A Preliminary Study of Age and Sex of People with Hemophilia

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Abstract

Aim: This paper aims at providing more information of people with hemophilia for more targeted treatment. **Methods:** 1149 people with hemophilia are surveyed in 45 units, and then established by EpiData software. The number of people with hemophilia in 9 age intervals for the male and female is analyzed by Population Pyramid and Pareto Analysis. **Results:** It is found that the people with hemophilia are appearing in every age interval. Relative to the number of male patients, the number of female patients is extremely rare. Of 1134 male patients, relative frequencies for male ranked the first (23.0%), second (17.4%), third (17.2%) are 7 - 12, 2 - 3, 13 - 18 years old, respectively, while of 15 female patients, relative frequencies for female in these age intervals are only 13.3%, 13.3%, 6.7%, respectively. However, the most relative frequency of female patients is between 26 - 45 years old. **Conclusion:** There is a challenge of the aging hemophilia population. Most of male patients are between 7 - 12 and 2 - 3 years old. Most of female patients are between 26 - 45 years old.

Keywords

Hemophilia, Survey, Age, Sex

1. Introduction

Hemophilia, an X-linked genetic blood disorder that affects boys and men primarily, is the most well-known [1] [2] [3] [4]. Women carry the gene and their sons develop the disease [5] [6]. Hemophilia is one of genetic disorders characterized particularly by three highs (high bleeding rate, high mortality and high morbidity). The hallmark of haemophilic bleeding manifestation is haemarthroses,

most frequently in severe disease with elbows, knees, and ankles most commonly affected. Repeated haemarthroses lead to arthropathy [3]. Nowadays, hemophilia is harmful, distributed widely and lack of effective treatment measure [7], which causes great pain, burden and economic crisis to patients and their family. In order to supply assistance treatment information of hemophilia, many researchers have studied demographic characteristics, quality of life, age, sex, etc. [8]-[13]. Patricia A. *et al.* [8] studied health information of 1243 women with hemophilia aged 18 - 25 years. C. Hermans *et al.* [9] researched the clinical management of older people with hemophilia. However, there is no report on special age and sex of people with hemophilia [8]-[16]. The present paper focuses on hemophilia patient's age and sex for providing more information for patients with hemophilia in order for more targeted treatment.

2. Materials and Methods

The method of sampling survey is used in this study. The people with hemophilia from various administrative units (hospitals and research institutes) were collected in China. The inclusion standard: the subjects who participate in the study are in accordance with the diagnostic criteria of World Federation of Hemophilia (WFH): hemophilia A (HA) and hemophilia B (HB), which are hereditary X-chromosomal recessive disorders caused by deficiency or absence of coagulation factors VIII (encoded by F8) or IX (encoded by F9), respectively [3]. The exclusion standard: the congenital genetic disease deficiency of other coagulation factors, von willebrand disease (vWF), and the disease deficiency of vitamin K are all eliminated. 1149 people with hemophilia were tested in 45 units distributed randomly the North District, the East District, the Northeast District, the Central south District, the Southwest District, and the Northwest District in China. These units were located in 20 provinces, cities, special administrative regions, and autonomous regions of China. These people with hemophilia were located in 256 cities and counties from 30 provinces, cities, special administrative regions, and autonomous regions of China. The age of the subjects ranged from 0 to 75 years old.

The database with 1149 cases is established by EpiData software [17] after finishing encoding data.

According to the United Nations age interval, the age interval is divided into juveniles (age < 18 years), youth (age $\in$ [18, 45) years), mid adults (age $\in$ [45, 59) years), and the elderly (age $\in$ [59, 75) years) (Table 1).

3. Results

3.1. Statistical Analysis

A total of 1149 people with hemophilia have been researched, of which hemophilia A (HA) is 1000 cases, hemophilia B (HB) is 149 cases (Table 2). Most of the subjects are han nationality, is 1131 cases, which account for 85.2% of the total.

Table 3 presents most of the patients are juveniles aged 0 - 18 years old, which

Table 1. Relative frequency of patients in different age intervals.

Category	The standard	Category	The standard	Age interval (year)
		Baby		0 - 1
		Infancy		2 - 3
Juveniles		Pre-school age	Chinese children ages	4 - 6
		School age		7 - 12
	The United Nations ages	Teenagers		13 - 18
		Young adults		19 - 25
Youth		Youth	The United Nations ages	26 - 45
Mid adults		Mid adults	The United Nations ages	46 - 59
The elderly		The elderly	The United Nations ages	60 - 75

Table 2. Relative frequency of types of people with hemophilia

Type	Number of patients	Relative frequency (%)
Hemophilia A (Factor VIII)	1000	87.0
Hemophilia B (Factor IX)	149	13.0
Total	1149	100.0

Table 3. Relative frequency of patients in different age intervals.

Category	Age interval (year)	Number of patients	Relative frequency (%)
Juveniles	0 - 18	786	68.4
Youth	18 - 45	338	29.4
Adults	45 - 59	23	2.0
The elderly	60 - 75	2	0.2
Total	Total	1149	100.0

account for 68.4% of the total, followed by the youth aged 18 - 45 years old, which account for 29.4% of the total. Fewer patients are adults aged 45 - 59 and the elderly aged 60 - 75 years old. However, of 1149 people with hemophilia, 25 people are over 45 years old. It is a remarkable fact that there is more aging hemophilia population.

In order to differentiate and comprehensive the number of each age interval more obviously. It is important to subdivide age intervals according to the United Nations ages and Chinese children ages. Table 4 shows relative frequency of patients in different age intervals. The most number of patients are in 7 - 12 age intervals which are 263 numbers of patients and constitute 22.9%, followed by the patients aged 1 - 3 years are 199 numbers of patients and constitute 17.3%. The least number of patients are in 60 - 75 age intervals which are 2 numbers of patients and constitute 0.2%.

3.2. Pareto Analysis and Population Pyramid Analysis

Study the number of each age interval for male and female with Population

Table 4. Relative frequency of patients in different age intervals.

Category	Age interval (year)	Number of patients	Relative frequency (%)
Baby	0 - 1	37	3.2
Infancy	2 - 3	199	17.3
Pre-school age	4 - 6	91	7.9
School age	7 - 12	263	22.9
Teenagers	13 - 18	196	17.0
Young adults	19 - 25	171	14.9
Youth	26 - 45	167	14.5
Mid adults	46 - 59	23	2.0
The elderly	60 - 75	2	0.2
Total	Total	1149	100.0

Pyramid Analysis and Pareto Analysis [18]. Table 5 presents relative frequency of patients in different age intervals for male and female. Figure 1 shows Pareto analysis summarizing the number of the male in different age interval and Pareto analysis based on the cumulative percentages. Figure 2 shows Pareto analysis summarizing the number of the female in different age interval and Pareto analysis based on the cumulative percentages.

A total of 1149 patients are researched, of the 1134 (98.7%) patients are male, and 15 (1.3%) patients are female. For the male, the number ranked the first (261), second (197), third (195) are 7 - 12, 2 - 3, 13 - 18 years old, which relative frequency is 23.0%, 17.4%, 17.2%. The least number is in 60 - 75 years old, which relative frequency is only 0.1% (Table 5, Figure 1). For the female, the relative frequency in 7 - 12, 2 - 3, 13 - 18 years old is only 13.3%, 13.3%, 6.7%, respectively. The most number is between 26 - 45 years old, which relative frequency is as much as 40.0%, while the least number is in 46 - 59 and 0 - 1 years old (Table 5, Figure 2).

Although from the point of single gender, the most number of female patients is in 26 - 45 years old, which relative frequency is as much as 40.0%. However, in contrast to the number of male patients, the number of female patients is extremely rare (Figure 3).
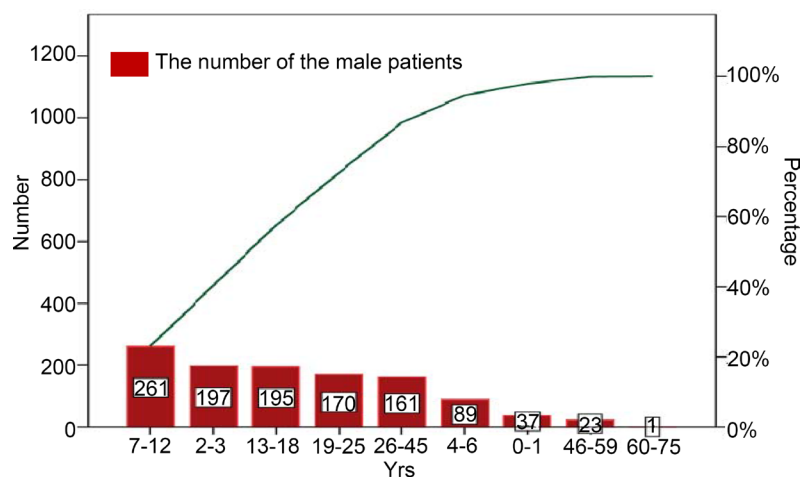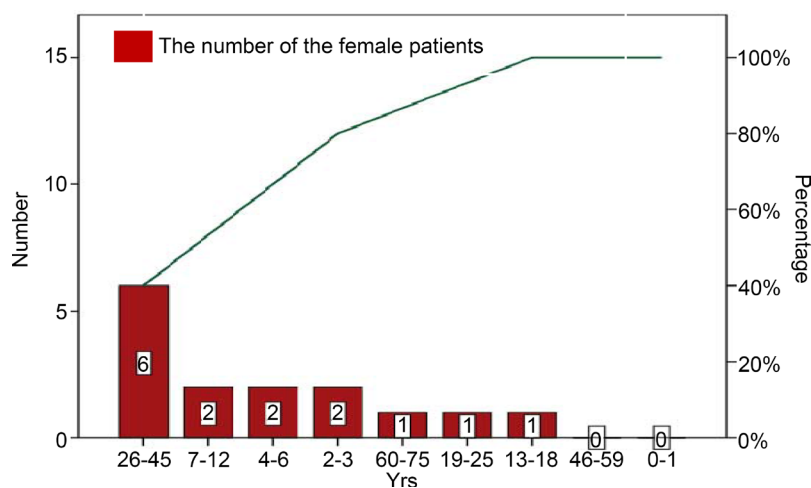
In Figure 3, red represents the number of the male with hemophilia; green represents the number of the female with hemophilia. It shows that compared with the male, the number of women can slightly displayed only in 26 - 45 years old from nine age intervals.

4. Discussion

Our results show that hemophilia A is more common than hemophilia B; the number of the male with hemophilia is far more than the female, and most of patients are juveniles aged 0 - 18 years old, which coincide with the biology characteristics of hemophilia [1] [2] [3] [4] [19]. Hemophilia is X-linked recessive disease,

Table 5. Relative frequency of patients in different age intervals for male and female.

Category	Age interval (year)	Male (N = 1134)	Female (N = 15)
		N (%)	N (%)
Baby	0 - 1	37 (3.3%)	0 (0.0%)
Infancy	2 - 3	197 (17.4%)	2 (13.3%)
Pre-school age	4 - 6	89 (7.8%)	2 (13.3%)
School age	7 - 12	261 (23.0%)	2 (13.3%)
Teenagers	13 - 18	195 (17.2%)	1 (6.7%)
Young adults	19 - 25	170 (15.0%)	1 (6.7%)
Youth	26 - 45	161 (14.2%)	6 (40.0%)
Mid adults	46 - 59	23 (2.0%)	0 (0.0%)
The elderly	60 - 75	1 (0.1%)	1 (6.7%)
Total	Total	1134 (100.0%)	15 (100.0%)

Figure 1. Pareto analysis summarizing the number of the male with hemophilia in different age intervals and Pareto analysis based on the cumulative percentages.

Figure 2. Pareto analysis summarizing the number of the female with hemophilia in different age intervals and Pareto analysis based on the cumulative percentages.
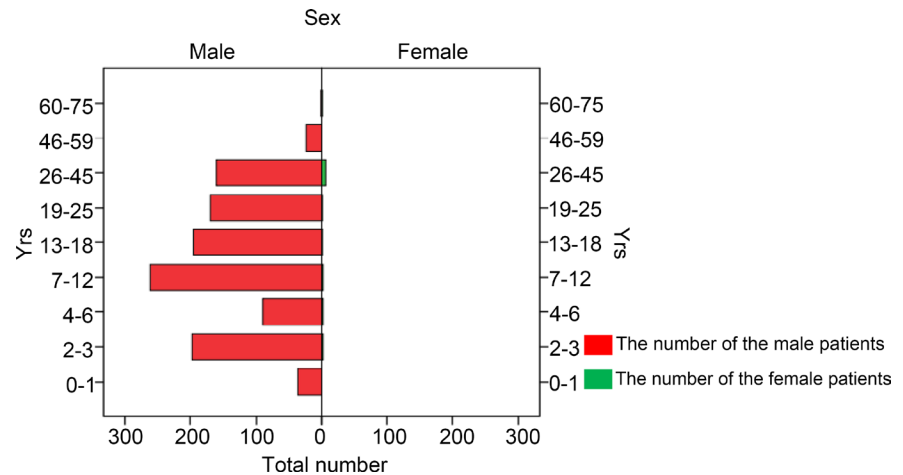
Figure 3. Population pyramid analyzes the number of patients in different age intervals.

of which disease pathogenesis is regular: if mother is a carrier, the probability of health or sick of her son will be respectively 50%. So hemophilia affects boys and men primarily, women carry the gene and their sons develop it. The causative mechanism of Hemophilia—deficiency in Factor VIII or IX—was recognized in the 1950s. The differences between haemophilias A and B are pharmacokinetics of coagulation factors, frequency of occurrence (haemophilia A > haemophilia B), proportion of patients in each level of severity, mutations that cause the disorder (more point mutations in haemophilia B than in haemophilia A), inhibitor development (more common in haemophilia A than in haemophilia B), risk of associated issues with inhibitor development (anaphylactoid reactions and nephrosis recorded in B and uncommon in A) [3].

Before modern substitution treatment was introduced at the end of the 1960s, hemophilia often resulted in severe disability at a young age and premature death [1] [2] [3]. However, in this study, there are some people with hemophilia in every age interval, such that there are 25 out of 1149 people aged over 45 years. The result at a societal level is that there are many more elderly people with hemophilia than in previous generations. It may be, life expectancy for people with hemophilia has improved and is now approaching that of the general population [9] [20] [21].

In order to facilitate and differentiate the comprehensive number of each age interval, we subdivide age intervals and find that the male with hemophilia are most around 7 - 12 and 2 - 3 years old, whereas the female with hemophilia are most around 26 - 45 years old. For male patients, most around 7 - 12 and 2 - 3 years old, coincide with the epidemiological characteristics of hemophilia [1] [2] [3] [4]. The reason for female patients, most around 26 - 45 years old may be that: on the one hand, women who carry one copy of the abnormal gene also can experience heavy bleeding symptoms and have mild hemophilia [6]. However, most of the women with a family history of hemophilia did not realize that they were at risk of bearing the gene [8]. On the other hand, most women have married at the age of 26 to 45. They have formed their own family and had children. At this time, mild symptoms resulting from hemophilia can be more severe for

women because of their associated effects on menstruation, pregnancy, child-birth [6] [10] [22] [23].

These data provide useful evidence on the trends in a measurable outcome of hemophilia. In recent years, though there is relatively small number of people with hemophilia, for meeting the challenge of the ageing hemophilia population, the management of hemophilia becomes more complex [9]. We will have come a long way to supply assistance treatment information for discovering new characteristic rules and seeking new treatment strategies [24] [25] [26]. One of the important challenging issues in the near future is registration available information for all affected individuals worldwide. Key elements of success include the enthusiasm and commitment of the Chinese professionals and patient leaders in their desire to advance hemophilia care and their commitment to work collaboratively in a coordinated manner.

Conflict of Interest Statement

None of the authors have any financial or other potential conflict of interest for this study.

Acknowledgements

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