



Prevalence of Viral Hepatitis (A, B and C) among Haemophilic Children Mohammed Salah Ali^{1*}, Mohammed Sayed Hameda², Ahmed Moheesn Abd El-hakem² and Kamel Soliman Hammad³

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ABSTRACT

Haemophilia is a rare haematological disease characterized by prolonged bleeding due to deficiency of coagulating factor 8 and factor 9. This is cross sectional study carried out at paediatric haematology unit Al-Azhar university hospital, Cairo, Egypt, and paediatric haematology unit of El Mabarah-Hospital-Health Insurance Organization, Zagazig, Egypt, during March 2014 to March 2016. One hundred male patients were screened for hepatitis (A, B, and C). Mean age was 11.47 ± 4.4 years old. About 95% with haemophilia A, 4% haemophilia B and 1 patient had combined haemophilia A and family history of hepatitis was 21%. Consanguinity was 28%. Similar condition in the family was 36%. Ecchymosis as clinical manifestation was 64%, haemarthrosis was 62% and jaundice detected in 35% of cases. Severity was mild 20%, moderate 47% and severe was 33%. Most affected joint was knee joint and represented 41%. Blood transfusion, cryoprecipitate were major risk factors for transmitting of hepatitis C positive cases. HAV was 7%, HBV was 0% and hepatitis C was 65%. **Conclusion:** HCV is still high in haemophilic and represent a major problem. **Recommendation:** Early detection, treatment, and further investigation of hepatitis C virus in haemophilic children.

Keywords: Haemophilia, viral hepatitis

INTRODUCTION

Haemophilia A and B are rare hereditary bleeding disorders, which are caused by mutations in the factor VIII and IX genes [1]. Haemophilia is a chronic disease characterized by bleeding in joints, muscles, and soft tissues [2]. Two most common forms of haemophilia are Haemophilia A (HA) and Haemophilia B (HB) and are caused by deficiency of factors VIII and IX respectively. HA accounts for 80-85% of cases and HB in 15% to 20% of cases. Both types are inherited as X linked recessive pattern characterized by prolonged bleeding and haemorrhages typically in joints and soft tissues [3].

Background

Haemophilia was recognized in ancient times. The Talmud, a collection of Jewish rabbinical writings from the second century AD, stated that male babies should not be circumcised provided two brothers had already died owing to excessive bleeding from the procedure. The Arabic physician Abacuses, who lived in the 12th century, described a family with males who died from bleeding after trivial injury [4].

Haemophilia is sometimes referred to as "The Royal Disease", because several members of royal families in Europe were affected by this scourge owing to the fact that Victoria, Queen of England from 1837 to 1901, was a haemophilia B carrier [5].

Haemophilia A is caused by a lack of active clotting factor VIII. About 1 out of every 5,000 male babies is born with

haemophilia A. Haemophilia B (Christmas disease) is caused by a lack of active clotting factor IX. It is less common and affects 1 out of 30,000 male babies [6].

In Egypt, which has a population of approximately (90 million) consanguineous marriage are frequent, therefore, recessive characteristic coagulation disorders reach a higher incidence than in many other countries. All ethnic groups affected. Exclusively affected males and females are carriers and rarely affected [7].

Individuals with less than 1% active factor are classified as having severe haemophilia, those with 1% to 5% active factor have moderate haemophilia, and those with mild haemophilia have between 5% to 40% of normal levels of active clotting factor [8].

Depending on the level of factor activity, patients with bleeding disorders may present with easy bruising, inadequate clotting of traumatic injury or in the case of severe bleeding disorders spontaneous haemorrhage [9].

Signs of haemorrhage include general (weakness, orthostasis, tachycardia, tachypnoea), musculoskeletal (tingling, warmth, pain, stiffness, and refusal to use joint) [10].

Screening tests show a long activated partial thromboplastin time (APTT), normal prothrombin time (PT), thrombin clotting time (TCT) and bleeding time, and a normal platelet count. Specific assays show factors VIII and IX clotting activity below 0.05 U/mL, with all other factors normal [11].

The articular problems of haemophiliac patients begin in infancy. These include recurrent haemarthrosis, chronic synovitis, flexion deformities, hypertrophy of the growth epiphyses, damage to the articular cartilage and haemophilic arthropathy. The most commonly affected joints are the ankle, the knee, the elbow, and the hip. The pain causes flexion deformities in affected joints, first correctable, but later becoming fixed [12].

In the past haemophilia replacement therapies were included fresh frozen plasma (FFP), cryoprecipitate and blood derived products without any viral inactivation. In 1950, plasma became available for treating haemophilia. In 1965, cryoprecipitate was used as a treatment for haemophilia. FIX and FVIII concentrates used for haemophilia patients in 1968. FIX and FVIII genes were cloned in 1982. Viral inactivated factor concentrates became available in 1985 and recombinant product became available in 1992 [13].

Before year 1985, using human's plasma derived factor concentrates which did not undergo viral inactivation increased the risk of transfusion transmitted viral infections in haemophiliacs [14].

To facilitate appropriate management in emergency situations, all patients should carry easily accessible identification indicating the diagnosis, severity of the bleeding disorder, inhibitor status, type of treatment product used, initial dosage for treatment of severe, moderate, and mild bleeding, and contact information of the treating physician/clinic [15].

The mainstay of haemophilia A and B care is intravenously delivered factor concentrates. Factor VIII and IX concentrates can be purified from plasma or recombinantly synthesized. The plasma-derived FVIII products contain varying amounts of von Willebrand factor (vWF), depending upon the manufacturing process [16].

Haemophilia and viral hepatitis

Haemophilia or haemorrhagic or hereditary haemorrhagic disease is a genetic disease that affects males more than females. It is a deficiency of the eighth coagulation factor called haemophilia. It represents about 85% of cases and the deficiency of factor IX is called haemophilia. About 15% after circumcision and removal of teeth, it is treated by giving the venous factor or intravenous blood derivatives as an alternative, such as plasma, blood or cryoprecipitate which makes the child susceptible to transmission of infection and liver viruses.

MATERIALS AND METHODS

Study protocol and design

This cross-sectional study was conducted from March 2014 to March 2016 on 100 male children at Al-Azhar University hospitals in Cairo in the Paediatric Haematology and Haematology Department at El Mabarrah-Hospital-Health Insurance Organization in Sharqia Governorate.

Clinical and biological data: The patient’s history was taken in detail, detailed examination and blood samples were taken under the necessary standards to control the infection. A blood image was performed, the ratio of the blood was measured, and the percentage of the bilirubin (yellow) was measured. Indications of hepatitis viruses (A, B, and C).

The mean age in the study was 4.4 ± 11.47 . Haemophilia type A 95% while haemophilia type B 4% was 1% with factor 8 and factor 9 together. 28% were related to the closeness of the father and the mother. The similar cases were 36% in the family and 21% in the family. Skin bruises were as satisfactory as 64%, whereas joint destruction was 62%. The knee joint was more affected by 41%. Bleeding is like 50%. In nose, it is 70%. Haemophilia was 20% mild, 47% moderate, and 33% severe.

The most dangerous agents for transmission of C virus were cryoprecipitate (90%) and blood transfusion (83%).

The results found that antibodies to the virus represented 7% while virus B was 0% and antibodies to C virus were 65%.

This is a cross sectional study, was done at paediatric haematology unit in Al-Azhar university hospital Cairo and paediatric haematology unit El Mabarah-Hospital-Health Insurance Organization, Zagazig, Sharkia governate from March 2014 till March 2016. We examined 100 haemophilic male children for prevalence of hepatitis (A, B, and C).

Ethical considerations

Patients were enrolled after written informed consents obtained from their parents or caregiver.

Types of participants

Inclusion criteria: Patients diagnosed with haemophilia with age between 2-18 years were included in the study. Patient who have received factor concentrate, cryoprecipitate and other blood product as blood transfusion or plasma were also included.

Exclusion criteria: Patients with age less than 2 years and more than 18 years were excluded from the study. Patients with other bleeding disorder such as thrombocytopenia were excluded from the study.

Clinical pathological test

Blood samples were screened for hepatitis markers using ELISA.

Statistical analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered, and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0).

RESULTS AND DISCUSSION

Our study carried out in paediatric haematology unit at Al-Azhar University hospital, Cairo, Egypt and paediatric haematology unit of El Mabarah-Hospital-Health Insurance Organization, Zagazig, Egypt. Our study carried on 100 haemophilic male patients with mean age was 11.47 ± 4.4 years (Table 1). This late age due to lack of early diagnosis, screening in early life and lack of interest with extensive study for haemophilic children. Figure 1 demonstrates that oldest and frequent number of examined cases was 17 years.

Table 1 Age distribution of study group

Age	N=100
Mean age in year \pm SD	11.47 \pm 4.4
Range in years	2.0-18.0

In our study, we found that positive HAV was 7%. The level of hygiene in different communities could be one of the most important reasons for these variations. Poor hygiene, poor water sanitation, and family crowding, which increase the chance of close contact with the virus, are several reasons for the increased prevalence of the infection. Mauser-Bunschoten, et al. showed that the anti-HAV prevalence in 197 haemophiliacs (treated with clotting factor concentrates produced from large plasma pools) was 20%, and in 144 patients (treated with small pool cryoprecipitate) it was 13% [17]. HAV was 22.4% [18] (Tables 2 and 3; Figure 2).

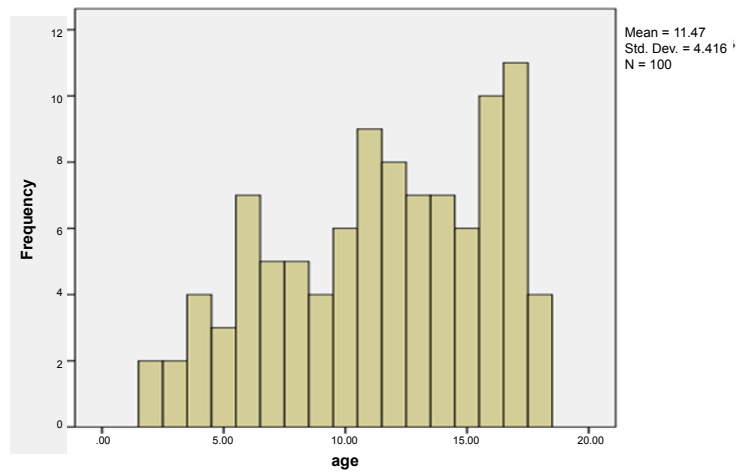


Figure 1 Age distribution of study cases

Table 2 Distribution of Severity in study cases

Severity	N	%
Mild	20	20.00%
Moderate	47	47.00%
Severe	33	33.00%

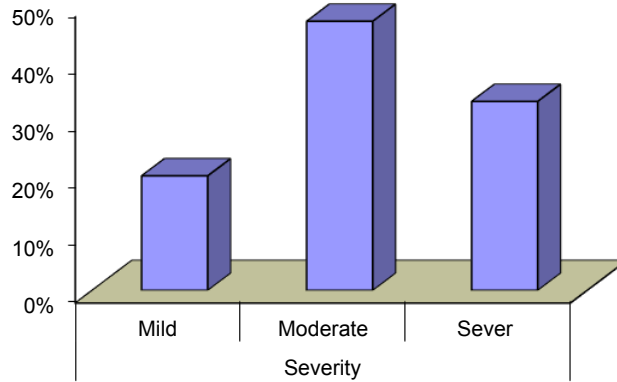


Figure 2 Severity of haemophilia in study

Table 3 Prevalence of hepatitis in study cases

Prevalence of hepatitis		N	%
HBV	-VE	100	100.00%
HCV	-VE	35	35.00%
	+VE	65	65.00%
HAV	-VE	93	93.00%
	+VE	7	7.00%

In contrast to our study, Mirzaei, et al. reported HAV IGM 59% [19]. Tantawya, et al. Egyptian study HAV seropositive was 87.8% [20]. This study showed no difference between haemophilic and normal children in prevalence of hepatitis A [21]. HAV was 43% among Spanish haemophilic patients.

Although in a cross-sectional study conducted among 1 to 15-year-old children, no difference in the seroprevalence of hepatitis A related to age groups, mean age, sex, and family size was observed [22].

In our study, the prevalence of HBsAg was 0% it seems that vaccination against HBV infection in newborn and high-

risk groups. And mandatory screening of blood donors by local blood banks since 1995 was successful in controlling HBV infection in haemophilia patients.

Our result was in agreement with the result of other studies Toyoda, et al. [23] Japanese study hepatitis A prevalence was 0%, Borhany, et al. [14] not detected 0%. in Iran: Ahvaz 1.1% Assarehzadegan, et al. [24], Isfahan 1.6% Kalantari et al. [25], Zahedan 4.9% Sharifi-Mood, et al. [26], Azarbaijan 2.7%, Yazd 1.4%, Rezvan, et al. [27], Kerman 6%, Tehran 1%, Ghazvin 1.1%, Semnan and Zanjan 0% Kalantari, et al. [25]. Windyga, et al. polish study the prevalence of HBV was 7.8% [28].

In our study, we found that prevalence rate of hepatitis C was (65%). Regarding the infection of hepatitis C, our results were high. It is known that the window period of this disease is very long and the haemophilic patients have received these blood components when they were supposed to be safe. This has occurred basically because the developing countries, such as ours, have continued using blood products, plasma, and cryoprecipitate, which were not submitted to viral inactivation.

Iranian studies have reported the prevalence of HCV in haemophilia patients as follows: Ahvaz 54% Assarehzadegan, et al. [24], Isfahan 80.5% Kalantari, et al. [25], Zahedan 29.6% Sharifi-Mood, et al. [26], Azarbaijan 51% Rezvan, et al. [27], Gilan 71.3% Mansour-Ghanaei, et al. [29], Tehran 60.2% Alavian, et al. [30].

In contrast to our result similar study conducted on 367 haemophilia patients in Shiraz (1992 to 2002) was also reported 15% HCV seropositive [31].

CONCLUSION

This study revealed that infection with hepatitis C rates was higher with higher number of blood products transfusion. Haemophiliacs who received only factor concentrates were less prone for infection with hepatitis C. It is quite possible that we might have missed some infected haemophilia patients during infectious window period who are seroconversion. Hepatitis B virus infection was 0% and hepatitis A virus infection was 7%.

Recommendations

Neonatal screening to detect haemophilic especially those with (family history of similar condition or baby to carrier mother).

Treatment as early as possible to prevent morbidity and mortality.

Prophylactic therapy preferable than on demand.

Build up haemophilia treating centres.

Repeated screening for hepatitis markers

Vaccination against hepatitis A and B viruses.

Health education and good sanitation.

Blood product screening.

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