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ORIGINAL ARTICLE

Epidemiological and Biological Profiles of Constitutional Coagulation Deficiencies at CHU Ibn Rochd Hematology Laboratory

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ABSTRACT

Background: **Rare coagulation factor deficiencies are uncommon inherited bleeding disorders that remain poorly understood in many parts of the world, including Morocco. They primarily involve factors I, II, V, VII, X, XI, and XIII, and are generally inherited in an autosomal recessive manner. This study aims to analyze the epidemiological and biological profiles of these deficiencies in a Moroccan population.**

Methods: **This is a retrospective descriptive study conducted over a ten-year period (January 2015 - May 2025) in the Hematology Laboratory of the Ibn Rochd University Hospital in Casablanca. Thirty-seven patients presenting with abnormal coagulation profiles were included. The data analyzed included the distribution by type of rare coagulation factor deficiency, gender, family history, type of bleeding syndrome, global means of prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen, as well as the range of the deficient factor levels. Laboratory analyses were performed using the Sysmex CN-3000 analyzer, and statistical processing was carried out using the Jamovi software.**

Results: **The study included 37 patients with rare coagulation factor deficiencies. Factor VII deficiency was the most frequent (40.54 %), followed by factor V (21.62 %), factor X (18.93 %), factor II (13.51 %), and factor XI (5.40 %). A female predominance was observed (62.17 %). Epistaxis was the most frequently reported clinical manifestation (24.34 %), followed by muscle hematoma (16.21 %) and hemarthrosis (10.81 %). Family investigations contributed to diagnosis in 16.22 % of cases. Factor levels varied widely depending on the type of deficiency, with several severe cases (< 1 %). Coagulation testing showed a mean PT of 30.86 %, a mean aPTT of 62.8 seconds, and a mean fibrinogen level of 3.27 g/L.**

Conclusions: **This study, the first of its kind in Morocco, highlights the need to strengthen diagnostic and management tools for these rare bleeding disorders. It also provides a solid foundation for future research, particularly at the molecular level.**

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INTRODUCTION

Blood coagulation is a complex physiological process involving a cascade of enzymatic reactions between various plasma factors. Among the coagulation disorders, rare inherited coagulation factor deficiencies represent a highly uncommon group, accounting for only 3 to 5% of all congenital bleeding disorders. These rare

deficiencies primarily affect coagulation factors I (fibrinogen), II (prothrombin), V, VII, X, XI, and XIII [1]. Most of these conditions follow an autosomal recessive inheritance pattern, with the exception of certain cases of factor XI deficiency or fibrinogen abnormalities, which may be transmitted in a dominant manner. These disorders may present in a homozygous or compound heterozygous form and have been reported in various populations worldwide. The prevalence of these deficiencies varies depending on the factor involved: approximately 1 in 500,000 for factor VII deficiency, 1 in 1,000,000 for deficiencies in factors I, V, X, and XI, and between 1 in 2 to 3 million for factor II and XIII deficiencies [1]. In North African countries such as Morocco, Algeria, and Tunisia, the true frequency of these disorders remains poorly documented due to the scarcity of epidemiological and laboratory-based studies. However, data from the 2022 report of the World Federation of Hemophilia (WFH) provide a regional overview. In Algeria, factor VII deficiency is the most frequently reported, with 499 cases, followed by factor V (84 cases), fibrinogen (64 cases), factor X (36 cases), combined factor V and VIII deficiency (31 cases), factor XI (21 cases), factor II (10 cases), and factor XIII (19 cases). In Morocco, a similar predominance of factor VII deficiency is observed (63 cases), followed by fibrinogen (16 cases), factor V (11 cases), factors II and X (6 cases each), and factor XIII (2 cases). In Tunisia, the available data report 139 cases of factor VII deficiency, 119 of factor XI, 46 of fibrinogen, 40 of factor XIII, 19 of factor V, and 16 of factor X. These findings highlight a heterogeneous distribution of rare factor deficiencies across the Maghreb region, with a clear predominance of factor VII and factor XI deficiencies [2]. The aim of our study is to analyze the biological profiles of patients with rare coagulation factor deficiencies by examining demographic characteristics, first-line coagulation tests (PT, aPTT), and specific factor assays. This study seeks to better characterize these conditions in a Moroccan population and to contribute to improving diagnosis and clinical management.

MATERIALS AND METHODS

This is a retrospective descriptive study conducted over a 10-year period, from January 2015 to May 2025, at the Hematology Laboratory of the Ibn Rochd University Hospital Center in Casablanca. The study included 37 patients who presented with abnormalities in hemostatic screening tests, specifically prolonged prothrombin time (PT) and/or activated partial thromboplastin time (aPTT), in whom an isolated deficiency of coagulation factor II, V, VII, X, or XI was subsequently confirmed. Inclusion criteria encompassed all patients with a biologically confirmed deficiency in one of the aforementioned coagulation factors. Patients with combined factor deficiencies or incomplete laboratory data were excluded from the analysis. For each case, the collected data included gender, PT, aPTT, fibrinogen level, and the activity level of the deficient coagulation factor. Venous blood samples were drawn into sodium citrate tubes in accordance with standard recommendations. Biological analyses were performed using the Sysmex CN-3000 analyzer, which enables automated evaluation of coagulation screening tests and factor assays through a clotting-time-based method. In our laboratory, the normal reference ranges are as follows: PT: 70 - 140%, aPTT: 23 - 33 seconds, Fibrinogen: 2 - 4 g/L, coagulation factors II, V, VII, X, and XI: 70 - 140%. Data were collected from the local registry of coagulation factor deficiencies and the department's Kalisil information system. Statistical analysis was carried out using the Jamovi software, version 2.2.5.

RESULTS

Epidemiological data

This study included a total of 37 patients diagnosed with rare coagulation factor deficiencies. Data analysis revealed a heterogeneous distribution of the types of deficiencies. Factor VII deficiency was the most frequent, accounting for 40.54% of cases. This was followed by deficiencies in factor V (21.62%), factor X (18.93%), factor II (13.51%), and factor XI (5.40%). The distribution of deficiencies is illustrated in Figure 1. The gender distribution revealed a female predominance, with 62.17% of patients being female and 37.83% male, yielding a male-to-female ratio of 0.60. These data are summarized in the table below. A family history investigation contributed to the diagnosis in 16.22% of patients with rare coagulation factor deficiencies. When analyzed by deficiency type, factor VII deficiency accounted for the highest number of familial investigations, with a frequency of 33.33%. This was followed by factor II, V, X, and XI deficiencies, each representing 16.67% of the familial investigations.

Clinical data

Among the patients included in our study, clinical presentations were variable, reflecting the heterogeneity of rare coagulation factor deficiencies (Figure 2). Epistaxis was the most frequently reported symptom, occurring in 9 patients (24.34%). An equal proportion (24.34%) of patients were asymptomatic, highlighting the importance of systematic screening in the context of familial investigations. Muscular hematomas were observed in 6 patients (16.21%), followed by hemarthrosis in 4 patients (10.81%), which remains a significant indicator of joint involvement. Post-dental extraction bleeding was reported in 3 patients (8.10%), while the diagnosis was established during preoperative assessment in 2 cases (5.40%). Gastrointestinal bleeding was also noted in 2 patients (5.40%). Finally, hematuria and intracranial hemorrhage were each reported in one patient (2.70%).

Table 1. Patient distribution by gender.

Gender	Number of patients	Male-to-female ratio
Female	**23**	
Male	**14**	**0:60**
Total	**37**	

Biological data

Prothrombin (Factor II): Among the five patients with factor II deficiency, four had factor II activity levels below 1%, and one patient had a level of 2%. Proaccelerin (Factor V): In the group of eight patients with factor V deficiency, factor levels ranged from 1% (in three patients) to 7.6%, with intermediate values of 2%, 3%, 4%, and 7%. Proconvertin (Factor VII): Factor VII levels among the 15 patients ranged from 2% to 53%. Specifically, four patients had a level of 2%, three had 3%, two had 6%, and two had 32%. The remaining four patients had levels of 4%, 8%, 51%, and 53%, respectively. Stuart Factor (Factor X): Among the seven patients with factor X deficiency, levels ranged from < 1% to 4%. Four patients had levels < 1%, one had 1%, one had 2%, and one had 4%. Rosenthal Factor (Factor XI): Of the two patients with factor XI deficiency, one had a level < 1%, while the other had a level of 51%. Standard coagulation tests revealed a mean prothrombin time (PT) of 30.86%, a mean activated partial thromboplastin time (aPTT) of 62.8 seconds, and a mean fibrinogen level of 3.27 g/L.

DISCUSSION

Rare coagulation factor deficiencies encompass inherited insufficiencies in key components of the coagulation cascade, including fibrinogen, prothrombin (factor II), factors V, VII, X, XI, XIII, as well as combined deficiencies of factors V and VIII and vitamin K-dependent factors. These disorders are most often inherited in an autosomal recessive manner. Their prevalence is higher in populations with a high rate of consanguineous marriages, such as in the Middle East, India, and Pakistan, due to the increased likelihood of inheriting two mutated alleles responsible for the disease. These regions are also frequently characterized by limited economic resources, which can restrict access to diagnosis and management. Because of their rarity and the lack of in-depth knowledge regarding their etiology and pathophysiology, characterizing these deficiencies remains complex [3]. The diagnosis of a constitutional coagulation factor deficiency may arise following a spontaneous or triggered bleeding episode typically prolonged bleeding after an invasive procedure or postpartum hemorrhage or be prompted by a suggestive family history. In some cases, it is identified incidentally during routine coagulation testing. These deficiencies are characterized by significant clinical heterogeneity, ranging from asymptomatic presentations to mild, moderate, or severe bleeding symptoms. This variability is especially marked in cases with intermediate factor levels (5% to 50%). In fact, there is often no clear correlation between plasma factor levels and clinical severity: some patients with levels below 5% may remain asymptomatic, while others with levels above 30% may present with bleeding symptoms. This dissociation is particularly pronounced in factor VII (FVII) and factor XI (FXI) deficiencies, where factor levels poorly predict clinical outcomes. Conversely, in fibrinogen, factor X (FX), and factor XIII (FXIII) deficiencies, there is generally a stronger correlation between factor levels and hemorrhagic severity [4]. Blood clot formation can be assessed using two essential screening tests: the prothrombin time (PT) and the activated partial thromboplastin time (aPTT). PT evaluates the extrinsic coagulation pathway, triggered by tissue factor (TF), and involves factors II, V, VII, X, and fibrinogen. It is expressed as a percentage relative to normal pooled plasma, with 140% indicating normal clotting activity (though this may vary by laboratory standards). A prolonged PT reflects impairment of this pathway and indicates a delay in clot formation. The aPTT assesses the intrinsic pathway, activated *in vitro* by platelet-poor plasma (PPP) exposed to a contact phase activator and phospholipids. This pathway involves factors II, V, VIII, IX, X, XI, XII, and fibrinogen. aPTT is expressed as a ratio compared to normal plasma. Any disruption in this pathway results in a prolonged aPTT. The combined interpretation of PT and aPTT is essential for identifying coagulation disorders. In adults, further investigation is warranted when PT is ≤ 70% or aPTT is prolonged without explanation, as these abnormalities may reflect a hemostatic imbalance associated with bleeding risk. It should be noted, however, that neither PT nor aPTT evaluates primary hemostasis, and their abnormalities are not predictive of thrombotic risk [5]. Our study represents the first investigation conducted in Morocco that characterizes the epidemiological, clinical, and biological profiles of patients with rare coagulation factor deficiencies. Although these conditions are infrequent, they remain insufficiently explored in our context, which underlines the importance of this work. In our cohort, factor VII deficiency was the most common, consistent with findings from a Spanish study [6], which also identified factor VII as the most prevalent among rare deficiencies. However, unlike our series where factor XI deficiency was the least frequent the Spanish study ranked factor XI as the second most common. This discrepancy may be attributed to several factors. First, geographic and ethnic differences between populations may influence prevalence due to distinct regional genetic backgrounds. Additionally, consanguinity rates, which vary across regions, play a key role in the transmission of autosomal recessive disorders and thus impact the distribution of specific deficiencies. In our findings, we ob-

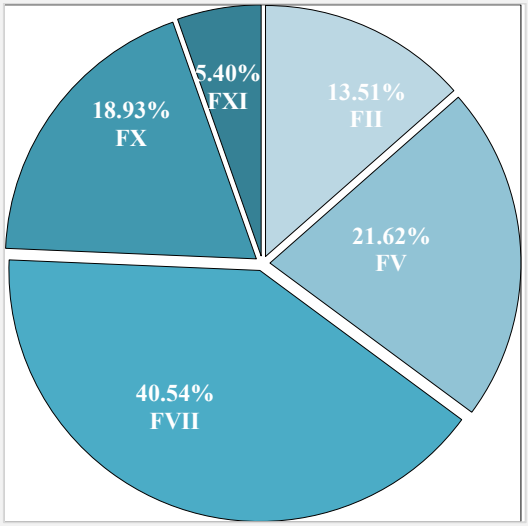

Figure 1. Distribution of rare coagulation factor deficiencies.

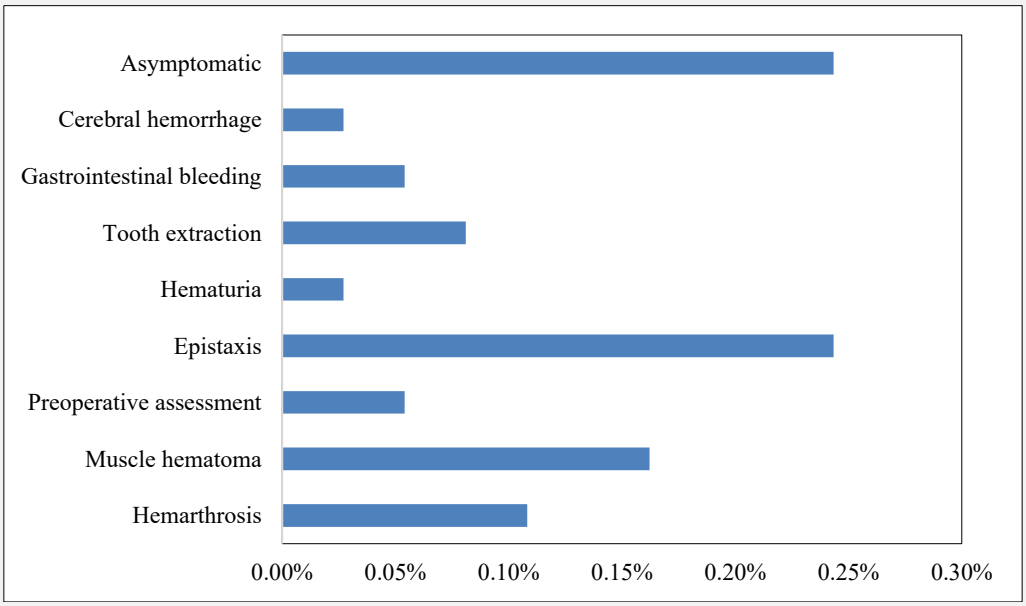

Figure 2. Distribution of hemorrhagic manifestations in the studied population.

served a female predominance, with 23 women and 14 men, corresponding to a male-to-female ratio of 0.60. These results are partially consistent with those reported in a Dutch study [7], which analyzed 1,092 patients with rare coagulation factor deficiencies and reported 427 males and 665 females, yielding a gender ratio of 0.64 again indicating a female predominance. In contrast, our data differ from those of a Saudi Arabian study [8], in which 347 males and 293 females were identified in a cohort of 640 patients, yielding a gender

ratio of 1.18 and thus a male predominance. In our series, 16.22% of patients were diagnosed through family history investigations. This rate is comparable to that reported in an Indian cohort [9], where 19% of 67 patients had a positive family history of an inherited bleeding disorder. Although slightly lower, our finding aligns with these results, reinforcing the importance of systematic collection of familial and genetic history. Among the clinical presentations, epistaxis was the most frequently reported symptom (24.34%), occurring at the same rate as asymptomatic cases. These were followed by muscular hematomas, hemarthrosis, post-dental extraction bleeding, abnormal findings during preoperative workup, gastrointestinal bleeding, and hematuria. These results are in line with those of a Turkish study [10], where epistaxis was also reported as the most common clinical manifestation. When comparing our findings to those of the study conducted at the University Hospital of Oran [11], notable differences emerge in the distribution of factor activity levels. In our cohort, a significant proportion of patients exhibited severely low factor levels, often below 10%, particularly for factors II, V, VII, and X. These differences may stem from various factors, including differences in inclusion criteria, assay sensitivity, and patient recruitment settings (hospital-based vs. familial screening). Our study found a mean PT of 30.86%, a mean aPTT of 62.8 seconds, and an average fibrinogen level of 3.27 g/L, calculated from all patients with deficiencies in factors II, V, VII, X, and XI. This approach, based on combined averages of standard hemostasis parameters, offers a comprehensive overview of coagulation status in our patient population. In the absence of directly comparable published data, it is challenging to confront our results with those of other studies. This constitutes both a methodological limitation and a unique feature of our study, which may serve as a foundation for future research adopting a similar approach.

CONCLUSION

This study, the first of its kind in Morocco, has enabled the characterization of the epidemiological, clinical, and biological profiles of rare coagulation factor deficiency conditions that remain largely underrecognized in routine clinical practice. The findings underscore the urgent need to strengthen national capacities for the screening, diagnosis, and management of these rare bleeding disorders. Moreover, they provide a valuable foundation for future, larger-scale studies that should include molecular analyses, with the aim of deepening our understanding of these rare hematological conditions and improving the patient care pathway.

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Consent for Publication:
Written consent for the publication of this report was obtained from the patients.

Declaration of Interest:
The authors declare that they have no competing interests.

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