Advances in Environmental and Life Sciences 3(1) (2023) 41-50



Contents lists available at Egyptian Knowledge Bank Advances in Environmental and Life Sciences journal homepage: https://aels.journals.ekb.eg



Sero-prevalence of human Parvovirus B19 Antibodies in Acute Leukemia Patients of Suez^{*}Canal University Hospital

Rabab H A Hasanain^{a,*} Hanaa H Gomaa^a, Fadia M Attia^b

 $Department of Botany and Microbiology, Faculty of Science, Suez \, Canal \, University, Ismailia, Egypt$

Department of clinical pathology, Faculty of medicine, Suez Canal University Ismailia, Egypt

Abstract

Background: Human parvovirus B19 (PB19) is a small-sized DNA virus that infects human erythroid progenitor cells causing a sudden cessation of erythropoiesis. PB19 infection constitutes a high risk and may contribute to acute leukemia and worsen the physiological conditions.

Objective: Screening acute leukemic patients in Suez Canal University Hospital for anti-human Parvovirus B19 antibodies.

Methods: 75 blood samples from acute leukemia patients and 75 blood samples from healthy individuals recruited from Suez Canal University Hospital were subjected to screening for antihuman parvovirus B19 IgM and antihuman parvovirus B19 IgG antibodies by implementing the ELISA technique.

Results: The prevalence of antihuman parvovirus B19 IgM and IgG antibodies in patients with acute leukemia was 22.7% and 98.7%, respectively. The prevalence of IgG antibodies against human parvovirus B19 within the control group was 14.7%.

Conclusion: This study reported the presence of both types of anti-human parvovirus B19 IgM and IgG antibodies in acute leukemia patients in Suez Canal University hospital, which constitutes a high risk for acute leukemia patients and worsens their clinical blood parameters as well.

Keywords: Myeloid leukemia, Lymphocytic leukemia, IgG, IgM, ELISA, Human parvovirus B191

1. Introduction

Human Parvovirus B19 is a small-sized DNA virus of the family Parvoviridae. It has some characteristics such as a 5.4 kb structure, erythroid progenitor cell specificity, and can be propagated only in-vitro with human erythroid bone marrow [1]. Infection with human parvovirus B19 in acute leukemia patients is considered an opportunistic infection; it is assumed that PB19 plays an important role in the pathogenesis of acute leukemia, and several studies reported an incidence of infection with B19 ranging from 8 to 18% in patients with acute lymphocytic leukemia. [2].

*Corresponding author.

Email address: pr.rabrab@gmail.com (Rabab H A Hasanain)

doi 10.21608/AELS.2023.179654.1026

Received: 15 December 2022, Revised: 6 January 2023 Accepted:8 January 2023: Published:12 January 2023

Human parvovirus B19 causes many clinical manifestations and is linked to many types of anemia, neutropenia, thrombocytopenia, and pure red cell aplasia. [3]. Human parvovirus B19 targets the red blood cell precursors and prevents the production of erythrocytes, causing anemia. In severe cases of anemia, B19 infection causes many serious complications, including circulatory collapse, cerebrovascular attack, acute splenic sequestration, and congestive heart failure. There is a link between acute human parvovirus B19 infection and low circulating Interleukin- 10 (IL-10) which is accompanied by a strong immune response; deficiency of the production of (IL-10) leads to subsequent development of acute leukemia [4], a specific methylation profile of human cancer genes in acute leukemia patients is linked to anti B19 IgG

antibodies that's why an extra mechanism of hit and run is suggested [4]. The presumed role of parvovirus B19 in the pathogenesis of acute leukemia fits well with the hypothesis of delayed infection as well as the model of the two-step mutation. in the two-step mutation model, the first mutation takes place before birth, and hematopoiesis is suppressed consequently [4], the result is a rapid proliferation of cells containing the first mutation, a second activating mutation is acquired, and after that, there will be an expansion of cells carrying both mutations, and consequently the development of acute leukemia takes place. [4]. Significance of the study: the study illustrates the prevalence of IgM and IgG antibodies of human parvovirus B19 among acute leukemia patients.

We aimed from conducting the current study to detect the IgM and IgG antibodies against human parvovirus B19 in acute leukemia patients to assess the risk of human parvovirus B19 transmission among the population of patients with acute leukemias in Suez Canal University hospital, Ismailia, Egypt.

2. Patients and methods

The current study was designed as a case-control study that has been conducted at Suez Canal University Hospital and the laboratories of the Botany Department, Faculty of Science, Suez Canal University. This study included seventy-five (75) Patients with acute leukemias and seventy-five (75) healthy control individuals at Suez Canal University Hospital.

In this study, blood samples were collected from acute leukemia patients (the study group) and healthy individuals (the control group), age group ranged from 4 to 55 years and genders included males and females for both patients with acute leukemia and the healthy individuals as well.

The 75 blood samples from patients with acute leukemia and the other 75 blood samples from healthy control blood donors were subjected to four screening core tests, including HIV antibodies, Hepatitis B surface antigen, Hepatitis C antibodies (subtypes 1 and 2), and a serologic test for Syphilis. These four screening tests returned negative results for the blood samples. The exclusion criteria were the acute leukemia patients' refusals or the healthy control blood donors' refusals, and data were collected from each patient with acute leukemia as well as from each healthy blood donor. Individuals were asked about the following data: name, age, gender, mobile phone number, and address. Sampling was conducted and included one hundred and fifty (150) blood samples collected into a 3-ml plain tube, and serum samples were separated and stored until use at (–20°C) for serological assessment.

2.1. Serological assessment of antihuman parvovirus B19 IgM and IgG antibodies

In this study, serum IgM and IgG antibodies against human parvovirus B19 were measured by ELISA (IBL-America Parvovirus B19 IgG/IgM ELISA) to get a better idea of how much human parvovirus B19 was in the blood of 75 healthy people and 75 people with acute leukemia.

2.2. Data Statistical analysis

Data were fed to the computer and IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) was used for the analysis. The normality of the distribution of variables was verified using the Kolmogorov- Smirnov; comparison between groups for categorical variables was done using the Chi-square test. The diagnostic performance of the markers was determined using Receiver operating characteristic curve (ROC). An area of about 100% is the best performance for the test. An area of more than 50% gives acceptable performance and the significance of the obtained results was judged at the 5% level.

Student t-test was used to compare two groups for normally distributed quantitative variables while Mann Whitney test was used to compare two groups for not normally distributed quantitative variables.

Ethical approval number for the current manuscript concerning the involvement of clinical patients (2019/022)

3. Results

In this study, antibodies against human parvovirus B19 were detected in the blood of healthy control individuals and patients with acute leukemias. The study was implemented at Suez Canal University Hospital. Samples included 75 healthy control individuals and 75 patients with acute leukemia; both male and female donors and children met the inclusion criteria.



Figure 1: Distribution of the studied sample according to diagnosis in the cases group

Figure 1 shows the percentage of acute lymphoid and acute myeloid leukemia patients among the 75 patients with acute leukemia represented within the study population; 41.3% of the acute leukemia patients who were included in this study were acute myeloid leukemia AML patients, and 58.7% were acute lymphoid leukemia ALL patients.

Compared the two studied groups, both acute leukemia patients and healthy control individuals, where human PV B19 IgM antibodies have been detected in 17 of the 75 acute leukemia patients included in the study; the prevalence of human parvovirus B19 IgM antibodies in acute leukemia patients in the study was 22.7%. The percentage of human PVB19 IgM antibodies in the healthy control individuals, on the other hand, was 0.0%, as PVB19 IgM antibodies were not detected in any of the 75 healthy control individuals, and the P value is significant (0.001).

In this study, human parvovirus B19 IgG antibodies were detected in 74 of the 75 acute leukemia patients; the prevalence of human parvovirus B19 IgG antibodies in acute leukemia patients was 98.7%. The percentage of human PVB19 IgG antibodies in healthy people (the control group) was 14.7%, as PVB19 IgG antibodies were detected in 11 of the 75 healthy people in the study, and the P value is significant (0.001). Table (1) shows the history of blood transfusion in the study group of acute leukemia patients (50 patients) and the control group of healthy individuals.

Table (2) shows that IgM antibodies against human parvovirus B19 have been detected in 17 of the acute leukemia patients within the study group; these patients also have a high leukocytic count (20–64), a decreased hemoglobin level (5-7), a decreased platelet count (8–25), and a high presence of blast cells (35–65); also, 67.7% of these leukemia patients have received blood or platelet transfusions during their treatment.

Table 3 shows that IgG antibodies against human parvovirus B19 have been detected in 74 of the acute leukemia patients within the study group, these patients also have a high leukocytic count (20–70), a decreased hemoglobin level (5-7), a decreased platelet count (5–30), and a high presence of blast cells (20–70).

Table (4) shows the prevalence of antihuman parvovirus B19 IgG antibodies within the control group of healthy individuals included. Of the 75 individuals in the control group, 11 have IgG antibodies against human parvovirus B19 in their serum. These 11 individuals have normal CBC blood parameters, with a leukocytic count ranging from 5 to 9, a hemoglobin level of 11 to 14, and a platelet count of 180–260.

4. Discussion

Screening acute leukemia patients for human parvovirus B19 antibodies is not yet applied in Egypt [5], although the virus is compromising this group of patients due to its ability to present in high titers, causing infection and serious complications in those patients. This virus is also capable of resisting heat inactivation procedures, so the need to examine the prevalence of antibodies against human parvovirus B19 in acute leukemia patients in Egypt is great [6].

| | Cases (n = 75) Control (n = 75) | | Test of Sig. | Р |
|------------------------------|--|----------------------|--------------|----------|
| Sex | | | | |
| Male | 27 (36.0%) 30 (40.0%) | | c2= 0.281 | 0.869 |
| Female | 38 (50.7%) | 35 (46.7%) | | |
| Child | 10 (13.3%) | 10 (13.3%) | | |
| Age (years) | | | | |
| Min. – Max. | 4.0-55.0 | 4.0 - 55.0 | U= 2535.00 | 0.296 |
| Mean \pm SD. | 31.51 ± 12.78 | 33.85 ± 11.85 | | |
| Median (IQR) | 33.0 (25.0-41.0) | 37.0 (32.50-40.0) | | |
| WBCs | | | | |
| Min. – Max. | 20.0 - 70.0 | 4.0 - 9.0 | t=21.635* | < 0.001* |
| Mean \pm SD. | 38.81 ± 12.73 | 6.84 ± 1.32 | | |
| Median (IQR) | 40.0 (30.0-47.0) | 7.0 (6.0-8.0) | | |
| Hb | | | | |
| Min. – Max. | 5.0-7.0 | 11.0 - 15.0 | t=42.027* | < 0.001* |
| Mean \pm SD. | 5.99 ± 0.68 | 12.68 ± 1.20 | | |
| Median (IQR) | 6.0 (5.60 – 6.30) | 12.50 (12.0 – 13.50) | | |
| Platelets | | | | |
| Min. – Max. | 5.0 – 30.0 | 170.0 - 320.0 | t=51.360* | < 0.001* |
| Mean \pm SD. | 15.45 ± 4.78 | 232.52 ± 36.29 | | |
| Median (IQR) | 15.0 (12.0 – 20.0) | 220.0 (200.0-250.0) | | |
| Blast cells | | | | |
| Min. – Max. | 20.0 - 70.0 | - | - | - |
| Mean \pm SD. | 45.27 ± 9.57 | - | | |
| Median (IQR) | 45.0 (40.0-50.0) | - | | |
| B19 IgM | _ | | | |
| Negative | 58 (77.3%) | 75 (100.0%) | c2=19.173* | < 0.001* |
| Positive | 17 (22.7%) | 0 (0%) | | |
| B19 IgG | | | | |
| Negative | 1 (1.3%) | 64 (85.3%) | c2=107.756* | < 0.001* |
| Positive | 74 (98.7%) | 11 (14.7%) | | |
| B19IgG level | | | | |
| Min. – Max. | 10.0 - 82.0 | 1.0 - 12.0 | U=7.500* | < 0.001* |
| Mean \pm SD. | 33.56 ± 20.96 | 4.85 ± 1.52 | | |
| Median (IQR) | 25.0 (20.0-47.50) | 5.0 (4.0-5.50) | | |
| History of blood transfusion | | | | |
| No | 25 (33.3%) | 75 (100.0%) | c2=75.00* | < 0.001* |
| Yes | 50 (66.7%) | 0 (0%) | | |

Table 1: Comparison between the two studied groups according to different parameters

| Table 2: | Relation between parvoviru | s B19 infection with diffe | rent parametersin case gr | oup (n= 75) | |
|----------------|----------------------------|----------------------------|---------------------------|---------------------|--|
| | PV B19 | IgM | PV B19 IgG | | |
| | Negative $(n = 58)$ | Positive $(n = 17)$ | Negative (n = 1#) | Positive $(n = 74)$ | |
| WBCs | | | | | |
| Mean ± SD. | 39.19 ± 12.82 | 37.53 ± 12.72 | 35.0 | 38.86 ± 12.81 | |
| Median | 40.0(20 - 70) | 35(20 - 64) | | 40(20 - 70) | |
| t (p) | 0.470 (0 | 0.640) | | _ | |
| HB | | | | | |
| Mean ± SD. | 5.97 ± 0.67 | 6.06 ± 0.71 | 6.0 | 5.99 ± 0.68 | |
| Median | 6(5-7) | 6(5-7) | | 6 (5 – 7) | |
| t (p) | 0.450 (0.654) - | | | | |
| Platelets | | | | | |
| Mean \pm SD. | 15.50 ± 4.87 | 15.29 ± 4.61 | 20.0 | 15.39 ± 4.79 | |
| Median | 15(5 - 30) | 15(8 – 25) | | 15 (5 – 30) | |
| t (p) | 0.155 (0 |).877) | | _ | |
| Blast cells | | | | | |
| Mean ± SD. | 44.90 ± 9.82 | 46.53 ± 8.83 | 56.0 | 45.12 ± 9.55 | |
| Median | 45.0(20.0-70.0) | 44.0(35.0-65.0) | | 44.50(20-70.0) | |
| t (p) | 0.616 (0 | 0.540) | | _ | |
| History of | | | | | |
| blood transfu- | | | | | |
| sion | | | | | |
| No | 19 (32.8%) | 6 (35.3%) | 1 (100.0%) | 24 (32.4%) | |
| Yes | 39 (67.2%) | 11 (67.7%) | 0 (0.0%) | 50 (67.6%) | |
| c2(p) | 0.038 (0.845) | | 2.077 (MCp=0.333) | | |

Table 3: Relationbetween parvovirus B19 IgG with CBC in the control group(n= 75)

| | B19 IgG | | • | | |
|----------------|------------------|-------------------|-------|-------|--|
| | Negative (n = | Positive (n = 11) | - L | þ | |
| | 64) | | | | |
| WBCs | | | | | |
| Mean \pm SD. | 6.78 ± 1.29 | 7.18 ± 1.47 | 0.034 | 0.354 | |
| Median (Min. – | 7(4-9) | 8 (5 – 9) | 0.554 | 0.534 | |
| Max.) | | | | | |
| Hb | | | | | |
| Mean \pm SD. | 12.75 ± 1.20 | 12.25 ± 1.18 | 1 269 | 0 200 | |
| Median (Min. – | 13 (11 – 15) | 12 (11 – 14) | 1.200 | 0.205 | |
| Max.) | | | | | |
| Platelets | | | | | |
| Mean \pm SD. | 233.9 ± 37.49 | 224.6 ± 28.41 | 0 797 | 0 434 | |
| Median (Min. – | 220 (170 - 320) | 220 (180 – 260) | 0.707 | 0.434 | |
| Max.) | | | | | |

Table 4: Validity(AUC, sensitivity, specificity) for B19 IgG level for diagnosis of infection of human parvovirus B19

| | AUC | р | 95% C.I | Cut off | Sensitivity | Specificit | yPPV | NPV |
|-----------------|-------|---------|-----------|---------|-------------|------------|------|------|
| B19IgG Level | 0.999 | <0.001* | 0.996-1.0 | >11 | 92.0 | 98.67 | 98.6 | 92.5 |



Figure 2: ROC curve for B19IgG level for diagnosis of parvovirusB19 infection

In this study, 66.7% of acute leukemia patients had previously received blood transfusions, and the study group of leukemia patients had a drop in both platelet count and hemoglobin level, as well as an elevated leukocytic count.

The study group included 36.0% males, 50.7% females, and 13.3% children; the control group included 40.0% males, 46.7% females, and 13.3% children; the age range for both the control and the study groups was 4–55 years.

The study showed that the anti-human parvovirus B19 IgG level is much higher in leukemia patients (10–82) compared to the control group (1–12). The study detected antihuman parvovirus B19 IgG antibodies in 74 patients of the study population. These 74 patients also had an elevated leukocytic count, decreased hemoglobin and platelet counts, and a high presence of blast cells in their blood samples. The study detected IgG antibodies against human parvovirus B19 in leukemia patients, which refers to a previous human parvovirus B19 infection. The prevalence of IgG antibodies against human parvovirus B19 in this study is higher than that in other studies. In 2004, Elmahlawy and colleagues performed a study to detect anti-PB19 IgG antibodies in acute leukemia patients. Their study included 50 patients suffering from both ALL and anemia and 34 patients with ALL but no anemia. These patients were receiving maintenance therapy. Screening for B19 IgG antibodies was implemented for the 2 groups of patients, and anti-B19 IgG antibodies have been disclosed in 19 of the 50 patients and 15 of the 34 patients, respectively.

In the current study, the prevalence of antihuman parvovirus B19 IgM antibodies within the study group was 22.7%, and 17 of the 75 serum samples from leukemia patients subjected to screening were positive for human parvovirus B19 IgM antibodies. 22.7% of the leukemia patients were in the early stage of viremia and had a recent infection with human parvovirus B19. These 17 patients also have an elevated leukocytic count, decreased hemoglobin and platelet counts, and a high presence of blast cells in the blood samples. The detected antihuman parvovirus B19 IgM antibodies in these patients, which refer to a recent infection with human PVB19, along with these previously mentioned CBC and Blast cells values strongly suggest that there is a link between the state of disease and their infection with human parvovirus B19 during their various stages of treatment. [7].

The number of leukemia patients with antihuman parvovirus B19 IgM antibodies is lower in this study than it was in a study done by Zaki and colleagues in 2006. In that study, they looked for the PB19 genome and IgM antibodies against the virus in 25 hemolytic anemia patients with aplastic crisis, 20 hemolytic anemia patients without aplastic crisis, 20 acute leukemia patients getting chemotherapy, 20 acute leukemia patients who had just been diagnosed, and 20 normal people. Six of the 25 people with hemolytic anemia went through an aplastic crisis. None of the other twenty people with hemolytic anemia went through an aplastic crisis, and only six of the twenty people with acute leukemia got chemotherapy. nine of 20 were recently diagnosed with acute leukemia, and 0 of 20 normal controls Serum IgM was found in 36% of the cases. nine of 25 hemolytic anemia in aplastic crisis, (5%) one of 20 hemolytic anemia without aplastic crisis, (35%) seven of 20 acute leukemia patients during chemotherapy, (50%) 10 of 20 recently diagnosed cases of acute leukemia, and 0 of 20 normal controls.

The prevalence of antihuman parvovirus B19 IgM antibodies in this study aligns with a previous study conducted in 2007, whereas the prevalence of IgG antibodies in our study was higher than a previous study conducted by Zaki and coworkers, their study detected the genome of human PB19, as well as antiB19 IgG and antiB19 IgM antibodies in bone marrow and serum of ALL patients receiving chemotherapy, the genome of the virus, was detected in serum and bone marrow of (20%) nine of 48 of the ALL patients, and genome of the virus wasn't detected in any of the individuals in the control group, anti-human PB19 IgM antibodies were detected in (26.7%) 12 of 48 ALL patients during chemotherapy as compared with none of the controls, and anti PB19 IgG antibodies were detected in 18 of 48 ALL patients during chemotherapy as compared with (10%) two of 20 controls.

The prevalence of IgM antibodies in our study is higher than in previous studies, in 2011, Kishore and coworkers, screened two groups of patients for B19 IgM antibodies and also to detect the genome of the virus, the first group included 35 children suffering from malignancies (13 suffering from lymphoma and 22 suffering from acute leukemia, the second group included 34 children suffering from solid tumors, antiB19 IgM antibodies were detected(active infection with B19) in 6 patients of the whole number of patients in the two groups, 5 ALL patients and one patient with lymphoma, of the five patients with ALL who were positive for IgM antibodies of the virus, two patients have the genome of the virus, and of these five patients two patients have prononrmoblasts which were detected in their bone marrow.

The prevalence of antihuman parvovirus B19 IgG and IgM antibodies in our study is much higher than in previous studies, in 2014, a study conducted by Jitschin and colleagues, the study included patients with malignancies and patients with non-malignant diseases, these patients were screened for infection with human parvovirus B19, the study included 24 patients with ALL, 10 patients (41.6%) were positive for anti-B19 IgG antibodies; one patient (4.2%) was positive for anti-B19 IgM, and 16.7% were positive for human parvovirus B19 genome, B19 genome present either in their bone marrow or serum.

The prevalence of B19 IgG antibodies against human parvovirus B19 in our study is much higher than in previous studies, in 2014, Ibrahem and coworkers conducted a case-control study, the study included 40 ALL patients recently diagnosed with leukemia and 60 individuals in the control group, both the study group and control group were screened to detect human B19 IgG antibodies, 19 out of the 40 ALL patients were positive for IgG antibodies, and 12out of 60 normal control individuals were positive for IgG antibodies against human B19.

The prevalence of IgG and IgM antibodies against human parvovirus B19 in this study is in consonance with previous study conducted in 2010, Zaki and coworkers conducted a case control study to detect B19 genome as well as IgG and IgM against the virus within the control group and the two study groups of patients, human B19 genome was detected in ten of the forty five ALL patients (22%), these patients were receiving chemotherapy, the DNA of the virus was also detected in eighteen of the forty ALL who were recently diagnosed with leukemia, and also DNA of the virus wasn't detected in any of the twenty healthy individuals within the control group, IgM antibodies against the virus were detected in fourteen of forty five (31%) ALL patients receiving chemotherapy, in twenty of the forty (50%) ALL patients recently diagnosed, and wasn't detected in any of the healthy control individuals, IgG antibodies against the virus were detected in 18 of the 45 (40%) ALL patients during chemotherapy and 16 of the 40%) ALL patients recently diagnosed, and wasn't detected in any of the healthy control individuals.

Fattet and coworkers in 2004 suggested a link between acute leukemia and parvovirus B19 infection, this link is caused by the immunosuppression caused by chemotherapy, and consequently, a persistent infection becomes activated or resulted from repeated blood transfusion [8], [9].

One of the causes of acute leukemia is some viruses, these viruses are also known as viral triggers, [10], [11], [12], human parvovirus B19 infects the erythroblasts found within the bone marrow, yet it is also capable of infecting different other cell types, infection with B19 in patients with hemolytic disorders such as patients with hemolytic disorders (shortened red cell survival) results in aplastic crisis which is a prodrome of acute lymphocytic leukemia in 2% of patients [13], [14].

PB19 also causes aplastic anemia, which takes place several months before the development of acute leukemia [15], [16].

Human cancer might develop as a result of viral infection by oncoviruses including human T-cell lymphotropic virus, Epstein–Barr virus, hepatitis B virus, hepatitis C virus, human papillomaviruses, Kaposi's sarcoma-associated herpesvirus (human herpesvirus 8), and Merkel cell polyomavirus, several distinct aspects of human parvovirus B19 life cycle resemble that of oncoviruses, also there are many recognized parvoviruses which causes cancer and considered oncolytic viruses like the rat parvovirus H-1 [17], [18], [19], [20].

Rat parvovirus H-1(known as ParvOryx virus) is now subjected to many clinical trials to treat human glioblastoma multiforme [21], [22], [23], [24].

PB19 is responsible for complicating the acute leukemia clinical course, either by an opportunistic infection exogenously acquired or by causing reactivation of a latent human parvovirus B19, also acute PB19 infection takes place before the diagnosis of acute leukemia by 180 days, and in certain cases, PB19 is responsible for causing an aplastic crisis, the aplastic crisis is known to proceed onset of acute leukemia in a few numbers of patients [25], [26], [27], .

In our study when the prevalence of antihuman

parvovirus B19 IgG and IgM antibodies is compared to parameters of blood and CBC in the study group of acute leukemia patients and the control group of healthy individuals in our study, it can be concluded that there is a high prevalence of the antibodies of the virus both types IgG and IgM antibodies combined with a decreased hemoglobin levels, decreased platelet counts, elevated count of blast cells and high leukocytic counts in the study group of leukemia patients, from this study it can be also concluded that the virus could have a major effect on the CBC and blood parameters of the leukemia patients in this study. Moreover, given that the virus constitutes a high risk for a certain group of patients, as it causes TAC and various other serious complications which could lead not only to a sudden drop of hemoglobin level but can cause congestive heart failure as well, so acute leukemia patients must be included within the high-risk categories of the patient who should be screened to human parvovirus B19 genome routinely during their treatment and before acquiring any blood transfusions, and as a previous study in Egypt in 2018 by Rabab H. A. Hasanain and coworkers suggested that screening for human parvovirus B19 genome and IgM antibodies should be mandatory for healthy blood donors, this study suggests that screening must be applied especially for the high-risk group of blood recipients referring here and suggesting the acute leukemia patients in particular.

The genome of human parvovirus B19 has been previously detected in ALL cases, and a significant association was suggested between the presence of parvovirus B19 IgG antibodies and aplastic anemia [29]. This finding showed the potential benefit of diagnostic screening for parvovirus B19 DNA by PCR in children with ALL, this could be explained by the finding of Kerr and Mattey (2015), who noted the evidence suggesting a possible role for B19 virus in the pathogenesis of a subset of cases of acute leukemia [30].

Human parvovirus B19 infection may aggravate the clinical course of acute leukemia patients and infection with B19 may also precede the development of acute leukemia by up to 180 days [27], there is a link between acute B19 infection and low levels of circulating IL-10 along with a strong immune response; deficiency of IL-10 production was presumed to be linked to a later emergence of acute leukemia [31].

In patients with inherited hemolytic anemias, these patients show high-titer replication and consequently resulting in bone marrow suppression, triggering a life-threatening drop of hemoglobin values causing profound anemia, or aplastic crisis, a B19 virus screening program is not applied till our present day either for high-risk patients such as leukemia patients or for the blood donations applied for the hemotherapy which is a cause of great concern, especially for this group of patients [31].

5. Conclusion

There is a high prevalence of human parvovirus B19 among the population of acute leukemia patients in Ismailia, Egypt, and this is a piece of evidence that there is active B19 transmission in this study group, therefore screening for human parvovirus B19 for the leukemia patients is highly recommended and can be considered as an essential procedure to be undertaken all through their treatment routine in the future to ensure that these patients will not encounter serious life-threatening complications that might worsen their state or delay their recovery process.

The majority of the adult population has acquired human parvovirus B19 infection previously during their lives, (the adult population is represented by the 75 healthy individuals and the 75 acute leukemia patients subjected to screening in this study), and this is concluded from the high prevalence of antihuman parvovirus B19 IgG antibodies in our study.

Acquiring an infection with B19 constitutes a high risk for patients with acute leukemia, but till the present day, there are no strict regulatory procedures to screen this group of patients for human parvovirus B19 to control and exclude any chances of B19 transmission to these patients.

6. Recommendations

Individual screening for anti-human parvovirus B19 IgG and IgM antibodies by ELISA should be im-

plemented for patients with acute leukemias.

References

- S. F. Cotmore, M. Agbandje-Mckenna, M. Canuti, J. A. Chiorini, A. M. Eis-Hubinger, J. Hughes, S. Modha, M. Ogliastro, D. J. Pintel, J. Qiu, M. Soderlund-Venermo, P. Tattersall, P. Tijssen.
- [2] T. Larkin, Peng Li and Biljana Horn Parvovirus B19 infection masquerading as relapsed acute lymphoblastic leukaemia following haematopoietic stem cell transplantation BMJ Case Rep (2020).
- [3] O. Naseem, A. Chaudhary, N. Sajid, Shahjahan and Shahida Mohsin Parvovirus B19 in patients of acute lymphoblastic leukemia with prolonged cytopenia, in: 10th World Hematology and Oncology Congress, Vol. 1, 2018.
- [4] M. A. Rahema, M. A. Arwa, Al-Shuwaikh, F. Waseem, Al-Tameemi role of human parvovirus b19 in persistence anemia in asample of iraqi patients with acute myeloid leukemia, Biochem. Cell. Arch 20 (2) (2020) 5165–5172.
- [5] Y. Jun, L.-Y. Sim, J.-M. Chang, P.-I. Chen, L.-M. Lee, C.-Y. Huang, Lu, Human parvovirus B19 infection in patients with or without underlying diseases, Immunology, and Infection 52 (2019) 534–541.
- [6] T. A. El-Khier, N, A. Darwish, M. E. S. Zaki, Molecular Study of Parvovirus B19 Infection in Children with Acute Myeloid Leukemia, Asian Pacific Journal of Cancer 8 Prevention: APJCP 19 (2) (2018) 337–342.
- [7] T. Larkin, P. Li, and Biljana Horn Parvovirus B19 infection masquerading as relapsed acute lymphoblastic leukaemia following haematopoietic stem cell transplantation, BMJ Case Rep 13 (8) (2020).
- [8] G. Jenan, Hassan, N. Wijdan, Ibrahem, J. Hassan, Hasony, Human parvovirus B19 in childhood acute lmphoblastic leukemia in Basra, International Conference on Immuno - Oncology and Cancer Science, 2018.
- [9] D. Erik, K. E. Heegaard, Brown, Human parvovirus B19, Clin Microbiol Rev 15 (3) (2002) 485–505.
- [10] C. Bartenhagen, U. Fischer, K. Korn, S. M. Pfister, M. Gombert, C. Chen, V. Okpanyi, J. Hauer, A. Rinaldi, J.-P. Bourquin, C. Eckert, J. Hu, A. Ensser, M. Dugas, A. Borkhardt (2017). [link].

URL https://doi.org/10.3324/haematol.2016.155382

- [11] A. Jain, P. Jain, S. Prakash, D. N. Khan, A. K. & amp; Ravi, Kant, Prevalence of Parvovirus B19V in Hematological Malignancies and Chronic Anemia 85 (2018) 77–78.
- [12] T. A. El-Khier, N. Darwish, A, E. S. Zaki, M, Molecular Study of Parvovirus B19 Infection in Children with Acute Myeloid Leukemia, Asian Pacific Journal of Cancer Prevention 19 (2) (2018) 337–342.
- [13] Y. L. L. D. X. L. W. W. X. Zhang (2015). [link]. URL https://doi.org/10.3892/ol.2015.3766
- [14] A. R. T. Clarke, V. Den, C. Bruel, Bankhead, D. Christopher, B. Mitchell, Phillips, J. Matthew, Thompson (2016).

- [15] T. Fisgin, N. Yarali, F. Duru, A. Kara, Parvovirus-B19 infection preceding acute myeloid leukemia with orbital granulocytic sarcoma, Leukemia and Lymphoma 43 (10) (2002) 2059–2061.
- [16] M. A. Rahema, M. A. Arwa, Al-Shuwaikh, F. Waseem, Al-Tameemi role of human parvovirus b19 in persistence anemia in asample of iraqi patients with acute myeloid leukemia biochem, Cell. Arch 20 (2) (2020) 5165–5172.
- [17] C. Bretscher, A. Marchini, H-1 Parvovirus as a Cancer-Killing Agent: Past, Present, and Future. Viruses (2019).
- [18] Giorgio Gallinella, Parvoviridae, Encyclopedia of Infection and Immunity.
- [19] A. Mahinbehzadifard, S. Atashi, Amiri, M. A. Saeidkaviani, M. Gholampour, Parvovirus B19 affects thrombopoietin and IL-11 gene expression in human bone marrow mesenchymal stem cells, Future Virology 16 (2021) 519–526.
- [20] L. Olivier-Gougenheim, F. Dijoud, A. Traverse-Glehen, S. Benezech, Y. Bertrand, S. Latour, E. Frobert, C. Domenech, Aggressive large B-cell lymphoma triggered by a parvovirus B19 infection in a previously healthy child, Hematological Oncology 37 (2019) 483– 486.
- [21] K. Geletneky, J. Huesing, J. Rommelaere, Phase I/IIa study of intratumoral/intracerebral or intravenous/intracerebral administration of Parvovirus H-1 (ParvOryx) in patients with progressive primary or recurrent glioblastoma multiforme: ParvOryx01 protocol, BioMed Central Cancer 12 (2012) 99–99.
- [22] S. Ramanathan, G. Narula, M. Prasad, T. Vora, G. Chinnaswamy, S. Banavali, Parvoviral disease in childhood cancer: Clinical outcomes and impact on therapy at a tertiary cancer center in India (2018) 11–11.
- [23] E. Rafet, M. Hilmi, D. Şermin, A. Osman, Y. Elif, Suyani, The seasonality in the diagnosis of acute leukemia: A single center data from Turkey, Marmara Medical Journal (2018) 112–115.
- [24] J. Hwee, C. Tait, L. Sung, C. Jeffrey, R. Kwong, J. D. Sutradhar, Pole, A systematic review and meta-analysis of the association between childhood infections and the risk of childhood acute lymphoblastic leukaemia, British Journal of Cancer 118 (2017) 127–137.
- [25] J. R. Kerr, A review of blood diseases and cytopenias associated with human parvovirus B19 infection, Reviews in Medical Virology (2015) 224–240.
- [26] M. Thvilum, F. Brandt, T. H. Brix, L. Hegedüs, Month of birth is associated with the subsequent diagnosis of autoimmune hypothyroidism. A nationwide Danish register-based study, Clinical Endocrinology 87 (2017) 832–837.
- [27] M. D. Usman, N. Garba, Diagnosis of acute myeloid leukemia: a review, BJMLS 3 (2) (2018) 2635–3792.
- [28] J. S. S. Ganaie, Qiu, Recent Advances in Replication and Infection of Human Parvovirus B19.Front Cell Infect Microbiol (2018).
- [29] A. Lindblom, M. Heyman, I. Gustafsson, O. Norbeck,

T. Kaldensjo, A. Vernby, Parvovirus B19 infection in children with acute lymphoblastic leukemia is associated with cytopenia resulting in prolonged interruptions of chemotherapy, Clin Infect Dis 46 (2008) 528–564.

- [30] J. R. Kerr, D. L. Mattey, The role of parvovirus B19 and the immune response in the pathogenesis of acute leukemia, Rev Med Virol 25 (2015) 133–55.
- [31] Slavov, S. N. Kashima, S. Pinto, A. C, C. D, Human parvovirus B19: general considerations and impact on patients with sickle-cell disease and thalassemia and on blood transfusions, FEMS Immunol Med Microbiol 62 (2011) 247–62.