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Epidemiological and Clinical Profile of Hemophilia Patients in Libya: A Cross-sectional Study

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Abstract:
Background: Hemophilia is a rare inherited bleeding disorder with significant public health implications. Limited epidemiological data are available on haemophilia in Libya, making evidence-based planning and care. Objective: To characterize hemophilia patients in Libya by examining their epidemiological, challenging clinical, and laboratory features, exploring correlations among demographic and clinical parameters, and providing an overview to improve care and analyze the frequency and patterns of bleeding disorders. Methods: A cross-sectional study was conducted on haemophilia patients in various regions of Libya, focusing on those registered with the Libyan Association for Hemophilia. Data were collected through structured questionnaires and laboratory records, covering demographics, haemophilia types, severity, coagulation deficiencies, antibody presence, bleeding patterns, family history, comorbidities, and treatment practices. Statistical analysis included descriptive statistics and chi-square tests, with significance set at $p < 0.05$. Results: A total of 230 patients were included. Most cases were concentrated in Tripoli (36.1%), followed by Zliten (8.3%), Benghazi (7%), and Al Khoms (5.2%). Haemophilia A was the most common type (67.8%), followed by haemophilia B (10.9%), von Willebrand disease (9.6%), and haemophilia C (3%). Factor VIII deficiency predominated (68.3%). Moderate severity was most frequent (50%), followed by severe (37%) and mild (13.5%) cases. Most patients were antibody-negative (80%). Joint bleeding was the most frequent site (36.5%). Kinship between parents was reported in 49.1% of cases, and 66.5% of participants reported relatives with haemophilia. Conclusion: This study highlights the predominance of haemophilia A and factor VIII deficiency in Libya, with a high proportion of moderate-to-severe cases. Joint bleeding remains the most frequent clinical complication, and consanguinity plays a considerable role in disease occurrence. Early diagnosis and targeted prevention strategies are needed to improve patient outcomes.

Keywords: Hemophilia, Libya, Epidemiology, Factor VIII deficiency, von Willebrand disease, Consanguinity, Joint bleeding.

الملف الوبائي والسريري لمرضى الهيموفيليا في ليبيا: دراسة مقطعية

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الملخص:
الخلفية: الهيموفيليا اضطراب نزيف وراثي نادر ذو آثار كبيرة على الصحة العامة، البيانات الوبائية المتوفرة عن الهيموفيليا في ليبيا محدودة، مما يجعل التخطيط والرعاية القائمة على الأدلة أمرًا صعبًا.
الهدف: توصيف مرضى الهيموفيليا في ليبيا من خلال فحص خصائصهم الوبائية والسريرية والمخبرية، واستكشاف الارتباطات بين المعايير الديموغرافية والسريرية، وتقديم نظرة عامة لتحسين الرعاية وتحليل وتيرة وأنماط اضطرابات النزيف.

المنهجية: أُجريت دراسة مقطعية على مرضى الهيموفيليا في مناطق مختلفة من ليبيا، مع التركيز على المسجلين في الجمعية الليبية للهيموفيليا. جُمعت البيانات من خلال استبيانات منظمة وسجلات مخبرية، شملت البيانات الديموغرافية، وأنواع الهيموفيليا، وشدتها، ونقص التخثر، ووجود الأجسام المضادة، وأنماط النزيف، والتاريخ العائلي، والأمراض المصاحبة، وممارسات العلاج. تضمن التحليل الإحصائي الإحصاء الوصفي واختبارات مربع كاي، مع قيمة دلالة إحصائية < 0.05.
النتائج: شملت الدراسة 230 مريضًا. تركزت معظم الحالات في طرابلس (36.1%)، تليها زليتن (8.3%)، وبنغازي (7%)، والخمس (5.2%). كان الهيموفيليا أ النوع الأكثر شيوعًا (67.8%)، يليه الهيموفيليا ب (10.9%)، ومرض فون ويلبراند (9.6%)، والهيموفيليا ج (3%). ساد نقص العامل الثامن (68.3%). كانت الشدة المتوسطة هي الأكثر شيوعًا (50%)، تليها الحالات الشديدة (37%) والخفيفة (13.5%). كان معظم المرضى سلبيين للأجسام المضادة (80%). كان نزيف المفاصل هو الموقع الأكثر شيوعًا (36.5%). تم الإبلاغ عن القرابة بين الوالدين في 49.1% من الحالات، وأفاد 66.5% من المشاركين بوجود أقارب مصابين بالهيموفيليا.
الخلاصة: تسلط هذه الدراسة الضوء على غلبة الهيموفيليا أ ونقص العامل الثامن في ليبيا، مع نسبة عالية من الحالات المتوسطة إلى الشديدة. لا يزال نزيف المفاصل أكثر المضاعفات السريرية شيوعًا، ويلعب زواج الأقارب دورًا هامًا في حدوث المرض. لذا، يلزم التشخيص المبكر واستراتيجيات الوقاية المُستهدفة لتحسين نتائج المرضى.

الكلمات المفتاحية: الهيموفيليا، ليبيا، علم الأوبئة، نقص العامل الثامن، داء فون ويلبراند، زواج الأقارب، نزيف المفاصل.

Introduction

Hemophilia is an X-linked inherited bleeding disorder characterized by a deficiency or dysfunction of clotting factors, leading to prolonged Bleeding episodes and large morbidity. Globally, haemophilia A (factor VIII deficiency) is the most prevalent subtype, followed by haemophilia B (factor IX deficiency) and rarer variants such as hemophilia C and von Willebrand disease [1]. In many countries, comprehensive national registries have provided valuable insights into the epidemiology, clinical characteristics, and treatment needs of haemophilia patients [2]. However, in Libya, epidemiological data are scarce, limiting the ability to develop targeted public health strategies and optimise resource allocation.

Haemophilia poses a considerable healthcare burden in developing countries, where diagnosis is often delayed and access to replacement therapy is limited [3]. Consanguinity, which is prevalent in North African populations, may increase the risk of haemophilia occurrence [4]. Moreover, complications such as joint bleeding (haemarthrosis), inhibitor development, and comorbidities including hepatitis C can significantly affect quality of life and life expectancy [5]. The inherited bleeding disorders were under-estimated in our country due to lack of awareness and patchy medical access in various areas in Libya. - Positive family history is low compared to the world. -Poor family adherence to treatment. - Decrease home-based therapy. - Most Von Willebrand disease patients' females with severe menorrhagia, make them receive frequent blood transfusion, exposing him to the risk of blood-borne infection [6].

Hemophilia is a non-contagious genetic disorder that is more common in males than in females. This condition leads to prolonged bleeding, which is often internal, and can cause swelling and pain if not treated promptly. The absence of clotting factors can result in repeated bleeding episodes in the muscles or joints. These episodes may occur spontaneously without any specific cause or may be triggered by an injury. The primary treatment for hemophilia involves injecting or infusing clotting factors directly into a vein to help the blood clot normally. If bleeding in the muscles or joints continues over time, it can lead to complications such as arthritis or joint damage, which may require surgery and can result in chronic pain.[7]. In hemophilia, the demographic data are extremely variable, with a prevalence rate worldwide of approximately 1:5000 to 10.000 males, with 85% hemophilia A, and 10% hemophilia B. [8].

This study aims to provide a comprehensive epidemiological and clinical profile of haemophilia patients in Libya, analysing distribution patterns, clinical severity, comorbidities, treatment use, and correlations between key demographic and laboratory variables.

Materials And Methods

Study Design and Setting

A descriptive cross-sectional study was conducted across multiple Libyan regions, including Tripoli, Zliten, Benghazi, and Al Khoms, as well as other provinces with smaller patient numbers.

Study Population

The study population consisted of all hemophilia patients registered with participating medical centres during the study period.

Inclusion criteria were:

Confirmed diagnosis of haemophilia (A, B, C) or von Willebrand disease,
Libyan nationality,

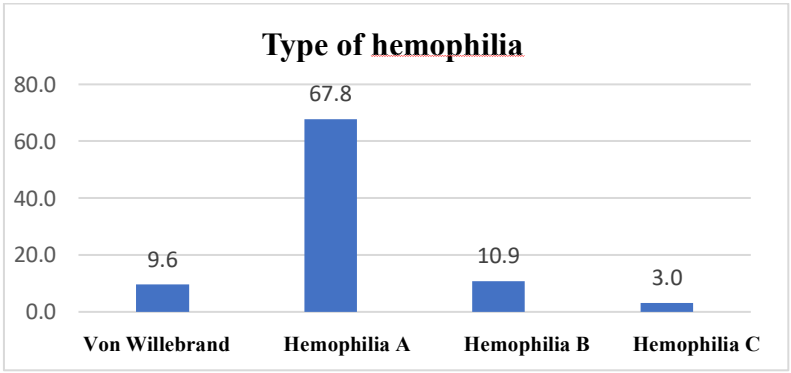
Availability of complete clinical and laboratory data.
Patients with incomplete records or uncertain diagnoses were excluded.
Data Collection: Data were obtained through structured interviews, patient medical files, and laboratory records.
Variables **collected included:** Demographic data: age, sex, region of residence, parental kinship
Clinical data: type and severity of hemophilia, bleeding patterns, comorbidities, disability, painkiller use
Laboratory data: deficient clotting factor type, antibody status, hepatitis C infection
Family history: presence of relatives with hemophilia and their relationship to the patient
Cause of hemophilia: hereditary or genetic mutation origin

Statistical Analysis
Data were entered into a statistical software package and analysed using descriptive statistics (frequencies, percentages) and inferential statistics. Chi-square tests were used to assess associations between categorical variables. Statistical significance was set at $p < 0.05$.

Ethical Considerations
The study was approved by the relevant institutional ethics committee. Informed consent was obtained from all participants or their legal guardians. Data confidentiality was maintained throughout the study.

Results
The frequency of cases of distribution in Libya
The majority of cases were concentrated in Tripoli, accounting for 36.1% of the total, followed by Zliten (8.3%), Benghazi (7%), and Al Khoms (5.2%). The remaining regions each contributed less than 5% of the total cases, indicating a marked concentration in major urban areas**.**

Frequency of the type of hemophilia
Hemophilia A was the most prevalent type, affecting 67.8% of patients, followed by hemophilia B (10.9%), von Willebrand disease (9.6%), and hemophilia C (3%).



Sex-specific analysis revealed hemophilia A in 80.4% of males compared with 19% of females. Conversely, von Willebrand disease was more frequent in females (61.9%) compared with males (4.8%).

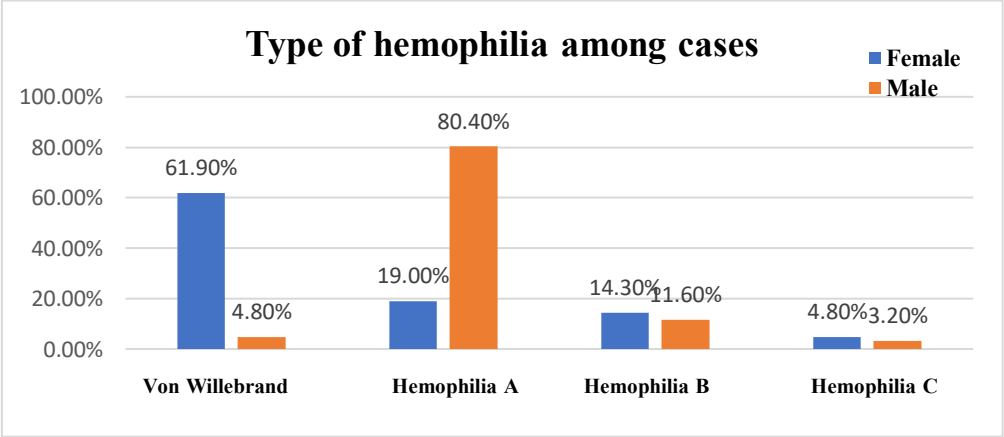


Figure 2. Distribution of hemophilia types overall and by sex.

Distribution of the type of factor

Factor VIII deficiency was the most prevalent, observed in 68.3% of cases. Other factor deficiencies each represented less than 10% of patients.

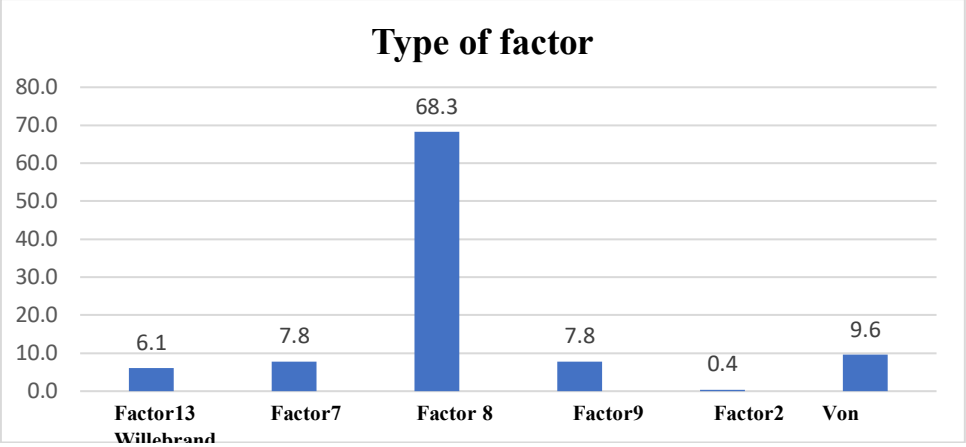


Figure 3. Frequency distribution of clotting factor deficiencies.

Distribution of the severity of hemophilia

Moderate severity accounted for 50% of cases, severe severity for 37%, and mild severity for 13.5%. Age analysis showed:

- **Mild hemophilia:** 12.1% (1–10 years), 14.4% (11–30 years), 13.0% (31–60 years)
- **Moderate hemophilia:** 37.9%, 53.4%, 56.5% respectively
- **Severe hemophilia:** 50.0%, 32.2%, 30.4% respectively

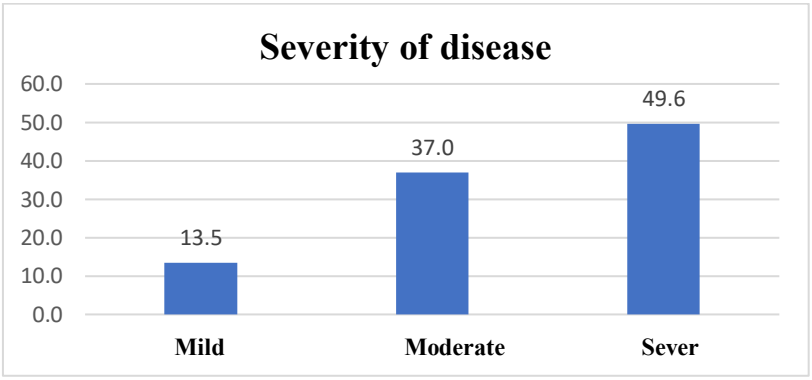


Figure 4. Severity distribution by age group.

Distribution of the presence of antibodies in hemophilia cases

Most patients (80%) were antibody-negative. Only 20% tested positive for inhibitory antibodies.

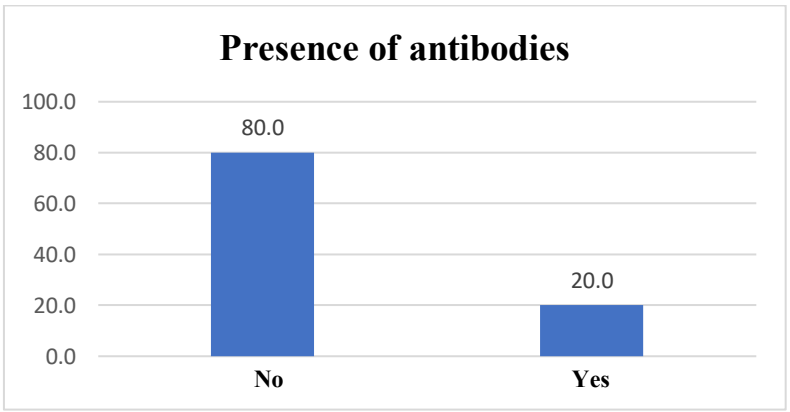


Figure 5. Proportion of antibody-positive and antibody-negative patients.

The frequency of bleeding locations among hemophilia patients

The most common bleeding site was joints (36.5%), followed by muscle bleeds (9.6%), oral bleeding (5.7%), and other sites (0.4–2.2%). Notably, 34.8% reported no recent bleeding episodes.

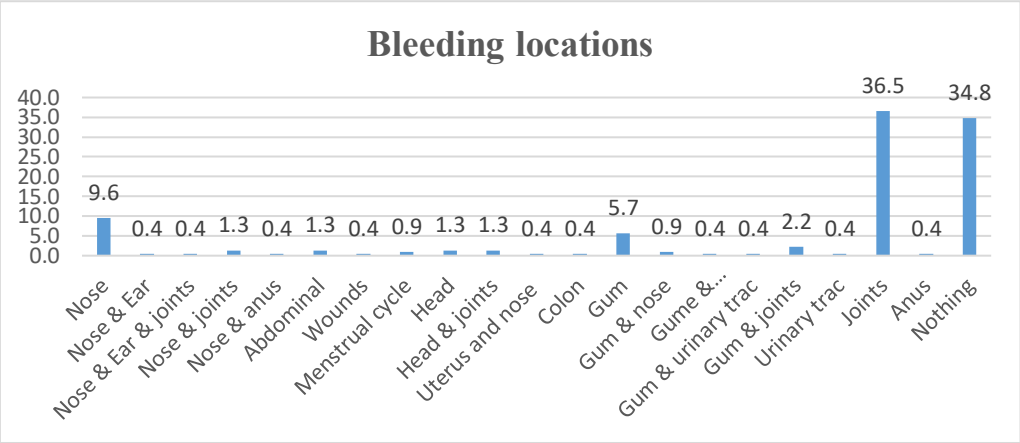


Figure 6. Frequency of bleeding locations.

The frequency of kinship relationships between parents in hemophilia cases

Parental kinship was present in 49.1% of cases, while 50.9% reported no parental relation.

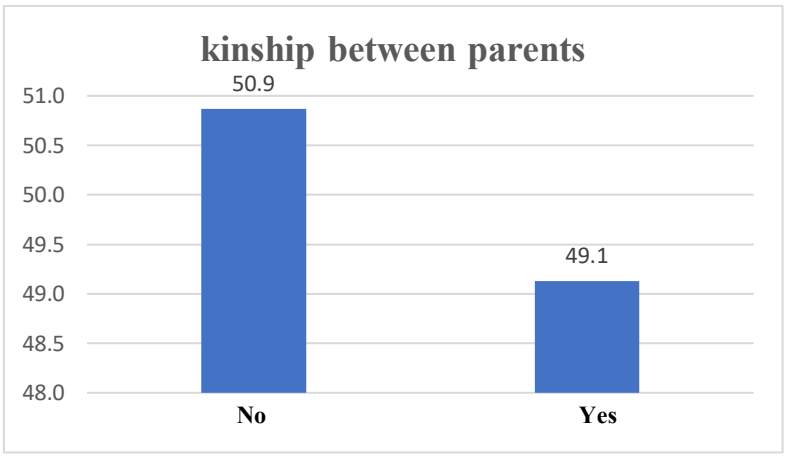


Figure 7. Proportion of cases with and without parental kinship.

Relative infection of participants

The bar chart illustrates the responses to whether relatives of the participants have hemophilia. A significant majority, 66.5%, responded (Yes), indicating they have relatives with hemophilia, while 33.5% responded (No), indicating no familial connection. This highlights a strong genetic link in the surveyed cases, as hemophilia is often inherited within families.

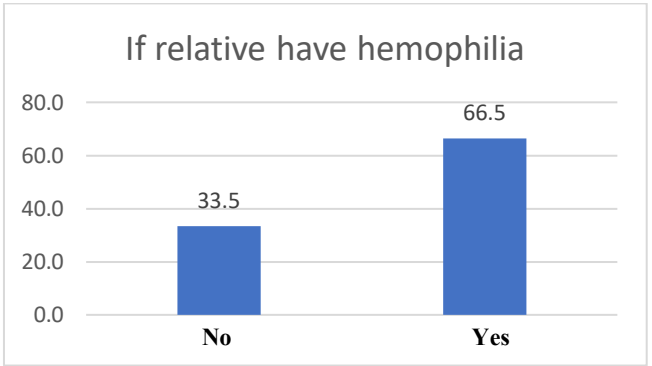


Figure 8. Relatives with hemophilia by relationship type.

The cause of hemophilia among participants

Hereditary transmission accounted for 60% of cases, while 40% resulted from genetic mutations without prior family history.

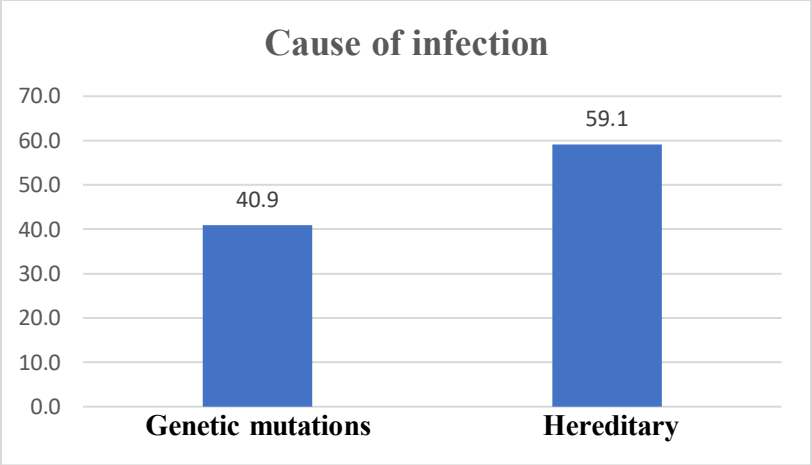


Figure 9. Causes of hemophilia.

Frequency and percentage distribution of age at diagnosis

Most cases (60%) were diagnosed at birth, 15.7% before age one, and progressively fewer thereafter.

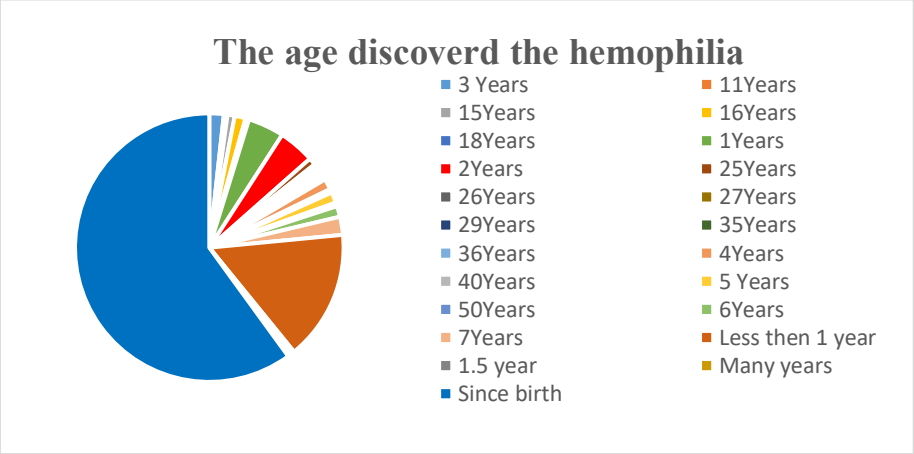


Figure 10. Age at diagnosis of hemophilia.

Chronic diseases among participants

The majority (84.3%) reported no chronic comorbidities, while 15.7% had one or more chronic diseases.

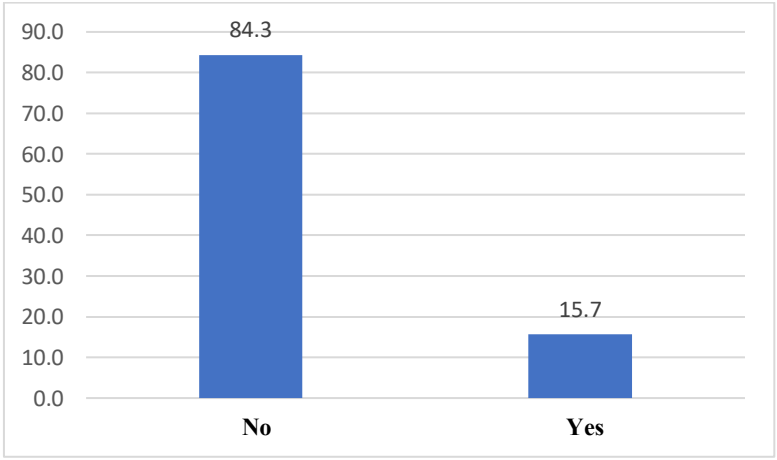


Figure 11. Presence of chronic comorbidities among participants

Disability among participants

Physical disability attributable to hemophilia was reported by 32.6% of participants, with a significant correlation between disability and recurrent bleeding ($p < 0.001$).

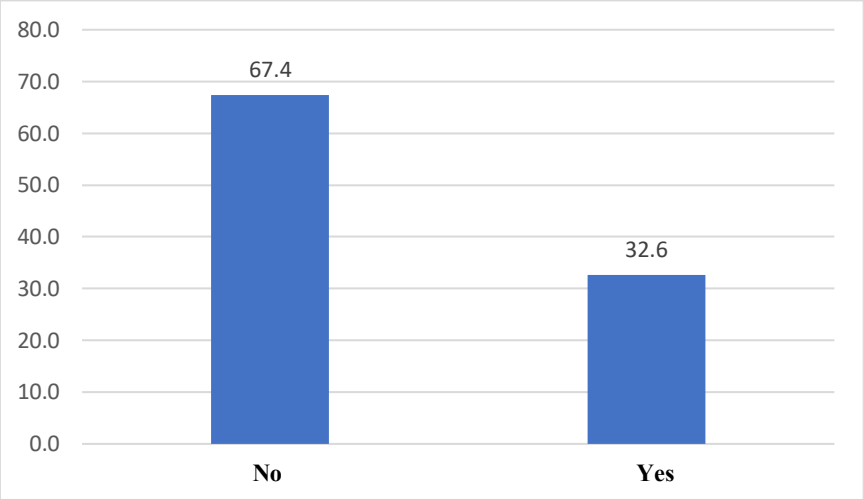


Figure 12. Disability status among hemophilia patients.

Use of painkillers among participants

Most (63%) did not use painkillers. Paracetamol was the most common medication (25.2%), with other agents (ibuprofen, Factor, morphine, tramadol, Voltaren) used rarely.

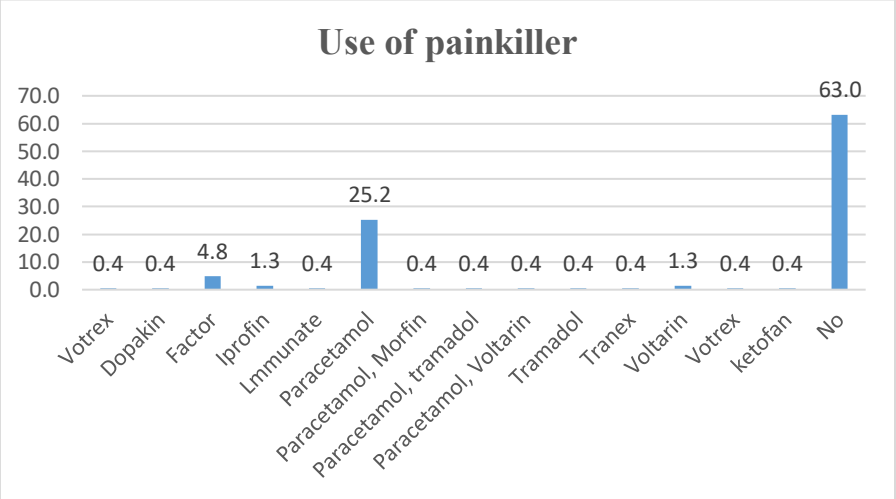


Figure 13. Types of painkillers used by hemophilia patients.

Hepatitis C infection among hemophilia participants

Hepatitis C was reported in 13.5% of patients, all of whom were male ($p = 0.041$).

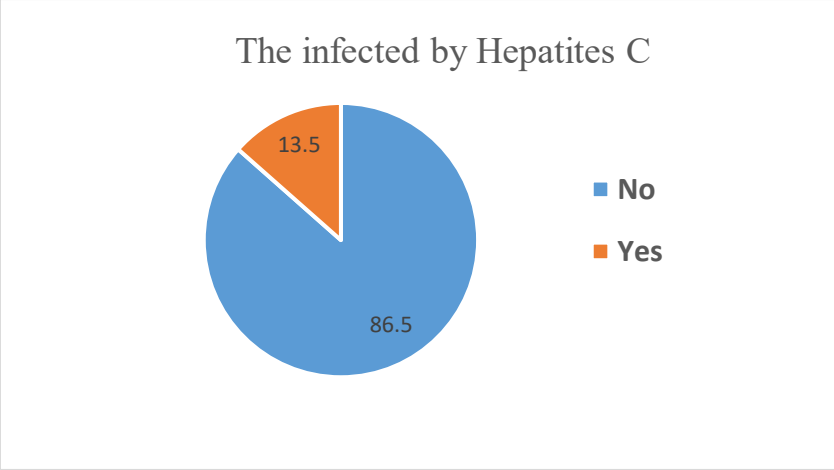


Figure 14. Prevalence of hepatitis C infection.

Correlation between sex and other variables

Significant associations were found between sex and hemophilia type ($p < 0.001$), type of factor ($p < 0.001$), hepatitis C infection ($p = 0.041$), and painkiller use ($p = 0.008$). No significant correlation was observed between sex and hemophilia severity ($p = 0.163$).

Table 1. Correlation between sex and selected variables.

Sex	Hepatitis C % from the total 100%		P value
	Yes	No	
Female	0.0	13.5	0.041*
Male	13.5	73.0	

Discussion

This study provides one of the most comprehensive epidemiological and clinical overviews of hemophilia in Libya to date. The findings highlight a predominance of hemophilia A, consistent with global trends where this subtype represents approximately 80–85% of cases [1]. The frequency of factor VIII deficiency further supports this observation and aligns with regional studies from North Africa and the Middle East [2].

Geographic distribution

The clustering of cases in Tripoli and other major urban areas may be partly due to population density and better diagnostic access in these regions. Rural and remote areas may have underdiagnosed or underreported cases, suggesting the need for nationwide screening and registry systems [3].

Type and severity distribution

According to the Indiana Hemophilia & Thrombosis Center's report, approximately 25% of individuals with hemophilia experience a mild variant of the condition, with 15% exhibiting moderate symptoms and a significant 60% enduring severe manifestations [12].

Our findings of a predominance of moderate hemophilia differ from several international reports where severe haemophilia is more common [4]. This could reflect earlier intervention or improved supportive care in some patients, or possibly regional genetic factors influencing disease expression. The strong association of severe hemophilia with younger age groups may indicate a natural progression towards milder clinical presentation with effective management, though this warrants longitudinal study.

Antibody development

The low prevalence of inhibitory antibodies (20%) is encouraging, as inhibitor formation can significantly complicate treatment [5]. However, ongoing monitoring is critical, particularly in patients with high exposure to factor replacement therapy.

Bleeding patterns
Joint bleeding was the most frequent site, consistent with hemarthrosis being the hallmark of hemophilia [9]. The relatively high proportion of patients with no recent bleeding episodes may reflect effective prophylaxis, though it may also be due to limited physical activity or recall bias in self-reported data.

Kinship and genetic predisposition
Consanguinity was reported in nearly half of the cases, consistent with cultural patterns in Libya and other Arab countries [10]. This highlights the importance of targeted genetic counselling to reduce haemophilia transmission risk in high-consanguinity populations**.**

Comorbidities and complications
The prevalence of hepatitis C (13.5%), entirely among males, is likely linked to historical use of unscreened blood products [11]. The relatively low chronic disease burden in this cohort is encouraging but should not detract from the significant disability burden (32.6%), most commonly due to joint damage.

Treatment patterns
Paracetamol use dominated pain management, reflecting adherence to recommendations avoiding NSAIDs in haemophilia due to their effect on platelet function [13]. However, the high proportion of patients not using any pain relief could suggest either good disease control or inadequate access to analgesics.

Implications for healthcare policy
These findings emphasize the need for:

- National hemophilia registry development
- Expansion of early diagnostic services
- Access to recombinant factor concentrates
- Regular inhibitor screening
- Community-based physiotherapy programmes to prevent disability

Conclusion
Hemophilia in Libya is predominantly of type A with factor VIII deficiency, with moderate severity being the most frequent clinical presentation. Joint bleeding remains the principal clinical complication, and consanguinity contributes significantly to disease occurrence. While most patients are antibody-negative and free from hepatitis C, the burden of disability is notable. Improved early detection, targeted genetic counselling, and enhanced access to prophylactic treatment are essential to improve patient quality of life and reduce complications.

Disclaimer
The article has not been previously presented or published, and is not part of a thesis project.

Conflict of Interest
There are no financial, personal, or professional conflicts of interest to declare.

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