2021;57(11):1–8.
17. Stewart GC, Lopez-Molina J, Gottumukkala RVSRK, Rosner GF, Anello MS, Hecht JL, et al. Myocardial Parvovirus B19 Persistence: Lack of Association With Clinicopathologic Phenotype in Adults With Heart failure. Circ Hear Fail. 2011;4(1):71–8.
18. Röhrer C, Gärtner B, Sauerbrei A, Böhm S, Hottenträger B, Raab U, et al. Seroprevalence of parvovirus B19 in the German population. Epidemiol Infect. 2008;136(11):1564–75.
19. Abraham M, Rudrarajau R, Kannangai R, Koshy G. A pilot study on the seroprevalence of parvovirus B19 infection. Indian J Med Res. 2002;115:139.
20. Anderson LJ, Tsou C, Parker RA, Chorba TL, Wulff H, Tattersall P, et al. Detection of antibodies and antigens of human parvovirus B19 by enzyme-linked immunosorbent assay. J Clin Microbiol. 1986;24(4):522–6.
21. Paszek E, Wilk A, Palacz J, Majer A, Kapelak B, Pfitzner R. An association between parvovirus B19 infection and the severity of coronary atherosclerosis. Kardiol Pol. 2019;77(9):875–7.
22. Liu SC, Tsai CT, Wu CK, Yu MF, Wu MZ, Lin LI, et al. Human Parvovirus B19 Infection in Patients with Coronary Atherosclerosis. Arch Med Res [Internet]. 2009;40(7):612–7. Available from: http://dx.doi.org/10.1016/j.arcmed.2009.09.002
23. Kühl U, Pauschinger M, Bock T, Klingel K, Schwimmbeck CPL, Seeberg B, et al. Parvovirus B19 infection mimicking acute myocardial infarction. Circulation. 2003;108(8):945–50.
24. Escher F, Modrow S, Sabi T, Kühl U, Lassner D, Schultheiss HP, et al. Parvovirus B19 profiles in patients presenting with acute myocarditis and chronic dilated cardiomyopathy. Med Sci Monit. 2008;14(12):589–97.