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Article

The Correlation between some Risk Factors and the Patients with Inherited Hemophilia Gender in the Province of Kerbala.

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ABSTRACT

The transcendent side effects normally correlate with the patients' organic sex, which signifies that the crippling instruments of bleeding problems are gendered, bleeding turmoil hereditary diseases. This includes debilitated blood clotting, which might prompt a handicap. The patients' gender determines the mechanism of inactivation of bleeding disorders because of the prevailing symptoms difference. It usually depends on the biological sex. In this study, ninety-one (91) of the male and female hemophilic patients had complete information taken for this study from their medical records in the special department for treating patients in the hospital of the city of Kerbala. The study aims to determine the association between a hemophilic patient's gender and the various risk factors and reveal how much these factors impact sex. The results of the current paper confirmed that males 86% were more affected than females 14% by hereditary hemorrhagic disease due to the correlation between this disease and the chromosome of sex. The age of the disease diagnosis in male patients was between one and five years. In female patients, a specific age of diagnosis did not appear. There were differences between sexes at the age of ten (10) of diagnosis and younger than that. The affected males were suffering from VIII and IX factors deficiency 54.94% and 23.07%, respectively, while the females did not suffer from the previously mentioned deficiency of those factors but suffered from XI factor deficiency 14.28%. Parental consanguinity significantly impacted 32.96% of the number of injuries in males, including the first 15.3 % and the fourth degree of kinship 17.5%. Concerning results of the history, they manifested that males are more than females in Epistaxis, Skin Bleeding, Join Bleeding, Muscle Bleeding, Bleeding after Trauma. No differences were found in rates of WBC and the amount of clotting factor deficiency, while we found a significant difference in platelet mean between the two genders. Conclusion: According to the data, hemophilia A and B are more frequent than C of all the studied hereditary bleeding diseases. The most prevalent symptom among male patients is skin bleeding. Consanguineous marriage is the main cause of the disease. Although the disease is linked to the sex chromosome, females are also affected.

Keywords: hemophilia, gender, risk factors, family history of bleeding, VIII factor deficiency, IX factor deficiency.

INTRODUCTION

Hemophilia is a disease that is widely spread all over the world and has no legitimate treatment. The majority of patients are still really suffering in the world. Hemophilia affects around 80 million Egyptians owing to inbreeding [1]. Hemophilia typically appears at the beginning of life or birth and is thus a precursor to an individual's advancement for themselves and their social life. The symptoms differ from one person to another concerning the type and severity of bleeding turmoil. Accordingly, it ranges from severe swelling and bleeding, unconstrained nosebleeds, to inner bleeding in joints and muscles, besides much blood loss during the menstrual cycle. An actual injury might cause bleeding. However, it frequently happens immediately with no conspicuous reason. Moreover, people with bleeding problems are in high danger of genuine involvement if no particular insurance is taken to prevent bleeding. [2]

A widespread misunderstanding about bleeding problems is that they exclusively affect men. Women are frequently assumed to 'simply' have the mutated gene and, as carriers, may pass the disease on to their sons. Women, on the other hand, might have severe symptoms [3]. Affected males have symptoms. They transfer the influenced X chromosome to their daughters rather than their sons. On the other hand, females with the influenced X chromosome usually do not show symptoms. However, they have a 50% chance of passing the influenced gene to their kids [4]. An inherited bleeding disorder is a disorder that is brought about by a reduction in blood coagulating factor VIII or factor IX (known as Hemophilia A and B respectively), Which leads to frequent bouts of bleeding [5] Hemophilia A and B are hereditary X-linked bleeding diseases and is caused by a lack of clotting factors FVIII or FIX respectively. Hemophilia A affects one (1) in every 10,000 male births, while hemophilia B affects one (1) in every 30,000 male births [6]. The absence of a functional intrinsic tenase complex leads to decreasing Thrombin production and the inability to form and sustain a stable clot when either FVIII or FIX is deficient [7]. Rare coagulation factor deficits are autosomal recessive bleeding diseases in which one or more clotting factors (factors I, II, V, VIII, VII, X, XI, or XIII) are absent or malfunctioning [8.]

MATERIALS AND METHODS

Data Set was obtained from the department of hemophilia in Al-Hussein Hospital for Children in the province of Karbala to describe gender, age at diagnosis, the diagnosis of the factor of deficiency, family history of bleeding, bleeding history, platelets, WBC and the amount of the clotting factor deficiency of ninety-one (91) study cases. The age of individuals with hemophilia ranges from one (1) day to thirty-three (33) years old. They were randomly selected. Fifty-nine (59) cases with incomplete data were excluded. Analytical statistics ((SPSS) software) was used to enter and manage the data of all patients (version 25). The variables' descriptive statistics were given for quantity, means, and standard deviation.

RESULTS

Table One uncovers the effect of the patient's gender on the incidence of hereditary hemorrhagic disease. The percentage of males is (85.71%), while that of females is (14.29%), presenting a highly significant difference ($P < 0.001$). As for the effect of age at diagnosis on the incidence of infection in both males and females, it is evident in Table 2, which manifests that males are more affected than females at the age of 10 years and even at a younger age than that while there is no difference between two sexes at the age >10. According to the three factors of deficiency: VIII, IX and XI, the male patients suffer from a deficiency in factors VIII at the rate of (54.94%) and IX at the rate of (23.07%), with a high moral difference. Females do not suffer from the deficiency of these two factors. As for the defi-

ciency in the XI factor is found in both of them at the same proportion. A significant difference, i.e. (P <0.001), is found between the males in the deficiency of factor VIII and females in factor XI, as in Table Three.

Gender	Patients No. (%)
(♀)Females	13 (14 %)
(♂)Males	78 (86 %)
Total	91 (100%)
P value	0.00001 **
* (P <0.05) , ** (P <0.001)	

Table 1. The Effect of Gender on the Infection of the Disease.

Age at diagnosis (year)	Female Numbers and rate (%)	Male number and rate (%)	Total number and rate (%)	P value
< 1	4 (4.39%)	26 (28.57%)	30 (32.96%)	0.00006 **
1 – 5	4 (4.39%)	35 (38.46%)	39 (42.85%)	0.00001 **
6 – 10	1 (1.01%)	10 (10.98%)	11(12.08%)	0.00666 *
11 – 15	1 (1.01%)	2 (2.19%)	3 (3.29%)	0.5637
> 15	3 (3.29%)	5 (5.49%)	8 (8.79%)	0.4795
Total	13 (14%)	78 (86%)	91(100%)	0.00001 **
P value	0.47205	0.00001 **	0.00001 **	
* (P <0.05) , ** (P <0.001)				

Table 2. The Difference between the Two Genders in the Percentage of the Disease Infection according to the Age at Diagnosis.

Factor deficiency	Female number and rate (%)	Male number and rate (%)	Total number and rate (%)	P value
VIII	0 (0%)	50 (54.94%)	50 (54.94%)	0.00001**
IX	0 (0%)	21 (23.07%)	21 (23.07%)	0.00003**
XI	13 (14.28%)	7 (7.69%)	20 (21.97%)	0.17791
Total	13 (14%)	78 (86%)	91 (100%)	0.00001 **
P value	0.00047 **	0.00001 **	0.00007 **	
* (P <0.05) , ** (P <0.001)				

Table 3. Difference between two genders in the diagnosis factor deficiency.

The family history of bleeding could prove that the relationship between first and fourth-degree kinship and parental kinship present, statistically, significant differences between males: (15.38%) and (17.58%) and females: (1.01%) and (2.91%) respectively. While it is found that the kinship of the third and the fourth degrees could acquire new mutation, kinship on the mother's behalf does not present any statistical differences between males and females affected, as is vivid in Table Four. The results of the bleeding type also could tell that the significant differences (P <0.001) between males (41.75%), (43.95%), (42.85%), (42.85%), (31.86%) and females (10.98%), (8.79%), (1.01%), (4.39%), (7.69%) exists in

epistaxis, skin bleeding, joint bleeding, muscle bleeding and post-traumatic bleeding respectively. A significant difference (P <0.05) between males (31.86%) and females (9.89%) in tooth or gum bleeding exists, where the number of males was higher than females. On the other hand, no difference between the two sexes in bleeding at birth, Hematuria, or GI bleeding is recorded. These findings are clearly presented in Table five.

Family's Bleeding History	Females' Number and Rate (%)	Males' Number and Rate (%)	Total Number and Rate (%)	P value
First	1(1.01%)	14(15.38%)	15(16.48%)	0.00079**
Second	0 (0%)	4(4.39%)	4(4.39%)	0.31731
Third	2 (2.91%)	5(5.49%)	7(7.69%)	0.25684
Fourth	2(2.91%)	16(17.58%)	18(19.78%)	0.00097**
Parental consanguinity	5(5.49%)	30(32.96%)	35(38.46%)	0.00002**
Acquired	3(3.29%)	7(7.69%)	10(10.98%)	0.2059
Mother side grandfather	0(0%)	1(1.01%)	1(1.01%)	0.5637
New mutation	0(0%)	1(1.01%)	1(1.01%)	0.5637
Total	13(14%)	78(86%)	91(100%)	0.00001 **
P value	0.47205	0.00002**	0.00004**	
*** (P <0.05) , ** (P <0.001)**				

Table 4. The Difference between two Genders in the Family's Bleeding History.

Type of Bleeding	Females' Number and Rate (%)	Males' Number and Rate (%)	Total Number and Rate (%)	P value
Bleeding at birth	4(4.39%)	10(10.98%)	14 (15.38%)	0.10881
epistaxis	10(10.98%)	38(41.75%)	48 (52.74%)	0.00005**
Skin bleeding	8 (8.79%)	40 (43.95%)	48(52.74%)	0.00001**
Join bleeding	1(1.01%)	39 (42.85%)	40 (43.95%)	0.00001**
Muscle bleeding	4(4.39%)	39 (42.85%)	43(47.25%)	0.00001**
Bleeding after trauma	7(7.69%)	29 (31.86%)	36 (39.56%)	0.00025**
Hematuria	1(1.01%)	6 (6.59%)	7(7.69%)	0.5878
GI bleeding	5(5.49%)	12 (13.18%)	17 (18.68%)	0.8956
Tooth or gum bleeding	9 (9.89%)	29(31.86%)	38(41.75%)	0.00118 *
P value	0.06268	0.00001**	0.00001**	
*** (P <0.05) , ** (P <0.001)**				

Table 5. The Difference between the Two Genders and the Type of Bleeding

Furthermore, this study manifests a similarity in the rate of the WBC and the amount of clotting factor deficiency in the blood samples for both sexes despite having a difference between the number of infected males and the infected females, as is clear in Tables 6 and 7, respectively. We note that the rate of platelets in females is lower than in males, with a significant difference at p<0.05, as shown in Table eight.

Gender	Number and rate (%)	Average	SD
Female	13(14%)	9.5	2.12132
Male	78(86%)	11.66613	7.988192
Total	91(100%)	11.53485	7.761386
P value	0.00001 **	0.3357	
*** (P <0.05) , ** (P <0.001)**			

Table 6. The Difference between the Two Genders in the average WBC

Gender	Number and rate (%)	The average	SD
Female	13(14.28%)	7.6290909	17.144322
Male	78(85.71%)	6.0928169	10.574451
Total	91(100%)	6.3618518	11.598840
P value	0.00001 **	0.6616	
*** (P <0.05) , ** (P <0.001)**			

Table 7. The Difference between the Two Genders in the Average of the Clotting Factor Deficiency

Gender	Number and rate (%)	Average	SD
Female	13(14%)	289.7692	114.0045
Male	78(86%)	378.0769	152.9229
Total	91 (100%)	315.6813	144.9143
P value	0.00001 **	0.04773*	
*** (P <0.05) , ** (P <0.001)**			

Table 8. The Difference between the Two Gender in the Average of the Platelets

DISCUSSION

This study is conducted to help identify factors associated with bleeding disorders in this region of Iraq. The results reveal that the disease of Hemophilia appears in both genders with no exception. Since C Hemophilia is passed on autosomal chromosome 4 and is unrelated to the patient's gender, it affects both sexes equally. Due to A and B Hemophilia transmission via a gender chromosome, the males are more affected than females [9]. Males suffer from factor VIII and IX deficiency, while females suffer from XI factor, as presented in the results. Inherited deficits or abnormalities in plasma proteins involved in blood coagulation can result in life-long bleeding problems with severe inversely proportion to the degree of factor deficiency. Hemophilia A and B are the most common deficits caused by a hereditary deficiency or defect in factors VIII and IX, respectively. Hemophilia A and B are inherited as X-linked recessive characteristics, with prevalence rates of around 1 in each 10,000 and 1 in each 50,000 in the general population, respectively, with no notable racial differences [10].

Other coagulation protein deficiencies, such as factors V, VII, X, and XI, are classified as rare inherited coagulation disorders (RICD) and are passed down as autosomal recessive features in both sexes, with a homozygous form frequency in the general population. Apart from consanguineous marriages, which are widely spread (such as in the Middle East, India, and Iran), all of these factor shortages are uncommon. The most frequent RICD (Recessively Inherited Coagulation Disor-

ders) is hereditary factor VII deficiency [11]. Factor XI deficiency (also known as hemophilia C) is fairly rare. However, it affects many of the Ashkenazi Jewish community [12] because these genes are on the X chromosome. Males have one X and Y chromosome (XY), whereas females have two X chromosomes (XX). The X chromosome is carried down through the generations from mothers to sons, whereas the Y chromosome is transmitted down through the generations from fathers to sons. A female receives one X chromosome from each father. This indicates that if a son receives an X chromosome from a woman with hemophilia, he will also develop the disease. However, since women have two X chromosomes, they can only get the condition if both parents have the faulty gene [13].

The results reveal that most patients have a family history of the disease, especially consanguineous marriage. Most hemophilia patients learn about their infection through family history; they examine the child and discover that he is a disease carrier. However, infected children who do not have a family history learn about their infection only after surgery or a traumatic injury that causes bleeding [14]. Due to the consanguineous marriage, the incidence of inherited diseases -including hemophilia- has increased, as stated in the current study's findings. "Consanguinity" refers to a relationship between two people with at least one ancestor [15]. Over half of all marriages in the province under study are consanguineous, ranging from first to distant cousins. This is true in Iraq and practically all of Iraq's neighbors [16]. Iraq is a Middle Eastern nation where weddings between first cousins are considered as an allowed one. In areas where such marriages are popular, close biological relatives account for up to 60% of all marriages. Consanguinity has been implicated in several studies as a cause of birth abnormalities and disorders such as hemophilia, among others [17].

It was first suggested by analysis of small groups of healthy adults that platelet count varied with age [18] and gender [19] being greater in youth than in old age and higher in women than in males. The larger investigations later confirmed these findings. After adjusting for age and gender, platelet count had a 54% heritability. However, environmental variables only accounted for 5% of phenotypic variance, indicating that genetic factors played a significant role in these disparities [20].

CONCLUSION

Hemophilia C is the most common disease of all the inherited bleeding diseases, which is evaluated as less in females than males. This can be associated with factor 11 deficiency, according to the findings. Skin bleeding is the most common symptom among male patients. Consanguineous marriage is the main cause of the disease among both genders. Although the disease is linked to the sex chromosome, females are also affected.

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