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Descriptive Epidemiology and Complications of Haemophilia in Assiut, Egypt

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Abstract

Background: *Haemophilia is a group of rare congenital disorders of blood where there's a defect in mechanism of clotting due to deficiency in factor VIII (Haemophilia A) or factor IX (Haemophilia B). It's inherited as x-linked recessive disorder but 30% of patients have no family history of the disease and they usually have spontaneous new mutation.*

Aim: *to describe the epidemiological situation of haemophilia in Assiut, assist the various complications and the type of treatment.*

Patients and Methods: *retrospective study was conducted on 75 hemophilic patients who were attending to Clinical Hematology Unit, Internal Medicine Department; Assiut University Hospital, Clinical Hematology Unit of Assiut Pediatric Hospital and Hematological Clinics in Assiut Health Insurance Clinics from the period between 2014-2016.*

Results: *haemophilia A represent 85.3% of the studied patients and 14.7% had haemophilia B. As regard residency 64% of haemophilia A patients and 13.3% of haemophilia B patients live in rural areas. We found positive consanguinity in 77.3% of hemophilic patients. Patients were classified according to the severity of bleeding manifestations into mild haemophilia in 84.4%, moderate haemophilia in 15.6%. As regards complications of hemophilic patients 76% had complication. The most common complications were hemarthrosis in 26.7% patients, muscle hematoma in16% and post transfusion infections as we found Positive HCV in 5.3%. As regard Treatment 54(72%) of all hemophilic patients were on demand treatment and 18(24%) with prophylaxis treatment while 3(4%) with no treatment. There was statistically significant ($P < 0.001$) increased complications in patients received on demand treatment compared to those received prophylaxis treatment.*

Conclusions: *The most common inherited bleeding disorder in our locality was haemophilia A followed by haemophilia B. Haemophilia was more common in rural area. Increase cases with consanguineous marriages. Hemarthrosis, hematoma and hepatitis C infection represented the main complications. Awareness, education and genetic counseling will be needed to decrease the spread of haemophilia in our community. Factor support (prophylaxis treatment) should be initiated for all patients as early as possible just diagnosis is confirmed to reduce the frequency of complications .Screening of blood and blood products to reduce the risk of viral hepatitis.*

Key Words: *Haemophilia, Bleeding, Factor VIII, Factor IX, Haemoarthrosis.*

INTRODUCTION

Haemophilia is a group of rare congenital disorders of blood where there's a defect in mechanism of clotting due to deficiency in factor VIII (Haemophilia A) or factor IX (Haemophilia B). It's inherited as x-linked recessive disorder but 30% of patients have no family history of the disease and they usually have spontaneous new mutation.[1]

Haemophilia is a rare disorder where patients can be presented by severe spontaneous life threatening episodes of bleeding in the early years of life. Not only haemophilia affects patients by its clinical consequences, it also causes a great economic problem to health care systems due to costs of hospitalizations, follow up visits and drugs in addition to costs due to decreased productivity of affected individuals at work and schools.[2]

For management of haemophilia to be effective, it's very important to get accurate diagnosis. So individuals presenting with history of easy bruising, spontaneous joint bleeding, soft tissue hematomas, hematuria or excessive bleeding after trauma or in the post operative setting should be suspected and evaluated for haemophilia.[3]

In Egypt which has a population of approximately (90 millions) and frequent consanguineous marriage , autosomal recessive disorders are more prevalent than other areas of the world. According to World Federation of Haemophilia(WFH) survey, 80% of haemophilia patients in the world don't receive any treatment and usually do not survive till adulthood. However, mortality in haemophilia patients has decreased due to increased availability of factor concentrates and improved management of bleeding episodes in haemophilia specialized centers.[4]

Haemophilia patients are prone to a lot of complications. However, the most common are musculoskeletal complications with spontaneous bleeding into joints and muscles where the first attack usually occurs before 2 years of age.[5]

PATIENTS AND METHODS

This retrospective study included 75 hemophilic patients who were attending Clinical hematology unit, Internal medicine department; Assiut University Hospital, Clinical hematology unit in Assuit pediatric hospital and Haematology clinic in Assiut health assurance during the period 2014-2016. All patients were subjected to complete history taking and complete clinical examination. Patients were divided according to factor VIII & factor IX levels into mild, moderate and severe. Laboratory Investigations including: CBC, Blood sugar, PT, PC, APTT, INR, HBsAg, HCVAb, HIV, factor VIII activity, factor IX activity, Liver and kidney functions were done to all patients.

Statistical analysis was performed using SPSS-version 16 software. The results were expressed as mean ± SD and percentages. Fisher's exact or chi-square test was used for comparisons of categorical variables. Paired samples t-test was used for comparisons of continuous variable before and after each procedures. Wilcoxon Signed Ranks Test was used for non-param-etric statics when comparing two related samples.

RESULTS

This retrospective study was conducted on 75 hemophilic patients in the period from 2013 to 2015. Haemophilia A represented 85.3% of patients and 14.7% had haemophilia B. Their age was 25± 13.6 years. Males represent 94.7% and 5.3% were females (Table 1). As regard residency 64% of haemophilia A patients and 13.3% of haemophilia B patients live in rural areas (Table 2). 68% of haemophilia A and 9.3% of haemophilia B showed positive history of consanguinity (Table 3). Clinical severity of hemophilic patients was classified as mild in 82.7% and moderate in 17.3% (Table 4). According to line of treatment among all hemophilic patients, 72% of them were on demand treatment and 24% with prophylaxis treatment while 4% with no treatment (Table 5). The commonest complications in this study were,

hemarthrosis in 26.7%, muscle hematomas in 16%, hepatitis C virus infection and intra abdominal hemorrhage in 5.3%, severe epistaxis in 4%, excessive post traumatic bleeding, hematuria and oral bleeding in 2.7% (Figure 1). There was statistically significant (P < 0.001) increased complications in patients received on demand treatment compared to those received prophylaxis treatment (Table 6).

Table (1): Personal characteristics of all the studied patients

	No. (n= 75)	%
Type of haemophilia:		
Type A	64	85.3
Type B	11	14.7
Age:		
< 18 years	14	18.7
18 - 25 years	37	49.3
> 25 years	24	32.0
Mean ± SD (Range)	24.95 ± 13.60 (5.0 – 61.0)	
Sex:		
Male	71	94.7
Female	4	5.3

Table (2): Distribution of type of haemophilia according to Residency

Residence	Type of haemophilia				Total (n= 75)	
	Type A (n= 64)		Type B (n= 11)			
	No.	%	No.	%	No.	%
Rural	48	64.0	10	13.3	58	77.3
Urban	16	21.4	1	1.3	17	22.7

Table (3): Distribution of type of hemophilia according Consanguinity marriage

Consanguinity	Type of haemophilia				Total (n= 75)	
	Type A (n= 64)		Type B (n= 11)			
	No.	%	No.	%	No.	%
Positive	51	68.0	7	9.3	58	77.3
Negative	13	17.4	4	5.3	17	22.7

Table (4): Clinical severity of all hemophilic patients

Classification	Type of haemophilia				P-value
	Type A (n= 64)		Type B (n= 11)		
	No.	%	No.	%	
Mild	54	84.4	8	72.7	0.609
Moderate	10	15.6	3	27.3	
Severe	0	0	0	0	

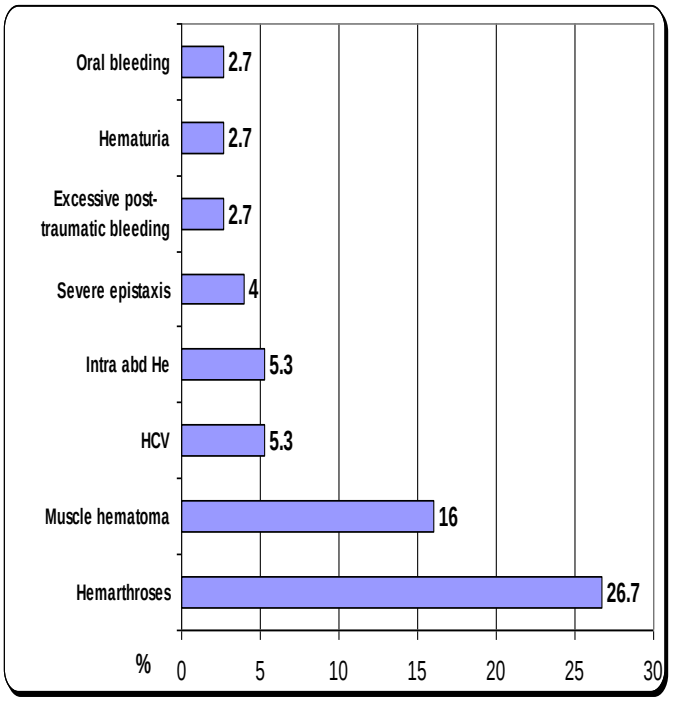
Table (5): Line of treatment among all hemophilic patients

Line of treatment:	No. (n= 75)	%
No treatment	3	4.0
On demand(Cryoprecipitate and fresh frozen plasma)	54	72.0
Prophylaxis(factor VIII & IX)	18	24.0

Table (6): Relation between complications and line of treatment

Complications	Line of treatment						P-value
	No treatment (n= 3)		On demand treatment (n= 54)		Prophylaxis treatment (n= 18)		
	No.	%	No.	%	No.	%	
Complications	2	66.7	47	87.0	8	44.4	0.001*
No complications	1	33.3	7	13.0	10	55.6	

Figure (1): Most common type of Complications among all hemophilic patients



DISCUSSION

The most common inherited bleeding disorder is Haemophilia especially haemophilia A which is five times more common than haemophilia B. The severity of these disorders is usually related to the degree of factor deficiency.[6]

In Egypt, haemophilias are considered to be one of the rare conditions with low prevalence and no real statistical analysis on the demography of the disease is available. So in this study we tried to describe the demographics of haemophilia in Assiut university which represents the largest pool of patients in the region of Upper Egypt.

In the present study, the majority of diagnosed haemophilia cases 64(85.3%) were haemophilia type A and only 11(14.7%) were haemophilia type B. These results were in concordant with the results of multiple previous studies [4], [7]–[9] where the majority of hemophilic cases in their studies were hemophilia A.

Also, in the present study, the majority of diagnosed hemophilia cases 51 (68%) their ages were less than 25 years old and only 24 (32%) were more than 25 years old, these results were in agreement with the results of Stonebraker et al [3] and with KAR et al [8], where the majority of diagnosed hemophilia cases were younger than 25 years old.

Gender distribution revealed that 71(94.7%) were males and 4(5.3%) were females. These results were in concordant with the results published by Al tonbary et al [4] as haemophilia is a x linked.

Residency distribution of all hemophilic patients in the current study revealed that 58 hemophilic patients (77.33%) were in rural areas and 17(22.67%) were in urban areas. These findings were in agreement with Alzubaidy [10] as 65% of all hemophilic patients were in rural areas and 35% were in urban areas, in comparison with KAR et al [8] (58%) of hemophilic patients residing in urban and peri-urban areas,(10%) in large towns, while (25%) were in rural areas, the reason for that difference hemophilic patients were clustered around the hemophilia centers or clinics that usually present in urban regions.

Positive consanguinity in the studied patients was present in 58 patients (77.33%) while negative consanguinity represented in17 patients (22.67%). These results were in concordant with the results of Alzubaidy [10] as positive consanguinity were reported in (71.7%) and negative consanguinity in (28.3%) of hemophilic patients, also with Borhany et al [11] positive consanguinity marriage in Pakistan were (62.7%) and negative consanguinity were (37.3%) of hemophilic patients.

In the current study, all hemophilic patients were classified as mild cases 62 (82.6%) and moderate cases 13 (17.4%) without severe cases. these results were in concordant with the results of Al tonbary et al [4] as they reported that mild cases were (73.6%) , moderate cases (19.4%) and severe cases were (6%). In comparison with the study of Ferreira et al [9], they reported that mild cases were (20.5%), moderate cases were (41%) while severe cases were (38.5%).

In the present study, 57 of the hemophilic patients (76%) had complications while 18 had no complications (24%). These findings are coinciding with that of Al tonbary et al [4] study, who found that 56.6% of the studied hemophilic patients had complications. That means complications are common in haemophilia.

The most common complications detected in the current study were hemarthrosis which represented in 26.7% of all studied hemophilic patients. These results were in concordant with that of Al tonbary et al [4]who reported that hemarthrosis was the most common complication among their hemophilic patients, and also with Ferreira et al [9] study as they also reported that hemarthrosis was the commonest complication among their hemophilic patients.

Our study showed that, 5.3% of hemophilic patients proved to be HCV positive. None of our studied cases had evidence of hepatitis B infection or HIV. Also Al tonbary et al [4] reported that 11% of their patients were HCV positive and none of them had serological evidences of hepatitis B virus, and also with Eshghi et al [12] who represented in his work the prevalence of HCV

infections among studied hemophilic patients was 15.6% and prevalence of HBV was 8%.This can be explained by the increased awareness and use of safe virus inactivated plasma transfusions and factor concentrates.

The current study showed that, the most common line of treatment used in our hemophilic patients was on demand factor concentrate treatment used by 54 patients representing 72% of studied group and prophylaxis treatment used by 18 patients representing 24% of studied group and only 3 patients were without treatment representing 4%. In comparison with the results of Carlsson et al [13] as most common line of treatment was prophylaxis treatment in 60.8% of their studied hemophilic patients and on demand therapy in 39.2% of their studied group. This could be explained by high economic state of Swedish and Norwegian population as prophylaxis treatment is much expensive than on demand treatment. This reflects the economic situation in our country where prophylaxis treatment with expensive factor concentrates is not affordable all the time to most patients and this explains the increased complications in this group of patients who are on demand therapy.

In the current study, the complications of hemophilic patients increased with on demand treatment 47/57 (82.45%) of complicated patients than patients with prophylaxis treatment 8/57 (14%) these results were in concordant with the results of Aznar et al [14] who reported that 71% of hemophilic patients with on demand treatment increased complications than those with prophylaxis treatment.

CONCLUSIONS

The most common inherited bleeding disorder in our locality was haemophilia A followed by haemophilia B.

- More common in rural area than in urban area.
- The number of total registered cases increasing with consanguineous marriages.
- The most common complications were hemarthroses followed by muscle hematoma and HCV.
- The most line of treatment was on demand treatment followed by prophylaxis treatment.
- The complications increased in hemophilic patients with on demand treatment more than those on prophylaxis treatment.

RECOMMENDATIONS

Initiation of a first step for a Hemophilia Center in Assiut city as a result of coordination between Egypt authorities & World Federation of Hemophilia (WFH).

Factor support a prophylaxis treatment should be initiated for all patients as early as possible just diagnosis is confirmed to reduce the frequency of complications .Screening of blood and blood products to reduce the risk of viral hepatitis.

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