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Parvovirus B19 viral infection and its incidence in Saudi Arabia

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Abstract:

Parvovirus B19 is a small non-enveloped single-stranded DNA virus of the family Parvoviridae and genus Erythrovirus. B19 virus is most known for causing erythema infectiosum (fifth disease) in children as well as numerous other diseases such as arthropathy in adults, Transient aplastic crisis in patients with increased erythropoiesis and persistent anemia in immunocompromised patients. Parvovirus B19 has been the topic of numerous reviews, however, not many studies have focused on B19 Virus Infection in Saudi Arabia. In this review we compile recent data on human parvovirus B19 and its Infection in Saudi Arabia.

Keywords: *Parvovirus B19, Saudi Arabia, fifth disease, malignant tumors, Transient aplastic crisis*

Introduction

Parvovirus B19 (recently renamed as erythrovirus) is most known for causing erythema infectiosum (fifth disease) in children, the virus has also been implicated in many other diseases such as arthropathy in adults, Transient aplastic crisis in patients with increased erythropoiesis, as well as persistent anemiain in immunodeficient and immunocompromised patients [1, 2]. Furthermore, Parvovirus B19 was recognized as the cause of hydrops fetalis and congenital anemia in fetuses [3].

Parvovirus B19 was first discovered in 1975 by yvonne cossart in London, when he observed an unusual reaction in a hepatitis B assay for a normal blood donor's serum (this serum sample was named B19) [4].

Parvovirus B19 is a small non-enveloped single-stranded DNA virus of the family *Parvoviridae* and genus *Erythrovirus*; it is the only member of *Parvoviridae* knouwn to cause disease in humans. This large family include numerous members that cause disease in animals such as canine parovirus [5], porcine parovirus [6] and Aleutian mink disease virus [7].

The name of parvoviruses comes from parvum the latin word which means small. Actually, parvoviruses are known to be among the smallest viruses with viral particles of only 22 to 24 nm in diameter [8]. Their structure is simple where the viral genome (length 5-6 kb) encodes three proteins. The first one is a nonstructural protein (NS1) with a molecular weight of 77 kDa, this protein is cytotoxic to host cells and subserveses multiple replicative functions. The other two are structural proteins (capsid proteins) known as viral protein (VP1) with 11 kDa and viral protein 2 (VP2) with 7.5 kDa [9].

Several studies have been conducted to identify B19V genotypes basing on nucleotide divergence. These studies were able to identify three B19V genotypes. Genotype 1 which is circulating worldwide, genotype 2 which is common in Europe, and genotype 3 which was believed to be confined in West Africa [10-12]. Interestingly,

Hübschen and co-workers found B19V genotype 3 in samples collected from Asia, Brazil and Europe. Their result suggest that B19V genotype 3 is more widely distributed outside Africa than previously described [13].

Recently, Jan-Hendrik Trösemeier and co-workers have reported the genome sequences of two references strains of parvovirusB19, these two references strains belong to genotype 1a1 and 1a2 [14].

Mode of transmission

The virus is usually transmitted by personal contact through respiratory secretions such as saliva and nasal mucus. It can be also transmitted through blood and blood products [15, 16]. However, recent studies demonstrated that parvovirus B19 can be transmitted from infected mother to her fetus [17].

Individuals acquire the B19V viral infection when the virus bind to a specific receptors that are present on the surface of host cells (P-blood group antigen globoside-4 [Gb4]). Then, the virus will be transported inside the host cell via endocytosis, where it can reach the nucleus and start its replication [18].

In addition, Parvovirus cannot encode its own DNA-polymerase, but instead depends on the host cell DNA-polymerase. This explains why individuals who do not have the P-blood group antigen are not susceptible to B19V viral infection [19].

Parvovirus B19 infection symptoms

Numerous patients infected by B19V are asymptomatic or usually show flu-like symptoms. Therefore, most patients with B19V infections do not need laboratory tests, because the illness is self-limiting and is usually resolved within a week [20, 21].

There are three categories of peoples in which parvovirus B19 may cause serious clinical consequences. The first category is peoples with haemolytic diseases; such as patients with thalassaemia major or sickle cell disease. In those patients, B19V is well known for causing aplastic crisis. The second category contain immunocompromised patients where B19V was recognized to cause chronic anemia. The third category is pregnant women [15]

Parvovirus B19 infection is common in children, especially children aged between 4 and 11 years. In fact, a study performed in United States showed that 19% of children infected by B19V were less than 10 years old, whereas, 67% of patients infected were more than 49 years old.

In infected children, B19V causes erythema infectiosum (Fifth Disease) characterized by a “slapped cheek” rash, which can be accompanied in some cases by fever, headache and diarrhea.

In pregnant women, the infected mother can transmit B19V to the fetus, which can cause non-immune fetal hydrops (NIHF), spontaneous abortion, congenital anemia, or intrauterine fetal death [17, 20].

Laboratory diagnosis of Parvovirus B19

Laboratory diagnosis for B19V is usually carried out using different serological and molecular techniques. Serological techniques are based on the detection of anti-B19V IgM and IgG antibodies in sera or blood.

The IgM class is considered to be a specific marker to differentiate the acute phase from the convalescent phase of infection. It can be detected during the first few months after B19V infection. IgG anti-B19V antibodies, however, are considered to be a specific marker for remote infections.

Several Serological tests are used for B19V diagnosis, the most commonly used are: immunofluorescence tests, enzyme-linked immunosorbent assay (ELISA) test as well as Immunoblot tests. Numerous diagnostic assays for anti-B19V antibodies are currently commercially available; such an example is the ELISA test (EIAgen parvovirus B19 IgM and IgG kit Adaltis, Italy).

Moreover, other serological techniques based on antigen detection are commercially available. In fact**,** many researchers focus on developing rapid diagnostic methods like haemagglutination tests for the detection of either the virus or its infected tissues [22].

Recently, molecular techniques based on the detection of B19V DNA have been developed and used, such as conventional polymerase chain reaction (PCR) and Quantitative PCR (qPCR). These molecular techniques seem to be more sensitive than serological tests for B19V diagnosis. Furthermore, molecular techniques like qPCR allow the identification of past and recent parvovirus B19 Infection in immunocompetent individuals [23].

Human B19 virus vaccine

The sequencing of human parvovirus B19 genome has encouraged researcher to develop an effective and safe vaccine to protect people against B19V infection. Numerous researches have worked for the production of the recombinant vaccine (MEDI-491) which is composed of two capsid proteins VP1 and VP2. The first clinical trials indicated that MEDI-491 was safe and immunogenic, and the overall results seemed promising [24].

B19 Virus Infection in Saudi Arabia

In Saudi Arabia, few studies have been performed to determine the seroprevalence of immunoglobulin-G (IgG) to B19V in Saudi blood donors in the western areas of Saudi Arabia [25, 26].

In 1993, a study was conducted by Al-Frayh and his colleagues to detect parvovirus B19-specific-IgG and IgM antibodies in the serums of patients and general blood donors in Saudi Arabia. in this study, all samples were tested using indirect enzyme-linked immunosorbent assay (ELISA) and the results demonstrated that specific IgM antibodies were detected in 94 % of all tested samples, whereas, specific IgG antibodies were detected in 85 % of all samples. [25]

Recently, another study has been performed by Johargy in Makkah city in Saudi Arabia. Johargy has tested 578 samples of Saudi blood donors using commercially available ELISA tests. Interestingly, results showed that among 578 samples tested, parvovirus B19-specific-IgG antibodies were detected in only 441 of them; which means that 76.3% of blood donors have been previously exposed to this virus. These results were in good agreement with previous published studies in others countries [26].

Discussion and Conclusion

It was strongly believed that there is a correlation between parvovirus infection and occurrence of malignant tumors. In 2012, LI and co-workers have investigated the effect of parvovirus B19 infection on the occurrence of malignant tumors. In fact, they have showed that the prevalence of B19 DNA in cancer patients was 50.69% whereas the prevalence of B19 DNA was only 4.5% in healthy controls. This result suggested that there is a potential correlation between B19 virus infection and the occurrence of cancer [27].

As of yet, our information regarding the seroprevalence of human parvovirus B19 and its role in cancer pathogenesis in Saudi Arabia is sparse and needs further investigation. Further studies are required to determine

the seroprevalence rate of immunoglobulin-G and immunoglobulin-M against human parvovirus B19 in the general population of Arabic countries, especially in women of childbearing age in Saudi Arabia.

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