Prevalence of Viral Hepatitis (A, B and C) Among Hemophilic Children

Mohammed Sayed Hemeda [1], Ahmed Mohesn Abd el-hakem [1], Kamel Soliman Hammad [2], Mohammed Salah Ali[1]

[1] Pediatric department, Faulty of medicine AL Azhar University, [2]. Clinical pathology department faculty of medicine AL-Azher University, Egypt.
Roaarody721@gmail.com

Abstract: Hemophilia is a rare hematological disease characterized by prolonged bleeding due to deficiency of coagulating factor 8 and factor 9. This is cross sectional study carried out at pediatric hematology unit al Azhar university hospital Cairo Egypt, and pediatric hematology unit Almabra health insurance hospital zigzag Egypt, in period from March 2014 to March 2016. one hundred male patient screened for hepatitis (A, B and C). mean age was 11.47±4.4 years old.95% with hemophilia A,4% hemophilia B and 1 patient had combined hemophilia A and Family history of hepatitis was 21%. consanguinity was 28%. similar condition in the family was 36%. Ecchymosis as clinical manifestation was 64%, hemearthrosis 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 still high in hemophilic and represent a major problem. Recommendation early detection, treatment and further investigation of hepatitis C virus in hemophilic children.
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Key word: Hemophilia, viral hepatitis**,** Hemophilic Children

1. Introduction

Hemophilia A and B are rare hereditary bleeding disorders, which are caused by mutations in the factor VIII and IX genes **(Franchini and Mannucci, 2012).**

Haemophilia is a chronic disease characterized by bleeding in joints, muscles and soft tissues **(Kaushansky et al., 2010).**

Two most common forms of hemophilia are Hemophilia A (HA) and Hemophilia B (HB) and are caused by deficiency of factors VIII and IX respectively. HA accounts for 80-85% of cases and HB in 15-20% of cases. Both types are inherited as X linked recessive pattern characterized by prolonged bleedingand hemorrhages typically in joints and soft tissues (**Kulkarni and Soucie, 2011).**

Historyof hemophilia:

Hemophilia 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 12thcentury, described a family with males who died from bleeding after trivial injury. (**Hoyer, 1994).**

Hemophilia 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 hemophilia B carrier **(Rogaev et al., 2009).**

Hemophilia A is caused by a lack of active clotting factor VIII (8). About 1 out of every 5,000 male babies is born with hemophilia A. Hemophilia B (Christmas disease) is caused by a lack of active clotting factor IX (9). It is less common and affects 1 out of 30,000 male babies **(Chitlur and Kulkarni, 2015).**

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. **(Youssef Al Tonbary et al., 2010).**

Individuals with less than 1% active factor are classified as having severe haemophilia, those with 1-5% active factor have moderate haemophilia, and those with mild haemophilia have between 5-40% of normal levels of active clotting factor **(Dimitrios Agaliotis et al., 2009).**

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 hemorrhage (**Kessler, 2007).**

Signs of hemorrhage include general (Weakness, orthostasis, tachycardia, tachypnea), musculoskeletal (Tingling, warmth, pain, stiffness, and refusal to use joint) **(Richards et al., 2012).**

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 **(Ballas and Kraut, 2008).**

The articular problems of hemophiliac patients begin in infancy. These include recurrent hemarthroses, chronic synovitis, flexion deformities, hypertrophy of the growth epiphyses, damage to the articular cartilage and hemophilic 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. **(Rodriguez-Merchan, 2012).**

In the past hemophilia replacement therapies were included fresh frozen plasma (FFP), cryoprecipitate and blood derived products without any viral inactivation. In 1950, plasma became available for treating hemophilia. In1965, cryoprecipitate was used as a treatment for hemophilia. FIX and FVIII concentrates used for hemophilia 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 **(Hough and Lillicrap, 2005).**

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 hemophiliacs **(Borhany et al., 2011).**

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. **(Singleton, 2010).**

The mainstay of hemophilia 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 vWF, depending upon the manufacturing process **(Boedeker BG, 2011).**

2. Patient and methods:

This is a cross sectional study, was done at pediatric hematology unit in Al azhar university hospital Cairo and pediatric hematology unit Almabara health insurance hospital Zagazig Sharkia governate from March 2014 till March 2016. we examined 100 hemophilic male children for prevalence of hepatitis (A, B and C).

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

Inclusion criteria:

- Known hemophilic patients.
- Patient aged from 2-18 years.
- Patient received factor concentrate, cryoprecipitate and other blood product as blood transfusion or plasma.

Exclusion criteria:

- Age less than 2 years and more than 18 years.
- Other bleeding disorder as thrombocytopenia.

Blood samples used for screening for hepatitis markers using ELISA.

- 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).

3. Results

Table (1): Age distribution of study group

Age N=100	
Mean age in years± SD	11.47±4.4
Range in years	2.0- 18.0

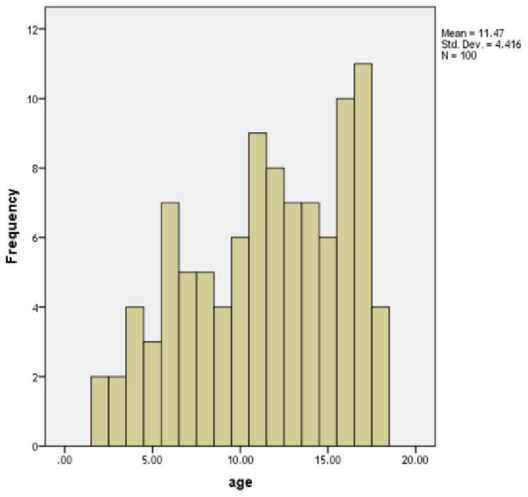

Figure (1): Age distribution of study cases

This figure demonstrates that oldest and frequent number of examined cases was 17 years.

Table (2): Distribution of Severity in study cases

Severity	No.	%
Mild	20	20.0%
Moderate	47	47.0%
Sever	33	33.0%

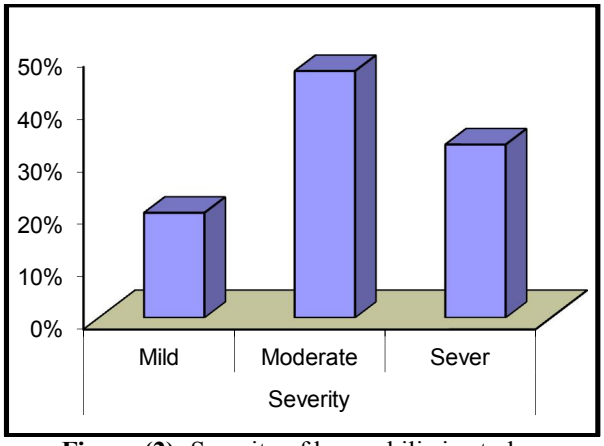

Figure (2): Severity of hemophilia in study

Table (3): Prevalence of hepatitis in study cases

Prevalence of hepatitis		No.	%
HBV	-VE	100	100.0%
HCV	-VE	35	35.0%
	+VE	65	65.0%
HAV	-VE	93	93.0%
	+VE	7	7.0%

4. Discussion

Our study carried out in pediatric hematology unit at al Azhar university hospital Cairo Egypt and pediatric hematology unit Almabara health insurance hospital Zagazig Egypt. Our study carried on 100 hemophilic male patients with mean age was 11.47±4.4 years. This late age due to lack of early diagnosis, screening in early life and lack of interest with extensive study for hemophilic children.

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., (1995)*** showed that the anti-HAV prevalence in 197 hemophiliacs (treated with clotting factor concentrates produced from large plasma pools) was 20%, and in 144 patients (treated with small pool cryoprecipitate) it was 13%. ***Hayashi K et al., (2001)*** HAV was22.4%.

In contrast to our study***Jamal Mirzaei et al. (2016)*** HAV IGM was 59%. ***Azza Tantawya et al. (2012)*** Egyptian study HAV seropositivity was 87.8%. This study showed no difference between hemophilic and normal children in prevalence of hepatitis A. ***(Molina et al., 1996)***. HAV was 43% among Spanish hemophilic 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 ***(Taghavi Ardakani et al., 2013)***.

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 hemophilia patients.

Our result was in agreement with the result of other studies ***Toyoda et al., (2004)*** Japanese study hepatitis A prevalence was 0%, ***Borhany et al., (2011)*** not detected 0%. in Iran: Ahvaz 1.1 % ***Assarehzadegan et al., (2012)***, Isfahan 1.6 % ***Kalantari et al., (2011)***, Zahedan 4.9 % ***Sharifi-Mood et al., (2007)***, Azarbaijan 2.7 %, Yazd 1.4 % ***Rezvan et al., (2007)***, Kerman 6 %, Tehran 1 %, Ghazvin 1.1 %, Semnan and Zanjan 0 % ***Kalantari et al., (2011).***

Windyga et al. (2006) polish study the prevalence of HBV was 7.8%.

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 hemophilic 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 hemophilia patients as follows: Ahvaz 54 % ***Assarehzadegan et al., (2012),*** Isfahan 80.5 % ***Kalantari et al., (2011),*** Zahedan 29.6 % ***Sharifi-Mood et al., (2007),*** Azarbaijan 51 % ***Rezvan et al. (2007),*** Gilan 71.3 % ***Mansour-Ghanaei et al. (2002)***, Tehran 60.2 % ***Alavian et al. (2003).***

In contrast to our result similar study conducted on 367 hemophilia patients in Shiraz (1992 to 2002) was also reported 15 % HCV seropositivity ***(Karimi et al., 2002).***

Conclusion

This study revealed that infection with hepatitis C rates was higher with higher number of blood products transfusion. Hemophiliacs who received only factor concentrates were less prone for infection with hepatitis C. It is quite possible that we might have missed some infected hemophilia 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 hemophilic 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 hemophilia treating centers. Repeated screaming for hepatitis markers Vaccination against hepatitis A and B viruses. Health education and good sanitation.

Blood product screening.

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