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Profile of Pediatric Hemophilia A Patients: One Hospital Study

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ABSTRACT

Introduction: This research is conducted to describe the characteristic of Hemophilia A patients.
Methods: Cross-sectional study conducted in 55 patients with Hemophilia A. The variables were age, bleeding episode, factor VIII level, and bleeding site. The data presented descriptively.
Results: The largest group was 2-10 years old (52,73%). The most common bleeding episode occured in the patients was moderate level (60,0%). The most common patient's factor VIII level was moderate level (52,7%). The patient's bleeding most likely took place in muscle or known as hematoma (41,8%). While the less likely bleeding were intracranial and nose bleeding.
Conclusion: 2-10 years old patient are the largest group because of hemophilia A mostly diagnosed in childhood, where children are actively moved so that the spontaneous bleeding or abnormal bleeding can be seen easily. Parents needs to be aware if there were abnormal or spontaneous bleeding which takes place in muscle or known as hematoma with moderate episode of bleeding which meant that the occurrence of spontaneous bleeding is periodically happened or in prolonged bleeding accompanied by minor trauma or invasive action.

Introduction

Hemophilia is the most frequent inherited bleeding disorder and is clasified into 2 types, which are Hemophilia A and Hemophilia B type.[15] Hemophilia A is a type of congenital disease of blood coagulation disorder caused by deficiency of Factor VIII in the blood and inherited by X-linked recessive.[13] This cause the bleeding in patient would be prolonged due to disruption of the intrinsic pathways in the blood clotting process.[14] The prevalence of Hemophilia A is greater than Hemophilia B, which is around 85%.[12] In the United States, as many as 20 in 100,000 boys suffer from hemophilia A. Hemophilia A can be categorized as mild, moderate, and severe hemophila.[5] In the United States, every 1 per 5,000-10,000 men suffer from Hemophilia A. Every year, around 400 babies are born with hemophilia.[2]

Hemophilia is one of the oldest genetic diseases ever recorded. The inherited bleeding abnormality that occurred in a man was recorded in Talmud file in the second century. The modern history of hemophilia began in 1803 by John Otto who explained the existence of children suffering from hemophilia. Proof of the existence of a blood clotting process abnormality in hemophilia was carried out by Wright in 1893. Factor VIII was only identified in 1937 when Patek and Taylor managed to isolate clotting factors from the blood, which was then called an antihemophilic factor (AHF). In 1952, Christmas disease was first described, and the cause was different from hemophilia A (classic), so hemophilia was later divided into hemophilia A and B.[4]

Prolonged bleeding and the occurance of bleeding in vital organs can be fatal in Hemophilia A patients. Patient's death which caused by intracranial bleeding in which over a long period of time a long period of time can increase the intracranial pressure and cause fatality to the brain.[1] In patients with Hemophilia A, bleeding can be occur in the area of joints or hemoarthrosis, bleeding in the muscles or hematoma, intracranial bleeding, bleeding post circumcision, bleeding in the gums and mouth, bleeding in the gastrointestinal tract, bleeding in the urinary tract or hematuria, bleeding from the nose or epistaxis, and others. In cases of acute bleeding due to trauma or surgery, hemophilia patients can experience hemorrhagic shock. In Europe, the life

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expectancy of hemophilia patients is less than 60 years.

The incidence of intracranial hemorrhage varies between 2.2% - 7.5% in children with hemophilia and adult patients, and about 1% - 4% in neonates. Intracranial hemorrhage is one of the most fatal mortality cause in hemophilia patients, and also result in serious long-term complications such as seizures/ epilepsy, behavioral disorders, speech disorders, and intelligence. In the era before 1960, the death rate from intracranial bleeding in hemophilia patients was around 70%. With the widespread use of freezing factor concentrates, this figure dropped by 20% in 2005.[3]

The level of Factor VIII in the blood of Hemophilia A patients can affect the severity of bleeding in certain sites (bleeding site) in patients, but this is not clearly known at the time of the initial diagnosis of Hemophilia A.

Based on the descriptive above, the researcher was interested in conducting this reasearch to determine the characteristics of Hemophilia A patients in Dr. Soetomo General Hospital Surabaya.

Methods

This study used a cross-sectional conducted from April 2018 to October 2018. Subjects were the Hemophilia A patients who were first registered at Pediatric Outpatient Clinic of Dr. Seotomo General Hospital, Surabaya for the period of January 2012 – December 2017. This research has been approved ethically by Research and Development Department of Dr. Seotomo General Hospital Surabaya (0182/KEPK/IV/2018). All data recorded from medical records.

The inclusion criteria were all hemophilia A patients who were first diagnosed within January 2012 – December 2017. While the exclusion criteria were all hemophilia A patients who were control patients, were not first diagnosed in Pediatric Outpatient Clinic of Dr. Seotomo General Hospital Surabaya, and non-active patients because of getting treatment in other hospital or passed away. The category for grouping the factor VIII level and bleeding episode were used the classification based on the guidelines for the managemet of Hemophilia published by World Federation of Hemophilia. The factor VIII level were categorized into 4 criterias which are normal (40%-100%), mild (5%-40%), moderate (1%-5%), and severe (0-<1%).11 The bleeding episode were categorized into 3 criterias which are mild (acute bleeding in major trauma or spontaneous bleeding rarely occur), moderate (periodic spontaneous bleeding or prolong bleeding with minor trauma), and severe (often spontaneous bleeding in joints and muscles or sudden bleeding without trauma).[11]

Results

There are total 55 patients in this study who were included in inclusion criteria. The result of the 55 patients are categorized by their age, gender, coagulation factor VIII level, and bleeding site as seen in table 1.

Table 1.Characteristic of Hemophilia A Patients

Variable	Frequency	Percentage
Age		
0-28 days (neonates)	0	0%
28 days-1 year (infant)	0	0%
1-2 years (toddler)	6	10.91%
2-10 years (child)	29	52.73%
10-19 years (adolescent)	20	36.36%
Gender		
Male	51	92.73%
Female	4	7.27%
Coagulation Factor VIII Level		
5-<40 (mild)	25	45.5%
1-5 (moderate)	29	52.7%
0-<1 (severe)	1	1.8%
Bleeding Episode		
Mild	5	9.1%
Moderate	33	60.0%
Severe	17	30.9%
Bleeding Site		
Intracranial bleeding	1	1.8%
Joint bleeding or hemarthrosis	10	18.2%
Muscle bleeding or hematoma	23	41.8%
Gum bleeding	12	21.8%
Post circumcision	5	9.1%
Nose bleeding or epistaxis	1	1.8%
Lip or mouth bleeding	3	5.5%

Based on table 1, the results showed that there were variations in the age of patients at the time of initial diagnosis was between 1-16 years. The largest age group was 2-10 years old (52,73%). There were no patients diagnosed with Hemophilia A in the range of 0-1 year old. This might caused by there was a limitation for early diagnose for neonates and infants in health care. Neonates and infants are less actively move than toddlers and children.

The results also showed that there were variations in the patient's coagulation factor VIII level at the time of initial diagnosis in 55 samples of patients. The patient's coagulation factor VIII level group that has the highest percentage is the patients with coagulation factor VIII level 1-5% also known as moderate level. Whereas the patient's coagulation factor VIII level group with the lowest percentage is the patients with coagulation factor VIII level 0-<1% also known as severe level which only consist of 1 patient.

Three categories of classification of hemophilia, which are mild, moderate, and severe episodes. The results showed that moderate episode of bleeding has the highest

percentage. While the mild bleeding episode group was the least percentage.

Besides, the result also showed that the bleeding in Hemophilia A patients at the time of initial diagnosis most likely took place in muscle bleeding or known as hematoma. While the least percentage cases of bleeding occur in intracranial bleeding and nasal bleeding or known as epistaxis.

Discussion

From the 55 samples, there was a variation in the age of patients at the time of the initial diagnosis, from 1-16 years old. The highest percentage is in the 2-10 years, while the group with the lowest percentage of the age group is 1-2 years. The results showed that moderate episode of bleeding most likely happened to the patients with manifestation at the time of initial diagnosis most likely hematoma, gum bleeding and joint bleeding (hemarthrosis). While the fewest percentage of bleeding occur in intracranial and epistaxis.

In the United States, many patients with hemophilia are diagnosed at a young age. Patients with mild hemophilia are diagnosed from the age of 36 months, patients with hemophilia are being diagnosed from the age of 8 months, and patients with severe age are diagnosed from the age of 1 month. In patients who have no known history of blood coagulation physiology in the family history, hemophilia is generally diagnosed when abnormal bleeding occurs.[6] Diagnosis of hemophilia A in patients over the age of 3 years old can be due to limited health facilities and services, especially for areas in developing countries.

Moderate bleeding episode is when the occurrence of periodic spontaneous bleeding or in prolonged bleeding accompanied by minor trauma or invasive action. Severe bleeding episode is when there is frequent spontaneous bleeding in the muscles or joints or in the absence of identified homeostasis. While the mild bleeding episode was the least percentage of bleeding group. Mild bleeding episode is when the occurrence of acute bleeding in major trauma or invasive action, or if spontaneous bleeding rarely occurs.[7]

In a survey conducted by the Association of Indonesian Hemophilia Society (HMHI) in Jakarta in July 2005 there were 219 hemophilia patients with 192 people (88%) suffering from Hemophilia A. From the survey, 83 people (43%) suffered from severe Hemophilia A, 72 people (37%) had moderate Hemophilia A, and 37 people (20%) had mild Hemophilia A.

Based on the HMHI survey and the results of this study have the same tendency, the largest population is in the group of patients with Hemophilia A with moderate to severe bleeding. While the group of patients with mild Hemophilia A is fewer.[4]

Spontaneous bleeding in hemophilia A is common takes place in the joints. Bleeding in the joints can occur in the synovium, causing inflammation called synovitis.[8] Synovium is a thin layer on the inside of the joint that lubricate joints and provide nutrients to the joints. The synovium contains a lot of blood vessels. So this is the reason why most bleeding often to occur in the joint area, especially in the joints of the limbs.[9] Besides, the spontaneous bleeding can also occured in muscle and known as hematoma. Hematoma happened because muscle contains many blood vessels and in children which actively move, the blood vessels can be ruptured which caused by any trauma or the bleeding happened spontaneously because of diapedesis process.[7] In a study in Iran in 2015 it was stated that the type of bleeding that most occurs in Hemophilia A patients is hemarthrosis, with hematoma in second place, and it is mentioned that gum bleeding, vertebral bleeding, and sublingual bleeding are rarely happened.[10] In this case, there is a similarity between this research and Mansouritorghabeh's study, which is that joint bleeding or hemarthrosis and muscle bleeding or hematoma are a group of bleeding sites that occur quite a lot in patients with Hemophilia A. However, there are differences, which in this research, gum bleeding occurs quite a lot. Whereas in Mansouritorghabeh (2015), gum bleeding is one of three types of bleeding that are rarely found in patients with Hemophilia A. Coagulation factor VIII is used in blood clotting process in order to stop bleeding. In hemophilia A patients which lacks of factor VIII, the bleeding cannot be stopped easily and caused prolonged bleeding.[15] So that, the therapy for hemophilia A patients is by giving coagulation factor VIII injection and this treatment is given for the patient's lifetime.[4]

Conclusion

Hemophilia A is generally occurs in patient which are 2-10 years old with most common bleeding takes place in muscle or hematoma with most coomon bleeding episode was moderate level of bleeding.

Conflict of Interest

The author stated there is no conflict of interest

References

1. Tonbary, Y. Al, Elashry, R., El, M., & Zaki, S. (2010). Descriptive Epidemiology of f Hemophilia and nd Other Coagulation Disorders in, 2(3).
2. Plug, I., Van Der Bom, J. G., Peters, M., Mauser-Bunschoten, E. P., De Goede-Bolder, A., Heijnen, L., Rosendaal, F. R. 2006. Mortality and Causes of Death in Patients with Hemophilia, 1992-2001: a prospective cohort study. Journal of Thrombosis and Haemostasis : JTH, 4(3), 510–6.
3. Guyton, A. C., & Hall, J. E. 2006 . Hemostasis and Blood Coagulation. Textbook of Medical Physiology. 11th ed., p. 465. Philadelphia, Pennsylvania: Elsevier, Inc.
4. Chozie, N. A., Gatot, D., Windiastuti, E., & Handryastuti, S. 2011. Perdarahan Intrakranial pada Hemofilia: Karakteristik, Tata Laksana, dan luaran. Sari Pediatri. 13(6), 250–6.
5. Stonebraker, J., Bolton-Maggs, P., Michael Soucie, J., Walker, I. and Brooker, M. 2010. A Study of Variations in the Reported Haemophilia A Prevalence Around the World. Haemophilia. 16(1), 20-32.
6. Centers for Disease Control and Prevention. 2017. Data & Statistics | Hemophilia | NCBDDD|CDC.
7. Kulkarni, R. , Soucie, J. M., et all. 2009. Sites of Initial Bleeding Episodes, Mode of Delivery and age of Diagnosis in babies with hemophilia diagnosed before the age of 2 years: a report from The Centers for Disease Control and Prevention's (CDC) Universal Data Collection (UDC) project. Hemophilia, 15: 1281-1290.
8. Centers for Disease Control and Prevention. 2017. Diagnosis | Hemophilia | NCBDDD | CDC. [online]
9. Van Vulpen, L. F. D., Holstein, K., & Martinoli, C. 2018. Joint disease in hemophilia: Pathophysiology, pain and imaging. Hemophilia, 24 February, 44–49.
10. Knobe, K., & Berntorp, E. 2011. Hemophilia and joint disease : pathophysiology, evaluation, and management. Journal of Comorbidity, 1(1), 51–59.
11. Mansouritorghabeh, H. 2015. Clinical and laboratory approaches

to hemophilia A. Iranian Journal of Medical Sciences, 40(3), 194–205.Medlineplus.gov. 2017. Hemophilia A: MedlinePlus Medical Encyclopedia.

12. World Federation of Hemophilia. 2012. Guidelines for The Management of Hemophilia. In Hemophilia. 2nd ed.. Montréal, Québec: Blackwell Publishing Ltd.
13. Sharma, R. S., Arya, A. K., & Rao, Y. K. (2016). Clinico-epidemiological profile of hemophilia with special reference to development of inhibitors in Indian scenario : a crosses sectional study at tertiary care centre in north India, 3(3), 922–925.
14. Wang, J. (2016). Comorbidities of cardiovascular disease and cancer in hemophilia patients. Thrombosis Journal, 14(Suppl 1).
15. Gatot, Djajadiman, Arwin. (2007). The prevalence of factor VIII inhibitor in patients with severe hemophilia-A and its clinical characteristics. Paediatrica Indonesiana, 45(7), 177–181.