Review Article

Viral Infections Associated with Anemia

Seyed Gholamreza Azimi[1], Hossein Goudarzi[2], Ebrahim Faghihloo[2*]

[1]Department of Biology, Shahr-e-Qods Branch, Islamic Azad University, Tehran, Iran
[2]Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Received: 26 February, 2025; Accepted: 15 April, 2025

DOI: 10.22037/nbm.v13i4.48404

Abstract

Background: Anemia is a serious blood disorder characterized by the bone marrow's inability to produce new blood cells, which can be either acquired or inherited. Exposure to viral infections can lead to anemia, including diseases caused by parvovirus B19, Epstein-Barr virus, cytomegalovirus, human immunodeficiency virus, hepatitis C virus, varicella-zoster virus, and SARS-CoV-2. While these infections are often subclinical in immunocompetent individuals, they can become critical and cause anemia in high-risk populations, such as immunocompromised individuals or those with underlying conditions like sickle cell disease, particularly in infants and pregnant women.

Materials and Methods: The search was performed using PubMed and Google Scholar for articles published from 2000 to 2024.The primary search string was: ("anemia" OR "erythroid aplasia") AND ("virus" OR "viral infection"), "Parvovirus B19", "Human Immunodeficiency Virus" OR "HIV", "Hepatitis C Virus" OR "HCV", "SARS-CoV-2" OR "COVID-19", "Varicella-Zoster Virus" OR "VZV", "Cytomegalovirus" OR "CMV", and "Epstein-Barr Virus" OR "EBV".

Results: Viral infections are important causes of anemia, through various mechanisms. Parvovirus B19 causes aplastic anemia by targeting red blood cell precursors, while HIV leads to anemia through chronic disease. Hepatitis C causes anemia via bone marrow suppression. SARS-CoV-2 disrupts iron metabolism through inflammation. Other viruses like CMV mainly cause anemia in immunocompromised patients.

Conclusion: This article aims to review the evidence regarding virus-induced anemia, detailing mechanisms such as erythroid progenitor cytotoxicity, chronic inflammation, and treatment-related haemolysis. Diagnostic strategies, ranging from serological assays to pathognomonic bone marrow findings, are discussed to assist laboratory science professionals and clinical specialists in diagnosing, treating, and managing patients with anemia.

Keywords: Viruses, Anemia, Immunocompromised

***Corresponding Author:** Ebrahim Faghihloo Department of Microbiology, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: faghihloo@gmail.com, ORCID ID: 0000-0002-8669-305X

Please cite this article as: Azimi SG, Goudarzi H, Faghihloo E. Viral Infections Associated with Anemia: A Review Study. Novel Biomed. 2025;13(4):240-53.

Introduction

Anemia is a hematological disorder characterized by the bone marrow's failure to produce a sufficient number of blood cells [12]. There are several causes of anemia, including genetic conditions, autoimmune diseases, exposure to certain chemicals or medications, and infections, particularly viral infections [27]. This review aims to (1) examine the data related to anemia and viral infections, (2) clearly define pathogen-

specific processes, and (3) describe diagnostic approaches. Additionally, we searched for any pathognomonic signs associated with each viral infection linked to anemia. Furthermore, we outlined the mechanisms of each virus and its respective diagnostic criteria.

A wide range of viral infections has been related to anemia, each exhibiting distinct biological behaviors that disrupt hematopoiesis. A diverse array of viruses, including parvovirus B19 (B19V), Epstein-Barr virus (EBV), cytomegalovirus (CMV), human immunodeficiency virus (HIV), hepatitis C virus (HCV), varicella-zoster virus (VZV), and SARS-CoV-2 [27, 75], have been identified as potential causes of anemia. These viruses can particularly affect individuals with underlying health conditions. Understanding how to approach and diagnose anemia in patients infected with these viruses is crucial for their treatment.

Parvovirus B19

Evidence: Parvovirus B19 (B19V) is a single-stranded DNA virus that exclusively infects humans. It is a significant pathogen responsible for a wide range of clinical manifestations, particularly anemia. Two similar studies involving 26 patients [56] and 27 patients [92] with aplastic anemia were conducted to examine the levels of B19V IgM and DNA. Among the 26 patients, twenty-four tested positive for B19V IgM, and thirteen had detectable B19V DNA. In the group of 27 patients, DNA was detected in 10 individuals, while IgM was identified in 11. Although B19V infection is typically minor in healthy individuals, the prevalence of B19V infection increases in specific populations, such as those affected by underlying conditions, such as sickle cell disease (SCD)[1], or individuals who are immunocompromised[28], for example, organ transplant recipients[18], as well as in children and pregnant women. Studies have shown that B19V infection is a major cause of aplastic crisis, a condition that halts red blood cell (RBC) production and leads to severe anemia[49]. E. Kaitlynn Allen [1] states that in patients, particularly children, with SCD, B19V infection can result in an aplastic crisis and subsequently lead to anemia. Additionally, another study [57] examined 322 pediatric patients with SCD for the presence of B19V. The results show that among the 322 patients, 113 tested positive for IgG, while 119 tested positive for IgM at enrolment. Individuals with immunocompromised conditions, like immunodeficiency syndrome (AIDS), are particularly at risk of B19V infection [28, 69]. In this case, in one study [70], 113 HIV-positive patients were tested for the presence of B19V DNA, as well as for anti-B19V IgM and IgG antibodies. The results showed that, out of the 113 patients, nineteen tested positive for B19V DNA, three had IgM antibodies, and seven had IgG antibodies. In transplant recipients**,** B19V infection is a significant cause of severe anemia, particularly among kidney, liver, and renal transplant recipients [17, 58]. In a study [17], researchers virologically examined 38 transplant recipients with anemia who received renal transplants from donors. The results demonstrated an active B19V infection following renal transplantation in 12 of the 38 recipients who presented with anemia. In pregnant women, while 30-50% are susceptible to B19V, only a small percentage will actually become infected with the virus [32]. Fetal infection by B19V is a common cause of fetal anemia and non-immune hydrops fetalis, which can lead to fetal death [33]. The risk of hydrops is higher if the infection occurs during the first trimester or between 13 and 20 weeks of gestation [32]. A study [53] investigated possible relations between B19V infection and fetal mortality and spontaneous abortion due to anemia. In this study, 100 placental tissues with unknown causes of fetal death were examined for the presence of B19V DNA. The results indicated that 6 out of 100 cases were positive for B19V. The researchers concluded that the infection can affect the fetus because fetal tissues express the viral P antigen receptor, which may lead to anemia, hydrops, and even high-output cardiac failure [54]. Currently, there are no specific treatments available for B19V infection in pregnant women; however, counselling for non-immune mothers and actively monitoring maternal infections may help reduce mortality [52].

Mechanism: The mechanism of anemia induced by B19V is multifaceted, involving direct viral cytotoxicity to erythroid progenitor cells, disruption of the cell cycle, and an often inadequate immune response that allows for persistent viral replication [32]. B19V primarily causes anemia through its selective infection of human erythroid progenitor cells [33], facilitated by its binding to the P antigen receptor on

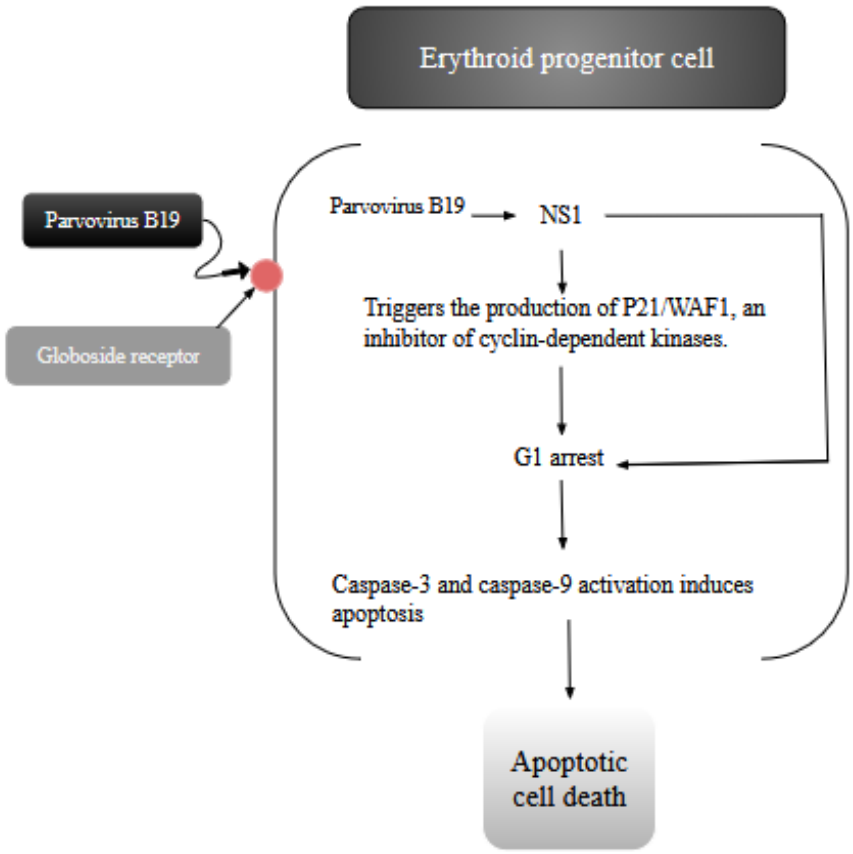

Figure 1. The mechanism through which Parvovirus B19 induces cell death in erythroid progenitor cells.

these cells. The NS1 protein induces the expression of P21/WAF1, a cyclin-dependent kinase inhibitor, resulting in G1 arrest. Furthermore, NS1 promotes both G1/G2 cell cycle arrest and apoptosis (Figure 1); this leads to transient RBC aplasia, particularly in patients with haemolytic disorders [53, 81]. Consequently, there is a rapid decline in erythropoiesis, which clinically manifests as a transient aplastic crisis in patients with haemolytic disorders and potentially as chronic red cell aplasia in immunocompromised individuals [53, 81.]

Diagnosing: There are several tests for B19V-related anemia shown in Table 1. Besides detecting anti-B19 IgM/IgA antibodies and B19V DNA viral loads, a pathognomonic sign for diagnosing B19V-induced anemia is the presence of pure erythroid hypoplasia observed in a bone marrow biopsy. This is particularly evident in cases of transient aplastic crisis. Additionally, the biopsy may reveal giant pronormoblasts[20] with intranuclear inclusions and surrounding cytoplasmic clearing, characteristic of parvovirus B19 infection (Figure 2).

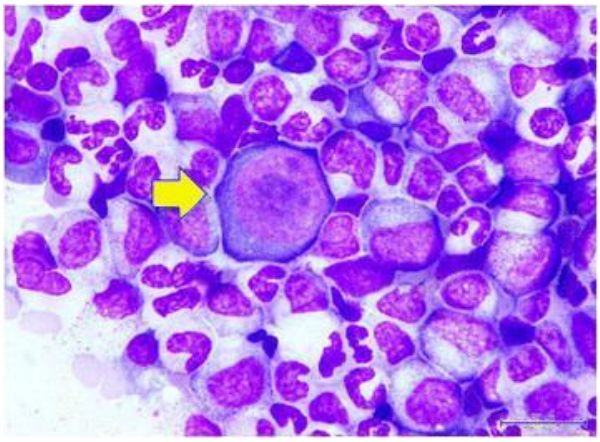

Figure 2. An enormous pronormoblast may be seen in the bone marrow, as indicated by the yellow arrow.

Table 1. Several tests for diagnosing the presence of B19V in anemic patients.

Diagnostic Method	Marker Detected	Clinical Relevance	References
Complete Blood Count (CBC)	Normocytic, normochromic anemia with low reticulocyte count	Help distinguish different types of anemia	(78)
Peripheral Blood Smear	Abnormal RBC shapes(e.g., poikilocytosis)	May represent possible hemolysis or bone marrow dysfunction.	(82)
Bone marrow biopsy	Erythroid hypoplasia, giant pronormoblasts	Confirms parvovirus B19 infection by showing characteristic giant pronormoblasts.	(14)
Serological Assays (ELISA)	Parvovirus B19-specific IgM (acute) and IgG (past)	Distinguishes recent from past infection in immunocompetent patients. In immunocompromised patients, IgM/IgG may appear 10–12 days and 2 weeks post-infection.	(37)
Real-time PCR	Detect low B19 viral loads	Preferred method for detecting active infection, especially in immunocompromised patients.	(18)

Human immunodeficiency virus

Evidence: Human immunodeficiency virus (HIV) is a member of the Retroviridae family, characterized by two copies of a single-stranded RNA genome encased in a capsid, which is surrounded by a plasma membrane. Anemia is the most prevalent haematological abnormality observed in HIV-positive patients [80]. Various types of anemia are commonly observed in individuals infected with HIV, including anemia of chronic disease, iron deficiency anemia (IDA), hypochromic microcytic anemia, macrocytic anemia, normocytic normochromic anemia, and vitamin B12 deficiency anemia[80], as well as immune haemolytic anemia[83]. In a study[43], 73 HIV-positive children were examined to confirm the presence and type of anemia. The results demonstrated that 47 of the 73 children had anemia, with 26% experiencing mild anemia, 60% moderate anemia, and 15% severe anemia. Among the 47 affected children, the following types of anemia were identified: hypochromic microcytic (40%), macrocytic (32%), and normocytic normochromic (28%). In the same study[32], 55 HIV-infected patients were examined. Among these patients, anemia was present in 45 individuals, with the following types identified: normocytic normochromic anemia (66.66%), iron deficiency anemia (37.77%), and anemia of chronic disease (62.22%). In an Ethiopian study [43], the overall prevalence of anemia was found to be 34.6% among individuals living with HIV/AIDS. In this study, researchers reported that approximately 5% of participants had severe anemia, 15.6% had moderate anemia, and 14% had mild anemia. A cross-sectional study conducted in Iran [35] found that 46% of HIV-positive participants exhibited mild anemia, with an overall prevalence of anemia at 71%. Normocytic anemia, characterized by a decreased reticulocyte count, was the most commonly observed type. In a study conducted in Nepal[59], the estimated prevalence of anemia was 66.7%, with mild anemia at 14.3%, moderate anemia at 40.5%, and severe anemia at 11.9%. Similarly, a study in Ethiopia[85] reported that

Table 2. Several tests for diagnosing HIV in anemic patients.

Step	Action	HIV-Specific Considerations	References
Initial Assessment	Complete blood count, reticulocyte count	HIV patients often present with normocytic normochromic anemia; can be hyporegenerative with low reticulocyte count	(24)
Iron Status Evaluation	Serum iron, total iron-binding capacity (TIBC), transferrin saturation, ferritin	HIV patients with anemia show significantly lower transferrin saturation and serum iron compared to HIV patients without anemia	(45)
Specialized Biomarkers	Erythrocyte zinc protoporphyrin (ZPP), serum hepcidin	Serum hepcidin and erythrocyte ZPP levels could help detect iron deficiency anemia in HIV-positive patients	(3)
CD4 Count Assessment	Measure CD4 lymphocyte count, determine HIV stage	Higher prevalence of anemia with lower CD4 counts; guides diagnostic approach based on disease stage	(91)
Medication Review	Evaluate current medications, especially AZT	Zidovudine (AZT) is particularly associated with anemia in HIV-positive patients	(86)
EPO Level	Measurement of serum EPO concentrations in HIV patients with anemia (range: 9–3,390 mU/mL), particularly in those with AIDS receiving zidovudine (ZDV)	HIV infection increases the risk of chronic kidney disease, which reduces EPO synthesis and exacerbates anemia due to insufficient erythropoietin production	(19)

approximately 5% of participants had severe anemia, 15.6% had moderate anemia, and 14% had mild anemia. Finally, a study in Indonesia [7] enrolled a total of 243 HIV-infected patients, including both those receiving antiretroviral therapy (ART) and those who were ART-naive. The prevalence of anemia among ART-naive patients was 60.8%, while it was 40.3% in patients receiving ART.

Mechanism: The mechanisms of anemia in individuals with HIV are complex and multifaceted, involving alterations in cytokine production that subsequently affect haematopoiesis[7], decreased erythropoietin (EPO) concentrations[103], and opportunistic infectious agents such as Mycobacterium avium complex and parvovirus B19, which can lead to red cell aplasia in HIV patients [93, 85,70]. Nutritional deficiencies, including those of iron, folate, vitamin B12, and vitamin A, have also been linked to anemia associated with HIV infection[74]. A hallmark of HIV infections is chronic inflammation, which disrupts iron homeostasis, adversely affecting erythropoiesis and contributing to the development of anemia[13]. Direct viral effects on bone marrow function further cause deficiencies in red blood cell production. T-cells infected with HIV can directly suppress the growth of progenitor cells in the bone marrow, negatively impacting haematopoiesis and leading to anemia[76,74]. One study explained that anemia induced by antiretroviral medication, particularly zidovudine, is a significant concern due to its bone marrow-suppressive effects. Approximately 22% of anemia cases in HIV-positive patients have been attributed to zidovudine-induced anemia [50, 86]. Zidovudine has the destructive effect of causing anemia, and research demonstrates that the duration of zidovudine use correlates with the severity of anemia in individuals living with HIV[22]. Additionally, several studies have suggested a relationship between viral load and anemia; however, this relationship remains poorly understood. According to one study[60], viral load profiles investigated in drug users with asymptomatic HIV infections found no direct association between viral load and anemia[60].

Diagnosing: Various types of HIV-induced anemia diagnoses are presented in Table 2. However, there is no specific pathognomonic sign for diagnosing HIV-induced anemia. Nevertheless, certain markers play a significant role in the diagnosis of this condition, such as hepcidin levels, EPO levels, and CD4 lymphocyte counts [19,45,91].

Hepatitis C Virus

Evidence: Hepatitis C Virus (HCV) is a member of the Flaviviridae family. Anemia is one of the most common and significant haematological abnormalities associated with HCV, particularly during treatment, such as blood transfusion[62]. According to a study in Egypt, 200 pregnant women with a history of bad

pregnancy were investigated for possible HCV infection; in this study, anemia was diagnosed in pregnant women with a hemoglobin level below 11 gm/dl[5]. The prevalence of anemia due to HCV infection is persistently greater in patients, especially those undergoing dialysis, than in the general population[71]. Studies evaluating the frequency of pancytopenia in patients with chronic viral liver disease, like HCV, have found significant rates of occurrence, with some reports indicating prevalence rates of around 28.57%[63]. Interestingly, some studies have found higher endogenous erythropoietin levels in hemodialysis patients with HCV infection compared to those without infection, suggesting complex interactions between HCV, kidney function, and erythropoiesis [62]. Additionally, in the treatment of HCV-infected patients, ribavirin-induced haemolytic anemia is frequently seen, which is directly correlated with the dosage of Ribavirin and exacerbated by interferon-induced bone marrow suppression[46,97].

Hepatitis-associated aplastic anemia (HAAA): Also, hepatitis-associated aplastic anemia (HAAA) is a distinct variant of aplastic anemia in which pancytopenia appears two to three months after an acute attack of hepatitis. HAAA occurs most frequently in young male children and is lethal if left untreated. The etiology of this syndrome is proposed to be attributed to various hepatitis and non-hepatitis viruses such as HAV, HBV, CMV, EBV, HCV, HDV, HEV, and HGV, which have been associated with this set of symptoms [79]. Due to evidence, the mechanism of HAAA includes a severe imbalance of the T cell immune system and an effective response to immunosuppressive therapy[80]. Diagnosis encompasses blood profiling, viral serological marker assessment, immune function evaluation, and examination of bone marrow hypocellularity. Patients diagnosed with HAAA have undergone treatment via bone marrow or haematopoietic cell transplantation from an HLA-matched donor; in the absence of such a donor, immunosuppressive therapy has been employed[79].

Mechanism: HCV can manifest as various types of anemia, including anemia of chronic disease, through multiple mechanisms that range from direct viral effects to complications induced by treatment. HCV can directly impact haematopoiesis through its effects on the bone marrow [87]. It is believed that HCV attaches to particular receptors and enters cells through endocytosis, potentially disrupting normal cellular processes. Following the uncoating process, the viral genome is translated into a precursor polyprotein, while viral RNA is produced by a polymerase complex encoded by the virus. Both of these processes can disrupt host cell functions. The direct impact of the Hepatitis C virus (HCV) on host cells may contribute to the onset of anemia by impairing erythropoiesis and altering normal cellular metabolic processes. In addition to HCV infection, it can also trigger immune-mediated processes that contribute to anemia[55]. The immunopathogenesis of liver disease in HIV/HCV co-infected patients is a process that can affect hematological parameters, including RBC counts. Several studies have demonstrated that HIV worsens the course of HCV infection, potentially exacerbating hematological complications, including anemia[26]. Furthermore, chronic HCV infection can lead to the development of mixed cryoglobulinemia type II, which is associated with immune complex formation and potential impacts on blood cell production [65]. Even so, in patients with liver dysfunction due to HCV, reduced production of erythropoietin and altered iron metabolism can contribute to anemia [10]. The liver plays a crucial role in the production of proteins involved in iron metabolism and erythropoiesis, and HCV-related liver damage can interfere with these processes[10]. At last, in cases of chronic HCV, treatment with interferon and Ribavirin can exacerbate bone marrow suppression, leading to significant anemia[38]. The suppression primarily affects the erythroid lineage in the bone marrow, resulting in insufficient production of red blood cells. The mechanisms involved include the inhibition of erythroid colony-forming units by inflammatory cytokines, such as interferon-gamma, which disrupt normal erythropoiesis and lead to anemia[5].

Diagnosing: Numerous laboratory tests are essential for confirming the diagnosis and identifying the underlying cause and severity of HCV-induced anemia, as shown in Table 3. However, there is no pathognomonic sign for diagnosing HCV-induced anemia.

Table 3. Several essential tests for diagnosing HCV in patients with anemia.

Test Type	Clinical Significance	References
Complete Blood Count (CBC)	Primary diagnostic tool for detecting the presence and severity of anemia; may present with low hemoglobin levels	(73)
Reticulocyte Count	Low reticulocyte counts may indicate impaired bone marrow response	(46)
Iron Studies	Evaluates iron status and helps differentiate anemia types (e.g., iron deficiency vs. anemia of chronic disease)	(41)
Erythropoietin (EPO) Levels	Measures EPO production; may be elevated in HCV-infected patients due to impaired red blood cell production	(10)
Liver Function Tests	Assesses the extent of liver damage, which may correlate with anemia; liver transaminases such as ALT are significantly higher in HCV-positive patients compared to HCV-negative individuals	(38)
Serological and Molecular Diagnosis	Detects anti-HCV antibodies and HCV RNA; correlates with hematological complications such as anemia	(39)

SARS-CoV-2 virus

Evidence: COVID-19, the disease caused by the single-stranded RNA virus named SARS-CoV-2, has been linked to various hematological abnormalities, including anemia [34]. A study [8] found that among 353 patients with an average age of 54.54 ± 18.28 years who were diagnosed with SARS-CoV-2 infection, 118 (41.93%) were affected by anemia. Anemia may be a pre-existing condition in many COVID-19 patients, as well as a complication that develops during the course [8]. The risk of severe COVID-19 increases in inherited anemias, such as sickle cell disease and β-thalassemia, due to the factors such as chronic inflammation, iron overload, and comorbidities[47]. Zhou et al.,[102] found that anemia in 15% of 191 patients hospitalized with COVID-19; however, these anemic patients had a greater frequency of comorbidities such as arterial cardiovascular disease, hypertension, and chronic kidney disease. Other researchers reported anemia in 35.5% of 222 hospitalized patients[94], and another study showed anemia in 61% of their 206 hospitalized COVID-19 patients[16]. Anemia was reported in 33.25% of COVID-19 patients in a Nepalese study[77], and another investigation reported anemia in 51.8% of older COVID-19 patients[95].

Mechanism: The connection between SARS-CoV-2 and anemia involves many pathways, ranging from inflammatory dysregulation to direct hematological consequences. SARS-CoV-2 produces a hyperinflammatory condition defined by increased cytokines (e.g., IL-6, TNF-α), which affect iron homeostasis. Pro-inflammatory cytokines raise hepcidin levels, a hormone that limits iron absorption in the gut and stores iron in macrophages. This results in chronic disease, characterized by low blood iron, normal/high ferritin levels, and reduced erythropoiesis[94,47,102]. This mechanism aligns with the classic anemia of chronic disease, where inflammation-induced iron restriction leads to normocytic/normochromic anemia[23]. SARS-CoV-2 may infect erythroid precursor cells via ACE2 receptors or decrease bone marrow function, resulting in reduced RBC production. There are some indications that viral RNA [94] has been found in hematopoietic stem cells, which signifies lymphopenia and anemia are common in severe COVID-19 cases, indicating bone marrow suppression [47].

Diagnosing: While there are no pathognomonic signs for SARS-CoV-2-associated anemia, diagnosing using a combination of standard hematological tests and markers of systemic inflammation or viral impact is the key to detecting the presence of anemia caused by SARS-CoV-2, as shown in Table 4.

Varicella-zoster virus

Evidence: Varicella-zoster virus (VZV) is a double-stranded DNA virus that is strongly cell-associated and a neurotropic alpha herpesvirus that only infects humans and causes specific disorders [89]. Several case studies provide possible evidence of an association between VZV and anemia through various pathways and syndromes.

Disseminated VZV infection in AA-PNH syndrome: In one case report, a 26-year-old man with aplastic anemia-paroxysmal nocturnal hemoglobinuria (AA-PNH) syndrome died from a disseminated VZV infection while on immunosuppressive medication (cyclosporine and corticosteroids). The study highlights that VZV can directly infect hematopoietic cells, thereby increasing cytopenias in conditions such as

Table 4. Several tests for diagnosing the presence of SARS-CoV-2 in anemic patients.

Diagnosing Method	Key Finding	Clinical Significance	References
Complete Blood Count (CBC)	Decreased hemoglobin (<13 g/dL in men, <12 g/dL in women); low RBC count	Anemia prevalence in COVID-19 ranges from 20–50%, often normocytic/normochromic; severity correlates with poor prognosis	(36)
Reticulocyte Count	Reticulocytopenia observed in 70% of severe COVID-19 cases	Indicates bone marrow suppression due to IL-6–driven inflammation or direct viral effects on erythropoiesis	(36)
Iron Studies & Inflammation Markers	Low serum iron, elevated ferritin (hyperferritinemia), high CRP	Helps differentiate iron deficiency anemia from anemia of chronic disease (ACD); hyperferritinemia correlates with severe COVID-19	(102)
Serological / Molecular Tests	SARS-CoV-2 RNA (PCR) or antigen detection; anti-SARS-CoV-2 antibodies	Confirms active infection or past exposure; anemia may correlate with viral load or prolonged inflammation	(51)

AA-PNH. Finally, the study highlights the vulnerability of immunocompromised patients to life-threatening VZV consequences, which worsen pre-existing anemia and cytopenias[98]. Another case study[99] reports that systemic inflammation caused by VZV reactivation can decrease erythropoiesis or enhance red blood cell death.

Autoimmune Hemolytic Anemia (AIHA) Secondary to Varicella: Following a varicella infection, an 11-year-old girl had severe AIHA, which included hemoglobin levels as low as 3.8 g/dL, jaundice, and high LDH. A positive direct Coombs test confirmed the diagnosis. Steroids and blood transfusions were used to treat the patient, who eventually recovered. This emphasizes VZV's role in inducing autoimmune destruction of red blood cells, particularly in pediatric populations[48].

***VZV Reactivation Reverses Pure Red Cell Aplasia (PRCA)*:** A 34-year-old lady with PRCA (marked by severe anemia and the absence of erythroid precursors in bone marrow) went into remission following a herpes zoster infection. Her hemoglobin returned to normal after VZV antiviral therapy, without the need for transfusions. This counterintuitive outcome suggests that VZV may enhance bone marrow regeneration in immunosuppressed individuals; however, the underlying mechanism remains unknown[6].

***Coinfection with VZV and hemolytic anemia*:** An 84-year-old lady with steroid-dependent hemolytic anemia died from pneumonia caused by coinfection with VZV and Pneumocystis jirovecii. While VZV was not the main cause of her anemia, her immunosuppression (due to continuous steroids) permitted significant systemic VZV reactivation, aggravating her underlying hematologic disease[66].

Mechanism: Possible mechanisms by which varicella-zoster virus (VZV) contributes to anemia, according to case studies, are a diverse range from bone marrow suppression to immune-mediated haemolysis. In terms of bone marrow suppression, VZV directly infects haematopoietic cells, thereby disrupting bone marrow function. This is especially critical in patients with aplastic anemia-paroxysmal nocturnal hemoglobinuria (AA-PNH) syndrome[98]. VZV infection can induce systemic inflammation, which may contribute to the development of anemia through various mechanisms, including hepcidin-mediated iron dysregulation, inflammatory cytokine-mediated (e.g., IL-1β, IFN-γ) inhibition of erythropoiesis, and reduced erythrocyte lifespan [72]. VZV reactivation worsens anemia in patients with nutritional deficiencies (e.g., vitamin B12) or autoimmune conditions (e.g., pernicious anemia) by compounding RBC production defects[54]. A case study suggests that VZV can trigger AIHA through molecular mimicry or immune dysregulation[55]. The study also notes that in infants with severe vitamin B12 deficiency, VZV infection may precipitate a hemolytic crisis by destabilizing RBC membranes or accelerating RBC destruction[54].

Diagnosing: However, there is no single pathognomonic symptom for VZV-induced anemia; various diagnostic procedures exist for identifying VZV infection, with PCR and serological assays being the most commonly employed. PCR is a highly sensitive test for detecting VZV DNA in a variety of specimens, including cerebrospinal fluid (CSF), vesicular fluid from skin lesions, and blood[25,100], and

serological tests, such as anti-VZV IgG, play an important role in diagnosing VZV antibodies, especially when direct viral detection is difficult [100].

Cytomegalovirus/Epstein-Barr virus

Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) are double-stranded DNA viruses characterized by an icosahedral nucleocapsid. These viruses are associated with a range of hematological and autoimmune disorders, most notably bone marrow suppression (CMV) and autoimmune hemolysis (EBV).

Evidence

***Cytomegalovirus evidence*:** CMV is a significant contributor to anemia, particularly in immunocompromised individuals and those with congenital infections. Slavov et al. [98] examined the presence of CMV DNA in individuals with sickle cell disease and beta-thalassemia, both of which are forms of anemia. The findings show that CMV DNA was detected in 13.8% of sickle cell patients and 7.6% of beta-thalassemia major patients. In this study, the CMV gB2 genotype was more prevalent (90.9%) in comparison with the gB1 genotype (9.1%). Another research study conducted in Brazil [98] found that CMV seroprevalence was 89.4% among 470 individuals with hematological disorders and other types of anemia. The observed prevalence was 78.9%, with 85% of persons suffering from various hematological illnesses such as sickle cell anemia, cancer, hemophilia, and hemoglobinopathies [98].

***Epstein-Barr virus evidence*:** EBV is common in anemia, particularly in immune-mediated variants (AIHA, HAAA), as well as in hematological diseases. Few studies have examined the frequency of EBV among individuals with hematological disorders. A research study [91] points out that in patients with hematological illnesses and those undergoing hemodialysis, the prevalence rates of anemia were 91.2% and 97.7%, respectively [90]. A comprehensive assessment of 60 patients (1973–2024) with EBV-associated hemolytic anemia indicated that 52% were cold-antibody-mediated, 30% were warm-antibody-mediated, and 3.3% had paroxysmal cold hemoglobinuria[11]. Two individuals died with warm-antibody AIHA[12]. According to this literature review, EBV and CMV may cause immune-mediated hemolytic anemia[11]. In a Brazilian cohort of 228 hematological patients, 85.09% tested positive for EBV, with 78.51% testing positive for both EBV and CMV. Elevated ferritin was associated with EBV infection (p=0.031) and coinfection (p=0.038), indicating inflammation-driven anemia [67]. EBV reactivation increases anemia risk in immunocompromised people (e.g., transplant recipients, HIV patients) due to immunological dysregulation and marrow suppression [68]. An observational research study [31] conducted in India with 120 patients suffering from aplastic anemia discovered active EBV infection in 20% of the patients. Of this group, seventeen had severe, five had very severe, and two had non-severe aplastic anemia. The author mentioned that at the time of laboratory diagnosis, none of the EBV IgM-positive individuals had mononucleosis. Two patients who tested positive for EBV and were also infected with parvovirus developed severe aplastic anemia.

Mechanism

While few researchers have confirmed CMV- and EBV-induced anemia, several case studies have illustrated how these infections can lead to various types of anemia, including immune-mediated mechanisms, direct impacts on hematopoietic cells, and inflammatory processes.

***Possible EBV mechanisms*:** In terms of immune-mediated hemolysis (AIHA), a study suggests that EBV induces autoantibodies against RBC antigens, resulting in cold agglutinin sickness or warm autoimmune hemolytic anemia [67]. A case report points out that EBV-associated hepatitis can advance to hepatitis-associated aplastic anemia (HAAA) [87], which is defined by bone marrow failure. A study explains how EBV elevates hepcidin, a hormone that inhibits iron absorption and recycling. This study suggests that EBV-induced inflammation (e.g., via the IL-6/IL-1β pathways) causes functional iron deficiency and anemia of chronic disease[22].

***Possible CMV mechanisms*:** Several case studies elucidate the potential CMV mechanisms in anemia, particularly in immunocompromised individuals, where these mechanisms encompass immune-mediated hemolytic anemia, bone marrow suppression, and even direct viral cytotoxicity. CMV infection can trigger autoimmune responses, where molecular mimicry

between CMV antigens and RBC surface proteins may lead to cross-reactive antibodies that target RBCs, which can lead to immune-mediated hemolytic anemia [96]. A study explained how CMV can suppress erythropoietin (EPO) production that happens when CMV infects renal interstitial fibroblasts, which are critical for hypoxia-induced EPO production. This study highlights that CMV inhibits hypoxia-inducible factor 2α (HIF-2α), a key regulator of EPO gene expression, resulting in reduced EPO levels and subsequent anemia[16]. In terms of bone marrow suppression, CMV infects bone marrow stromal cells, reducing the production of essential hematopoietic cytokines like stem cell factor (SCF), granulocyte colony-stimulating factor (G-CSF), and interleukin-6 (IL-6). This disrupts erythropoiesis and progenitor cell differentiation [68]. CMV can infect hematopoietic progenitor cells, leading to reduced RBC production. Although less common, this direct cytopathic effect has been observed in immunocompromised hosts [68]. At last, case studies declare that where CMV coinfection with viruses (e.g., parvovirus B19) or in HIV/AIDS or transplant patients, CMV reactivation often coincides with other infections, which worsen anemia through combined hemolytic and suppressive effects [96, 43].

Diagnosing

***Cytomegalovirus Diagnosing*:** CMV diagnosis involves a variety of procedures, including molecular testing, with the gold standard being quantitative PCR for CMV DNA, which has a sensitivity of approximately 95% in immunocompromised individuals[89]. Furthermore, viral load levels in the blood (>1000 IU/mL) suggest an active infection that requires therapy [91]. Serologic tests, such as CMV IgM/IgG, are also essential; however, they have a limited sensitivity in immunocompromised hosts [28].

***Epstein-Barr virus Diagnosing*:** The diagnostic approach for EBV diagnosis is as follows: (1) Positive VCA IgM + negative EBNA IgG signifies acute infection; (2) positive VCA IgG + positive EBNA IgG indicates past infection [11]. The direct Coombs test can play a significant role in the diagnosis of EBV-related AIHA patients, where, according to a case study, 52% of EBV-related AIHA patients were positive on the direct Coombs test [67]. Quantitative EBV DNA PCR (>1000 copies/μg DNA) is used to detect current infection [69].

Conclusion

Viral infections represent a significant and often underrecognized cause of anemia, with several pathogens—including B19V, HIV, HCV, SARS-CoV-2, VZV, CMV, and EBV—contributing to its development through various mechanisms. These viruses impact erythropoiesis by causing direct bone marrow suppression (e.g., B19V infecting erythroid progenitors), immune-mediated destruction (e.g., EBV leading to autoimmune hemolysis), or systemic inflammation (e.g., SARS-CoV-2 disrupting iron metabolism via hepcidin). Individuals who are immunocompromised, those with pre-existing hematologic diseases, and vulnerable groups, including youngsters and pregnant women, are more sensitive to viral-induced anemia. Diagnosis necessitates a multifaceted approach that combines clinical suspicion with specific laboratory testing such as PCR for viral identification, serology for immune response assessment, and bone marrow examination in select individuals. While certain infections, such as B19V, have pathognomonic features (e.g., enormous pronormoblasts), others require more extensive testing due to overlapping hematologic symptoms. Treatment methods range from antiviral medicine and immunosuppression to supportive care. Finally, increased recognition of viral etiologies in anemia is critical for early management, particularly in high-risk patients. Future research should focus on elucidating unknown processes, refining diagnostic algorithms, and developing targeted therapeutics to mitigate the hematologic effects of these infections. By merging virological and hematological perspectives, doctors may enhance patient outcomes in cases of virus-associated anemia.

Acknowledgment

None.

Conflict of interest

The authors further declare that they have no conflict of interest.

Funding

None.

References

1. Fsky RA, Jones RJ. Aplastic anaemia. Lancet. 2005;365(9471):1647–56.
2. Alves ADR, Cubel Garcia RDCN, Cruz OG, Pinto MA, Amado Leon LA. Quantitative real-time PCR for differential diagnostics of parvovirus B19 infection in acute liver failure patients. Expert Rev Mol Diagn. 2019;19(3):259–66.
3. Morinet F, Leruez-Ville M, Pillet S, Fichelson S. Concise Review: Anemia Caused by Viruses. Stem Cells. 2011;29(11):1656–60.
4. Pascutti MF, Erkelens MN, Nolte MA. Impact of Viral Infections on Hematopoiesis: From Beneficial to Detrimental Effects on Bone Marrow Output. Front Immunol. 2016;7:364.
5. Marascio N, Rotundo S, Quirino A, Matera G, Liberto MC, Costa C, et al. Similarities, differences, and possible interactions between hepatitis E and hepatitis C viruses: Relevance for research and clinical practice. World J Gastroenterol. 2022;28(12):1226–38.
6. Chorba T, Coccia P, Holman RC, Tattersall P, Anderson LJ, Sudman J, et al. The Role of Parvovirus B19 in Aplastic Crisis and Erythema Infectiosum (Fifth Disease). J Infect Dis. 1986;154(3):383–93.
7. Florea AV, Ionescu DN, Melhem MF. Parvovirus B19 infection in the immunocompromised host. Arch Pathol Lab Med. 2007;131(5):799–804.
8. Boubaker K, Mahfoudhi M, Battikh A, Bounemra A, Maktouf C, Kheder A. Higher Endogenous Erythropoietin Levels in Hemodialysis Patients with Hepatitis C Virus Infection and Effect on Anemia. Open J Nephrol. 2015;5:29–34.
9. Allen EK, Penkert RR, Hankins JS, Surman SL, Van de Velde LA, Cotton A, et al. Immune Cell Profiles of Patients with Sickle Cell Disease during Parvovirus B19-Induced Transient Red Cell Aplasia. Vaccines (Basel). 2024;12(9):984.
10. Lamont RF, Sobel JD, Vaisbuch E, Kusanovic JP, Mazaki-Tovi S, Kim SK, et al. Parvovirus B19 infection in human pregnancy. BJOG. 2011;118(2):175–86.
11. Naides SJ, Howard EJ, Swack NS, True CA, Stapleton JT. Parvovirus B19 infection in human immunodeficiency virus type 1-infected persons failing or intolerant to zidovudine therapy. J Infect Dis. 1993;168(1):101–5. [
12. Čapenko S, Kozireva S, Folkmane I, Bernarde K, Rozentals R, Murovska M. Anemia as a complication of parvovirus B19 infection in renal transplant recipients. Medicina (Kaunas). 2012;48(6):299–304.
13. Murer L, Zacchello G, Bianchi D, Dall'Amico R, Montini G, Andreetta B, et al. Thrombotic microangiopathy associated with parvovirus B19 infection after renal transplantation. J Am Soc Nephrol. 2000;11(6):1132–7.
14. Giorgio E, De Oronzo MA, Iozza I, Di Natale A, Cianci S, Garofalo G, et al. Parvovirus B19 during pregnancy: a review. J Prenat Med. 2010;4(4):63–6.
15. Goshua G, Pine AB, Meizlish ML, Chang CH, Zhang H, Bahel P, et al. Endotheliopathy in COVID-19-associated coagulopathy: evidence from a single-centre, cross-sectional study. Lancet Haematol. 2020;7(8):e575–82.
16. Mildvan D, Creagh T, Leitz G; Anemia Prevalence Study Group. Prevalence of anemia and correlation with biomarkers and specific antiretroviral regimens in 9690 HIV-infected patients: findings of the Anemia Prevalence Study. Curr Med Res Opin. 2007;23(2):343–55.
17. Lombardi F, Quitadamo AL, Notarangelo LD, Pelizzoni A, Accorsi P, Olivetti F, et al. Varicella zoster virus-induced hemolytic crisis in an infant with severe vitamin B12 deficiency. J Pediatr Hematol Oncol. 2010;32(4):317–8.
18. Levy R, Weissman A, Blomberg G, Hagay ZJ. Infection by parvovirus B19 during pregnancy: a review. Obstet Gynecol Surv. 1997;52(4):254–9.
19. Shabani Z, Esghaei M, Keyvani H, Shabani F, Sarmadi F, Mollaie H, et al. Relation between parvovirus B19 infection and fetal mortality and spontaneous abortion. Med J Islam Repub Iran. 2015;29:197.
20. Koduri PR. Novel cytomorphology of the giant proerythroblasts of parvovirus B19 infection. Am J Hematol. 1998;58(2):95–9
21. Ramezani A, Aghakhani A, Sharif MR, Banifazl M, Eslamifar A, Velayati AA. Anemia prevalence and related factors in HIV-infected patients: a cohort study. Iran J Pathol. 2008;3(3):125–8.
22. Helftenbein E, Kunz H, Hartter P. Labordiagnostik von Parvovirus-B19-Infektionen: Vergleich von zehn kommerziellen IgG- und IgM-Antikörpertests. Immun Infekt. 1994;22(5):181–6. German. [PMID: 7982714]
23. Muramatsu H, Kuriyama A, Anzai Y, et al. A co-infection of varicella-zoster virus and Pneumocystis jirovecii in a non-HIV immunocompromised patient: a case report. BMC Infect Dis. 2019;19:1092.
24. Gebremedhin KB, Haye TB. Factors associated with anemia among people living with HIV/AIDS taking ART in Ethiopia. Adv Hematol. 2019;2019:9614205.
25. Camacho J, Poveda F, Zamorano AF, Valencia ME, Vázquez JJ, Arnalich F. Serum erythropoietin levels in anaemic patients with advanced human immunodeficiency virus infection. Br J Haematol. 1992;82(3):608–14.
26. Sah S, Dahal P, Tamang G, Mandal D, Shah R, Pun S. Prevalence and predictors of anemia in HIV-infected persons in Nepal. HIV AIDS (Auckl). 2020;12.
27. Somia IK, Merati TP, Bakta IM, Putra Manuaba IB, Yasa WPS, Sukrama IDM, et al. High levels of serum IL-6 and serum hepcidin and low CD4 cell count were risk factors of anemia of chronic disease in HIV patients on combination antiretroviral therapy. HIV AIDS (Auckl). 2019;11:133–9.
28. ZainAlAbdin S, Aburuz S, Akour A, et al. Could anemia impact the severity of infections? COVID-19 as an example [version 2; peer review: 2 approved]. F1000Research. 2024;13:295.
29. Al-Anazi KA, Kanfar S, Aldayel A, Abduljalil O, Sayyed AH. Reversal of pure red cell aplasia by varicella zoster virus infection. J Hematol Clin Res. 2019;3:001–10.
30. Sah S, Dahal P, Tamang G, Mandal D, Shah R, Pun S. Prevalence and predictors of anemia in HIV-infected persons in Nepal. HIV AIDS (Auckl). 2020;12.
31. Nouri M, Kamakifar P, Khodabandehlou N, Sadri Nahand J, Tavakoli A, Norooznezhad F, et al. … Med J Islam Repub Iran. 2019;33:137.

32. Ong JP, Younossi ZM. Managing the hematologic side effects of antiviral therapy for chronic hepatitis C: anemia, neutropenia, and thrombocytopenia. Cleve Clin J Med. 2004;71 Suppl 3:S17–21.
33. Brown KE. Haematological consequences of parvovirus B19 infection. Baillieres Best Pract Res Clin Haematol. 2000;13(2):245–59.
34. Aka N, As M, Ah A, Gam AA. Correlation between liver function tests and polymerase chain reaction in chronic hepatitis C patients. … 2015.
35. Gürsoy V, Avcı S, Ermurat S, Erol A, Yazıcı M. Anemia and COVID-19. Eur Res J. 2023;9(5):1074–82.
36. An C, Oh HC, Chang JH, et al. Early triage of patients diagnosed with COVID-19 based on predicted prognosis: a Korean national cohort study. Res Sq. 2020.
37. Spivak JL, Barnes DC, Fuchs E, Quinn TC. Serum immunoreactive erythropoietin in HIV-infected patients. JAMA. 1989;261(21):3104–7. Also included in this entry as provided: Horsburgh CR. Mycobacterium avium complex infection in the acquired immunodeficiency syndrome. N Engl J Med. 1991;324:1332.
38. Lippi G, Salvagno G, Pegoraro M, Militello V, Caloi C, Peretti A, et al. Assessment of immune response to SARS-CoV-2 with fully automated MAGLUMI 2019-nCoV IgG and IgM chemiluminescence immunoassays. Clin Chem Lab Med. 2020;58(7):1156–9.
39. Meidani M, Rezaei F, Maracy MR, Avijgan M, Tayeri K. Prevalence, severity, and related factors of anemia in HIV/AIDS patients. J Res Med Sci. 2012;17(2):138–42. [Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3525030/]
40. Chen CC, Chen CS, Wang WY, Ma JS, Shu HF, Fan FS. Parvovirus B19 infection presenting with severe erythroid aplastic crisis during pregnancy in a woman with autoimmune hemolytic anemia and alpha-thalassemia trait: a case report. J Med Case Rep. 2015;9:58. [DOI: https://doi.org/10.1186/s13256-015-0542-7]
41. Shabani Z, Esghaei M, Keyvani H, Shabani F, Sarmadi F, Mollaie H, et al. Relation between parvovirus B19 infection and fetal mortality and spontaneous abortion. Med J Islam Repub Iran. 2015;29:197.
42. Hasan Y, Brown K. Viral eradication restores normal iron status in chronic hepatitis C patients with abnormal iron studies. Ann Hepatol. 2020;19(4):422–6.
43. Mahmood KA, Siddiqi H, Sajjad A, Shoukat S, Mehmood Z, Wasim A, et al. Iron-deficiency anemia: a study of risk factors among adult population of Quetta Valley. Health (NY). 2012;4:607–11.
44. Beader N, Kolarić B, Slačanac D, Tabain I, Vilibić-Čavlek T. Seroepidemiological study of Epstein–Barr virus in different population groups in Croatia. Isr Med Assoc J. 2018;20(2):86–90.
45. Sulkowski MS. Anemia in the treatment of hepatitis C virus infection. Clin Infect Dis. 2003;37(Suppl 4):S315–22.
46. Giridhar K, Sawhney R, Chichula D, Shet A. Serum hepcidin detects iron deficiency anemia in HIV infected patients with anemia of inflammation. Blood. 2015.
47. De Santis GC, Brunetta DM, Vilar FC, Brandão RA, de Albernaz Muniz RZ, de Lima GM, et al. Hematological abnormalities in HIV-infected patients. Int J Infect Dis. 2011;15(12):e808–11.
48. De Las Cuevas Allende R, Díaz de Entresotos L, Conde Díez S. Anaemia of chronic diseases: pathophysiology, diagnosis and treatment. Med Clin (Barc). 2021;156(5):235–42.
49. Rauff B, Idrees M, Shah SA, Butt S, Butt AM, Ali L, et al. Hepatitis associated aplastic anemia: a review. Virol J. 2011;8:87.
50. Moriishi K, Matsuura Y. Mechanisms of hepatitis C virus infection. Antivir Chem Chemother. 2003;14(6):285–97.
51. Sullivan PS, Hanson DL, Chu SY, Jones JL, Ward JW. Epidemiology of anemia in HIV-infected persons: results from the multistate adult and adolescent spectrum of HIV disease surveillance project. Blood. 1998;91(1):301–8.
52. Abraham AG, Palella FJ, Li X, Estrella MM, Kingsley LA, Witt MD, et al. The impact of impaired kidney function and HIV infection on the risk of anemia. AIDS Res Hum Retroviruses. 2012;28(12):1666–71.
53. Duque X, Mendoza E, Morán S, Suárez-Arriaga MC, Morales-Sánchez A, Fontes-Lemus JI, et al. Epstein–Barr virus infection is associated with elevated hepcidin levels. Int J Mol Sci. 2023;24(2):1630.
54. Majumdar S, Bean CJ, De Staercke C, Bost J, Nickel R, Coates T, et al. Parvovirus B19 infection in sickle cell disease: an analysis from the Centers for Disease Control haemoglobinopathy blood surveillance project. Transfus Med. 2020;30(3):226–30.
55. Saif MW. HIV-associated autoimmune hemolytic anemia: an update. AIDS Patient Care STDS. 2001;15(4):217–24.
56. Mishra B, Malhotra P, Ratho RK, Singh MP, Varma S, Varma N. Human parvovirus B19 in patients with aplastic anemia. Am J Hematol. 2005;79(2):166–7.
57. Bergamaschi G, Borrelli de Andreis F, Aronico N, et al. Anemia in patients with COVID-19: pathogenesis and clinical significance. Clin Exp Med. 2021;21(2):247.
58. Landry ML. Parvovirus B19. Microbiol Spectr. 2016;4(3):DMIH2-0008-2015.
59. Kakavandi S, Hajikhani B, Azizi P, Aziziyan F, Nabi-Afjadi M, Farani MR, et al. COVID-19 in patients with anemia and haematological malignancies: risk factors, clinical guidelines, and emerging therapeutic approaches. Cell Commun Signal. 2024;22(1):126.
60. Wiegering V, Schick J, Beer M, et al. Varicella-zoster virus infections in immunocompromised patients: a single-centre 6-years analysis. BMC Pediatr. 2011;11:31.
61. Aryastuti SA, Dewi SR, Masyeni S. High prevalence of anemia among HIV-infected patients: a cross-sectional study in Bali-Indonesia. Biomed Pharmacol J. 2021;14(1).
62. Butler LM, Dzabic M, Bakker F, Davoudi B, Jeffery H, Religa P, et al. Human cytomegalovirus inhibits erythropoietin production. J Am Soc Nephrol. 2014;25(8):1669–78.
63. Amer K, Mona R, Khaled M, AlKhazindar T, Elsayed D. Screening for viral infection and anemia among pregnant women with bad pregnancy outcome in Egyptian population. 2016;2(11):700–6.
64. Tun MM, Chowdhury T, Nway N, Noel P, Gousy N, Roy A, et al. Parvovirus infection leading to severe anemia in an adult patient with HIV disease. Cureus. 2022;14.
65. Haklar G. Liver function tests in chronic viral hepatitis cases. Marmara Med J. 2016;29(2):6–9.

66. Bain BJ. Pathogenesis and pathophysiology of anemia in HIV infection. Curr Opin Hematol. 1999;6(2):89–93.
67. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054–62.
68. Kotwal J, Singh V, Kotwal A, Dutta V, Nair V. Haematological and bone marrow changes in symptomatic HIV infection with special mention of functional iron deficiency, anaemia of critically ill and haemophagocytic lymphohistiocytosis. Med J Armed Forces India. 2013;69(4):319–25.
69. Mobin A, Manzoor I, Shaikh H, Ebrahim MA. Chronic liver disease. Prof Med J. 2018;25:292–6.
70. Krishnan SM, Dixit NM. Ribavirin-induced anemia in hepatitis C virus patients undergoing combination therapy. PLoS Comput Biol. 2011;7(2):e1001072.
71. Taisescu CI, Demetrian A, Biciusca V, Dricu A, Artene SA, Cioc C, et al. Ribavirin-induced anemia in patients with chronic hepatitis C virus infection. Rev Chim (Bucharest). 2018;69(12):3648–52.
72. Mitrani R, Gollomp K, Lambert MP, Obstfeld A. The immature reticulocyte fraction as an aid in the diagnosis and prognosis of parvovirus B19 infection in sickle cell disease. Blood. 2018;132(Suppl 1):3678.
73. Natov SN, Pereira BJ. Hepatitis C virus in chronic dialysis patients. Minerva Urol Nefrol. 2005;57(3):175–97.
74. Nabi S, Kahlon P, Goggins M, Patel A. VZV encephalitis following successful treatment of CMV infection in a kidney transplant patient. BMJ Case Rep. 2014;2014:bcr2014206655.
75. Gupta V, Pratap R, Kumar A, Saini I, Shukla J. Epidemiological features of aplastic anemia in Indian children. Indian J Pediatr. 2013.
76. Obeagu EI, Obeagu GU, Ukibe NR, Oyebadejo SA. Anemia, iron, and HIV: decoding the interconnected pathways: a review. Medicine (Baltimore). 2024;103(2):e36937.
77. Kebede SS, Yalew A, Yesuf T, Melku M, Bambo GM, Woldu B. Immune hemolytic anemia among HIV-infected adults: magnitude and associated factors, University of Gondar Hospital, 2021—cross-sectional study. PLoS One. 2022;17(10):e0274464.
78. Pertiwi D, Sofro MA, Winarni TI, Probandari A. Duration of zidovudine consumption correlates with anemia in people living with HIV. J Pharm Sci Community. 2023.
79. Poudel A, Pariyar R, Karki H, Giri A, Bhusal S, Poudel R, et al. Prevalence of anemia and mortality among anemic patients with COVID-19 in a tertiary care setting in Nepal. J Patan Acad Health Sci. 2023;10:72–8.
80. Kakavandi S, Hajikhani B, Azizi P, Aziziyan F, Nabi-Afjadi M, Farani MR, et al. COVID-19 in patients with anemia and haematological malignancies: risk factors, clinical guidelines, and emerging therapeutic approaches. Cell Commun Signal. 2024;22(1):126.
81. Kumar KJ, Kumar HC, Manjunath VG, Arun V. Autoimmune hemolytic anemia due to varicella infection. Iran J Pediatr. 2013;23(4):491–2.
82. Espy MJ, Teo R, Ross TK, Svien KA, Wold AD, Uhl JR, et al. Diagnosis of varicella-zoster virus infections in the clinical laboratory by LightCycler PCR. J Clin Microbiol. 2000;38(9):3187–9.
83. Djoerban Z. Viral load profiles in drug users with asymptomatic HIV infection and normal CD4 cell counts. Med J Indones. 2002;11(3):143.
84. Servey JT, Reamy BV, Hodge J. Clinical presentations of parvovirus B19 infection. Am Fam Physician. 2007;75(3):373–6.
85. Duque X, Mendoza E, Morán S, Suárez-Arriaga MC, Morales-Sánchez A, Fontes-Lemus JI, et al. Epstein–Barr virus infection is associated with elevated hepcidin levels. Int J Mol Sci. 2023;24(2):1630.
86. Ferrari de Freitas L, de Melo Silva J, Nogueira Barbosa A, Miranda Santos E, Pinheiro-Silva R, Soares Pontes G. Epidemiological and liver biomarkers profile of Epstein–Barr virus infection and its coinfection with cytomegalovirus in patients with hematological diseases. Biomolecules. 2021;11(8):1151.
87. Henry B, de Oliveira M, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in COVID-19: a meta-analysis. Clin Chem Lab Med. 2020;58(7):1021–8.
88. Lai JL, Chen YH, Liu YM, Yuan JJ, Lin J, Huang AQ, et al. Prevalence and risk factors of anaemia in hospitalised HIV-infected patients in southeast China: a retrospective study. Epidemiol Infect. 2019;147:e81.
89. Shkodrani E, Frangaj S, Cenko A, Xhaja A. Chronic HCV infection with cryoglobulinemia associated with cutaneous subacute lupus. 2018.
90. Saigal S, Singh RK, Kapoor G, Baronia A. Varicella zoster virus vasculopathy in adult: a rare case report. J Clin Case Rep. 2012.
91. Slavov SN, Kashima S, Wagatsuma VM, et al. Glycoprotein B genotyping of human cytomegalovirus strains isolated from Brazilian patients with sickle cell disease and beta thalassemia major. Viral Immunol. 2015;28(2):123–9.
92. de Matos SB, Meyer R, Lima FWM. Seroprevalence and serum profile of cytomegalovirus infection among patients with hematologic disorders in Bahia State, Brazil. J Med Virol. 2011;83(2):298–304.
93. Claster S. Biology of anemia, differential diagnosis, and treatment options in human immunodeficiency virus infection. J Infect Dis. 2002;185(Suppl 2):S105–9.
94. Meloni DF, Faré PB, Milani GP, Lava SAG, Bianchetti MG, Renzi S, et al. Hemolytic anemia linked to Epstein–Barr virus infectious mononucleosis: a systematic review. J Clin Med. 2025;14(4):1283.
95. Suii H, Ozeki I, Tatsumi R, Yamaguchi M, Kimura M, Arakawa T, et al. Safety of sofosbuvir and ribavirin combination therapy in a patient who developed anemia due to ribavirin. Case Rep Hepatol. 2017;2017:8793895.
96. Tao Z, Xu J, Chen W, et al. Anemia is associated with severe illness in COVID-19: a retrospective cohort study. J Med Virol. 2021;93(3):1478–88.
97. Taştemur M, Arık G, Heybeli H, Selvi Öztorun H, Sılay K, Ateş I, et al. The relationship between anemia and mortality in elderly COVID-19 patients. Cumhuriyet Med J. 2022.
98. Mayer A, Podlech J, Kurz S, Steffens HP, Maiberger S, Thalmeier K, et al. Bone marrow failure by cytomegalovirus is associated with an in vivo deficiency in the expression of essential stromal hemopoietin genes. J Virol. 1997;71(6):4589–98.
99. Natov SN, Pereira BJ. Hepatitis C virus in chronic dialysis

patients. Minerva Urol Nefrol. 2005;57(3):175–97.
100. Wang J, Yang Z, Ren D, Shi Z, Fang K, Li Z. Disseminated varicella-zoster virus infection in an aplastic anemia-paroxysmal nocturnal hemoglobinuria syndrome patient: a case report. Front Cell Infect Microbiol. 2023;13:1163872.
101. Mildvan D, Creagh T, Leitz G; Anemia Prevalence Study Group. Prevalence of anemia and correlation with biomarkers and specific antiretroviral regimens in 9690 HIV-infected patients: findings of the Anemia Prevalence Study. Curr Med Res Opin. 2007;23(2):343–55.
102. Yip CC, Sridhar S, Leung K, Cheng AK, Chan K, Chan JF, et al. Evaluation of RealStar® Alpha Herpesvirus PCR Kit for detection of HSV-1, HSV-2, and VZV in clinical specimens. Biomed Res Int. 2019;2019:5715180.
103. Shedid M, Abdelmonem M, Boraik A, Elmetwalli A, Hassan D. Hematological parameters throughout the first month of direct-acting antivirals plus ribavirin for HCV. Am J Clin Pathol. 2019.
104. Elnaggar MZ, Bichari W, Elshinnawy H. Effect of HCV infection versus HBV infection on the response to erythropoietin therapy in the treatment of anemia in prevalent haemodialysis patients. Egypt J Hosp Med. 2018;70(1):92–6.
105. Zauli G, Re MC, Visani G, Furlini G, Mazza P, Vignoli M, et al. Evidence for an HIV-1-mediated suppression of uninfected hematopoietic (CD34+) cells in AIDS patients. J Infect Dis. 1992;166(4):710–6.