

Concurrent Factor XI and Factor XII Deficiency with Suspected Diminished Factor XIII Activity in a Young Bangladeshi Male: A Rare Case Report

Md. Nazmul Hasan

rafimdnazmulhasan@gmail.com

Comilla Medical College, Bangladesh

Dr. Iftexhar Ahmed Sakib

Shaheed Suhrawardy Medical College

Fardin Shariar

Comilla Medical College, Bangladesh

Sanjida Islam Shuma

Mymensingh Medical College

Erfat Jahan Lubna

Mymensingh Medical College

Sudeshna Paul Tultul

Medical College for Women and Hospital

Case Report

Keywords: Combined factor deficiency, Factor XI deficiency, Factor XII deficiency, Factor XIII deficiency, Inherited coagulopathy, Prolonged activated partial thromboplastin time

Posted Date: July 7th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10056350/v1>

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Additional Declarations: No competing interests reported.

Abstract

Background

Rare coagulation disorders are inherited defects in the blood-clotting cascade. Factor XI deficiency is associated with trauma- or surgery-related bleeding, whereas Factor XII deficiency typically causes laboratory aPTT prolongation without clinical bleeding. The coexistence of both deficiencies is extremely rare and follows an autosomal recessive inheritance pattern.

Case Presentation

A 23-year-old Bangladeshi male presented with a lifelong history of prolonged bleeding following a lip laceration, first noted at 3 years of age. Initially misdiagnosed as von-Willebrand Disease in 2006, sequential coagulation factor assays ultimately confirmed FXI functional activity of 23.20%, FXII functional activity of 31.20%, and qualitatively diminished FXIII activity. The patient was ultimately diagnosed with concurrent FXI and FXII deficiency with qualitatively diminished FXIII activity. The prolonged APTT in this patient indicates intrinsic pathway involvement. Normal FVIII and FIX levels ruled out hemophilia A and B. FXI deficiency explains the bleeding manifestations, whereas FXII deficiency alone does not typically cause clinical bleeding but contributes to the abnormal coagulation profile. The addition of a diminished Factor XIII activity introduced a significant defect in clot stabilization. The coexistence of both deficiencies is extremely rare and follows an autosomal recessive inheritance pattern. For treatment purposes, Fresh Frozen Plasma (FFP) administered during bleeding episodes, with good hemostatic response.

Conclusion

This case demonstrates that persistently isolated aPTT prolongation with a mild provoked bleeding phenotype warrants systematic sequential investigation of all intrinsic pathway factors, including the frequently overlooked contact activation factors FXI and FXII. However, molecular and genetic research is needed for understanding the better pathophysiology and management criteria for such atypical bleeding disorders.

Introduction

Hereditary coagulation factor deficiencies determine a heterogeneous group of rare bleeding disorders, each resulting from quantitative or qualitative defects in particular blood coagulation proteins. Among these, Factor XI (FXI) deficiency (Hemophilia C or Rosenthal syndrome) and Factor XII (FXII) deficiency (Hageman factor deficiency), are two of the most infrequent autosomal recessive coagulopathies found in clinical practice. Their concurrent occurrence in a single patient poses an exceptionally rare diagnostic and management challenge [1].

In 1953, FXI deficiency or Rosenthal syndrome was first introduced and is estimated to affect approximately 1 in 100,000 individuals in the general population worldwide, though it is observed in up to 8% of Ashkenazi Jews owing to founder mutations [1, 2, 3]. Clinical presentation includes mild and variable bleeding phenotypes associated with bruises, epistaxis, hematuria, and postpartum hemorrhage and is usually detected during trauma or surgery-induced excessive bleeding, routine pre-surgical laboratory evaluation, or genetic screening of a proband's family members. Significantly, unlike Hemophilia A and B, FXI deficiency is an autosomal disorder affecting males and females equally which is not associated with the sex chromosomes [3].

FXII deficiency, first identified in John Hageman in 1955, represents a contrasting and paradoxical clinical phenotype. Approximately 1 in 1,000,000 individuals are diagnosed with factor XII deficiency and it is inherited in an autosomal recessive fashion, affecting men and women equally and occurring more frequently in Asians than in other ethnic groups [3, 4]. In contrast with FXI deficiency, FXII deficiency is not responsible for bleeding complications; rather, it is unexpectedly related to thromboembolic consequences, while its exact prevalence remains unknown, affected individuals are mostly asymptomatic under normal conditions. The laboratory hallmark of both deficiencies is an isolated prolonged activated partial thromboplastin time (aPTT) with a normal prothrombin time (PT), making their co-existence particularly difficult to distinguish on initial coagulation assessment [4].

The same patient having both FXI and FXII deficiency is exclusively rare. Although combined coagulation factor deficiencies have been documented, the genetic defects related to this pathology remain largely unknown. Very few cases of concurrent FXI and FXII deficiency have been reported in the literature globally [4, 5]. To our knowledge, no such case has been reported from Bangladesh, where diagnostic infrastructure for rare coagulopathies remains limited and systematic national registry data for FXI deficiency are absent.

Case Presentation

Initial Presentation (2006) at Age 3 years

We present a case of a 23-year-old Bangladeshi male, highlighting diagnostic complexity of atypical coagulopathy with its clinical implications in a limited resource setting. Initially, at approximately 3 years of age, the patient was brought to Dhaka Medical College Hospital with a 4-day history of continuous bleeding from the cut margins of the lips following minor trauma. In addition, a preceding history of prolonged bleeding from a minor injury at the age of 8 months was reported. Family history of any bleeding disorder was absent. On admission, physical examination demonstrated a source of bleeding over the upper incisor region with no other active hemorrhagic sites. Pallor was absent and temperature was normal.

Preliminary investigations (see the Table 1) disclosed a prolonged aPTT of 50 seconds (control: 28 seconds), a normal total platelet count of $350 \times 10^9/L$, bleeding time and coagulation time were 6 minutes and 13 minutes respectively. Von Willebrand Disease (VWD) was initially suspected, and the patient was referred to Dhaka Shishu Hospital, where he was admitted from 23rd to 28th November 2006 and treated with Fresh Frozen Plasma (FFP) transfusion (2 units). Factor VIII and IX activity, measured at the Armed Forces Institute of Pathology (AFIP), Dhaka Cantonment, was 70% and 110% respectively both within normal limits (reference: 60–150%), effectively excluding Haemophilia A and B [Figure 1]

Table 1
Summary of Factor VIII,Factor IX activity,Bleeding time,APTT, Coagulation time.

Parameter	Value	Normal Range	Status
Factor VIII Activity	70%	60–150%	Normal
Factor IX Activity	110%	60–150%	Normal
Bleeding Time	6 minutes	2–7 minutes	Normal
APTT	50 seconds	Control: 28 sec	Elevated
Coagulation Time	13 minutes	5–11 minutes	Prolonged

Re-evaluation at Age 12 Years (2015)

The patient re-presented to Dhaka Shishu Hospital when he was 12 years old with ongoing complaints of persistent bleeding after cut injuries, a longstanding symptom since 3 years of age (see the Table 2). Re-assessment of haematological parameters at AFIP (June 2015) demonstrated the following: [[Figure 2]:

Table 2
Summary of APTT, Prothrombin time,INR,Bleeding time, Coagulation time,Clot retraction test, Von willerband factor antigen, Haemoglobin, Total platelet count and ESR.

Parameter	Result	Reference Range	Interpretation
aPTT (Patient / Control)	54 s / 31 s	—	Prolonged
Prothrombin Time (Patient / Control)	15 s / 13 s	—	Normal
INR	1.19	—	Normal
Bleeding Time	3 minutes	2–7 min	Normal
Coagulation Time	9 minutes	5–11 min	Normal
Clot Retraction Test	70%	28–63%	Increased
Von Willebrand Factor Antigen (VWF:Ag)	102%	50–160%	Normal
Haemoglobin	11.80 g/dL	13.0–17.0 (M)	Low
Total Platelet Count	$337 \times 10^9/L$	150–410	Normal
ESR (Westergren)	18 mm/hr	0–10 (M)	Elevated

Specialist Haematology Referral and Definitive Diagnosis (2017)

At 12 years and 9 months of age, the patient was referred to Dr. Abu Jafar Mohammed Saleh, Consultant in Haematology and Stem Cell Transplant, Apollo Hospitals, Dhaka, for additional specialist opinion (Fig. 3). A consultation summary dated 16 May 2017 reported a history of prolonged bleeding from cut injuries since 3 years of age, repeated normal investigations of PT, FVIII, FIX, and VWF with persistently elevated aPTT (40–50 seconds), prior FFP management, and no family history of bleeding disorder,a factor deficiency involving FXI, FXII, or FXIII was clinically suspected, and targeted factor assays were requested.

Investigations performed on 27 July 2017 yielded the following results shown in Table 3.

Table 3 Summary of Factor XI,Factor XII,Factor XIII,Thrombin time and Fibrinogen level			
Parameter	Result	Reference Range	Interpretation
Factor XI, Functional	23.20%	70.00–120.00%	Mild–moderate deficiency
Factor XII, Functional	31.20%	70.00–120.00%	Deficiency
Factor XIII, Functional (Qualitative)	Diminished	Normal activity	Normal activity Deficiency

Clinical Summary at Current Presentation (Age 23)

The patient is now a 23-year-old male who has been monitored over nearly two decades. His bleeding history has been consistently confined to prolonged bleeding following minor trauma or mucosal injury, with no bruising, epistaxis, spontaneous haemarthroses, deep muscle haematomas, or intracranial bleeding episodes. There is no consanguinity reported in the family, and no first-degree relatives have been diagnosed with any bleeding disorder. The patient has never undergone any surgical procedure. He has been managed conservatively with FFP transfusion during bleeding periods [Figure 4].

Investigation and Intervention summary

Investigation and Intervention summary

Table 4 summarises prior bleeding episodes and procedures with corresponding treatment details.

Table 4
Summary of Clinical Findings, Diagnostic Workup and Management Timeline

Exact Date(s)	Patient Age	Event / Clinical Incident	Key Laboratory Findings	Treatments & Interventions
Nov 04, 2006 to Nov 28, 2006	3–4 Years	Major Episode 1: Continuous bleeding from cut margin of lips persisting for 4 days	Prolonged APTT: 50 sec (Control: 28s), later 40s. Normal: Platelets ($350 \times 10^9/L$), Bleeding Time (4 min), Clotting Time (10 min), Factor IX (110%), Factor VIII (70%).	Hospitalizations: 1. DMCH (Nov 4–14) 2. Dhaka Shishu Hospital (Nov 23–28) Medicines: Antibiotics, B-Complex, Oralon mouthwash.
Jun 16, 2015	12 years	Follow-up Profiling: Routine hematological testing (No active bleeding reported)	Prolonged APTT: 54 sec (Control: 31s). Prolonged PT: 15.0 sec (Control: 13.0s, INR 1.19). Normal vWF:Ag: 102% (Ref: 50–160%). Normal: BT, CT, Plt, Clot Retraction (70%).	Routine outpatient testing, no acute treatment required.
Jul 27, 2017	14 years	Follow-up Profiling: Outpatient testing at Apollo Hospitals Dhaka.	Normal Fibrinogen: 288 mg/dl (Ref: 180–350). Normal PT: 12.9 sec.	Routine outpatient testing, no acute treatment required.

Diagnosis

The patient's final diagnosis is “Combined congenital Factor XI and Factor XII deficiency with qualitatively diminished Factor XIII activity”.

Differential Diagnosis

01. von Willebrand Disease (vWD): The initial diagnosis. Ruled out in 2015 when vWF Antigen was found to be 102% (normal range).
02. Hemophilia A (Factor VIII Deficiency): Considered due to prolonged APTT, excluded with a normal Factor VIII activity of 70%.
03. Hemophilia B (Factor IX Deficiency): Eliminated as Factor IX activity was 110% (normal range).
04. Vitamin K Deficiency / Liver Disease: Excluded due to normal Prothrombin Time (PT) and INR (1.19) and a healthy clinical manifestation without jaundice or malnutrition.

Treatment :

The patient's therapeutic management focused on acute hemostasis during bleeding episodes rather than continuous prophylaxis:

01. Blood Component Therapy: Recurrent use of Fresh Frozen Plasma (FFP). Specific instances include:

- 2 units for dental bleeding at age 9.
- 2–3 units for mucosal (lip) laceration at age 3.

02. Pharmacotherapy: During hospitalizations, secondary infections were treated with antibiotics (Amoxicillin, Flucloxacillin).

Outcome and follow-up:

The patient has reached adolescence with a stable but cautious clinical status:

01. Clinical Outcome: Hemostasis was successfully accomplished in all documented acute hemorrhagic episodes using FFP. No intracranial or life-threatening hemorrhages were recorded.

02. Follow-up Instructions: The patient must avoid Intramuscular (IM) injections and physical sports to prevent hematomas.

Discussion

The prolonged aPTT reflected intrinsic pathway involvement [Figure 5]. Normal levels of FVIII and FIX in this patient effectively excluded hemophilia A and B. FXI deficiency explained the bleeding manifestations, whereas FXII deficiency which does not typically cause clinical bleeding contributed to the abnormal coagulation profile. The qualitatively diminished Factor XIII activity introduced an additional defect in clot stabilization. The coexistence of both deficiencies is extremely rare and likely inherited as an autosomal recessive disorder.

A. Diagnostic Challenge of Isolated Prolonged aPTT

Presence of an isolated prolonged aPTT in the setting of a clinically mild, trauma-associated bleeding phenotype illustrates one of the most diagnostically complex presentations in haematology. This patient presented a consistently prolonged aPTT, previously indicating von Willebrand Disease and Haemophilia A and B for nearly two decades, which were systematically eliminated through normal VWF antigen, Factor VIII, and Factor IX activity. According to Moiz et al., isolated prolonged aPTT that corrects on mixing with normal plasma should prompt assessment of Factors VIII, IX, XI, and XII and high molecular weight kininogen and prekallikrein where possible [12]. An isolated prolonged aPTT with a normal prothrombin time is the characteristic laboratory finding in both FXI and FXII deficiencies, making their co-existence particularly difficult to identify on early screening [4] and in this patient, that challenge manifested as a diagnostic delay for about two decades.

B. Clinical Significance of FXI Deficiency

The primary driving force of the bleeding phenotype is FXI deficiency at 23.20% functional activity, according to international standards, this patient is in the intermediate severity category (20–40% of normal) [7]. Approximately 1 in 100,000 individuals globally is affected by FXI deficiency, or Haemophilia C, and inherits this condition in an autosomal recessive manner, presenting variably with bruising, epistaxis, haematuria, and postpartum haemorrhage, most often detected after trauma or surgery [1, 2, 3]. Critically, bleeding severity shows minimal correlation with residual factor levels or genotype [8], and significantly reduced thrombin production can be seen in patients only with 40% residual FXI activity [9]. The absence of spontaneous haemarthroses or intracranial bleeding in this patient aligns well with the known phenotypic variability and does not diminish the aetiological centrality of FXI deficiency to his lifelong bleeding history.

C. Why FXII Deficiency is a Complicated Interpretation

The concurrent FXII deficiency at 31.20% functional activity introduced considerable challenges to both laboratory analysis and clinical risk assessment. FXII, or Hageman factor, is a single-chain glycoprotein facilitating initiation of the internal coagulation cascade and fibrin formation [3], and its deficiency produces a markedly prolonged aPTT that is disproportionate to any clinical bleeding tendency. FXII deficiency is neither associated with clinically significant bleeding tendency, nor does it reduce likelihood of thrombosis [3], and occasional manifestations such as menorrhagia or deep vein thrombosis are considered incidental findings unrelated to the coagulation defect [10]. In vivo and in vitro studies have further established a greater role for FXII in inflammatory responses than in haemostasis [11]. In this patient, FXII deficiency did not cause any bleeding but significantly enhanced aPTT prolongation, concealing the true haemostatic contribution of FXI deficiency; overall, complicating risk categorization. Recognising this contrast between laboratory findings and clinical haemorrhagic risk is essential to ensure appropriate therapy for the medically significant deficiency.

D. Potential Contribution of FXIII Abnormality

The qualitatively diminished FXIII activity provides a pathophysiologically distinct layer to this coagulopathy. Factor XIII cross-links fibrin polymers, and its reduction results in delayed bleeding due to premature clot lysis [7]. Unlike FXI and FXII deficiency, FXIII deficiency does not prolong the aPTT or prothrombin time and therefore remains undetectable on standard coagulation screening, revealing only when an inadequately stabilised clot undergoes early fibrinolysis. This mechanism directly explains the patient's four-day persistent haemorrhage following a minor lip laceration, where initial clot formation occurred but haemostasis was not sustained due to inadequate fibrin cross-linking. The triad of FXI, FXII, and FXIII abnormalities represent a convergence of defects across the contact activation, intrinsic pathway amplification, and clot stabilisation, producing a combined haemostatic vulnerability greater than any single deficiency would predict, and reflecting a complex autosomal recessive genetic structure [4, 5]. It must be noted that FXIII

was assessed qualitatively only, and a formal quantitative assay was not performed, preventing definitive confirmation of a third concurrent congenital deficiency.

E. Importance in Resource-Limited Settings

The nearly two-decade diagnostic delay in this case reflects not only clinical complexity but the critical resource limitations of haematology services in Bangladesh and comparable low- and middle-income settings. National registry data for FXI deficiency is entirely absent in Bangladesh, and diagnostic capacity for rare coagulopathies remains markedly constrained at public referral centres [1, 4]. Targeted factor assays for FXI, FXII, and FXIII are unavailable at primary or secondary levels, requiring referral to private tertiary institutions which remain inaccessible to most of the population. The concurrent occurrence of FXI and FXII deficiency is incredibly rare globally, with only a small number of published cases [5], and to our knowledge none previously reported from Bangladesh, where the absence of a national rare bleeding disorder registry further hinders recognition and follow-up. While FFP remains the principal approved treatment for FXI deficiency during surgery or significant bleeding in resource-limited settings [6], it fails to bridge the diagnostic gap that delays counselling, activity restriction guidance, and surgical risk stratification. Greater investment in accessible coagulation factor assay capacity and targeted clinician education on rare intrinsic pathway deficiencies is urgently needed.

F. Need for Molecular Diagnostics

Comprehensive discussion of this combined deficiency requires molecular genetic analysis, which could not be conducted as a result of logistical and resource limitations, representing the most significant constraint on the conclusions of this manuscript. Whole exome sequencing or targeted gene panel analysis of the F11, F12, and F13A1/F13B loci would enable genotype–phenotype correlation and clarify further whether the three deficiencies arise from a shared genetic mechanism or independent co-inherited mutations [4, 5]. As the genetic defects underlying combined coagulation factor deficiencies remain largely unknown, and this particular combination has not been previously described in the literature, molecular insight is indispensable for assessing whether this case represents a novel combined deficiency syndrome or not [4]. Moreover, family screening of first-degree relatives was also not conducted, precluding the determination of the familial versus de novo nature of the deficiencies as well as identification of at-risk individuals. To understand the exact pathophysiology and management criteria for such atypical bleeding disorders, molecular and genetic research is necessary [7], and whole exome sequencing holds definite promise for permitting personalised, genotype-informed therapeutic strategies beyond observational FFP transfusion.

Review of Literature:

An extensive review of major biomedical databases found no previously reported cases describing the simultaneous deficiency of Factors XI, XII, and XIII in a single individual, nor were there cases documenting a qualitative deficiency of Factor XIII in combined with deficiencies of Factors XI and Factor XII. While individual or dual factor deficiencies have been documented, this presentation appears to be an extraordinarily rare form of multi-factor coagulation disorder. To our knowledge, this is the first documented case of this nature, particularly in a South Asian patient population.

Search and Selection

To identify published clinical cases of concurrent Factor XI and Factor XII deficiency mentioned in the existing literature A literature review was performed in the PubMed database. The search protocol was according to the study's keywords, which, along with the use of Boolean operators (AND, OR, NOT), helped get the most relevant results in accordance with objectives. Considering this, the search was performed using the Medical Subject Headings (MeSH) phrase: **["Factor XI Deficiency"[MeSH] AND "Factor XII Deficiency"[MeSH]], (Factor 11 deficiency) AND (Factor 12 deficiency) AND (Combined Deficiency)**

A total of 10 results were identified. Based on the relevance of the publishing journal, the presence of duplicates, full-text accessibility, and the reading of abstracts, 6 articles were available in full text after detailed screening. The remaining 4 articles were unavailable because of institutional subscription restrictions and could not be added in the final review. To maximise retrieval of relevant literature, subsidiary searches were also performed using Google Scholar, Sciondirect, ResearchGate, and reference lists of all accessible articles were directly screened for further pertinent reference.

Subsequent to application of the inclusion criteria, clinical studies involving concurrent or combined Factor XI and Factor XII deficiency, cases suggesting the diagnostic procedures performed, and cases indicating the clinical management employed all 6 attainable articles were included in the final analysis. Together with the present case, these represent a total of 7 cases summarised in Table 5.

Table 5
Review of literature

Studies	Age/Sex	APTT	FXI Activity	FXII activity	First Sign of bleeding	Diagnosis	Treatment
Ye et al. (2011) [13]	40/F	> 180 seconds	43%	0%	None; the patient had no history of spontaneous or uncontrolled bleeding	Combined deficiency of factor XII and factor XI.	No specific hematological treatment or factor replacement was administered; she successfully underwent a planned hysterectomy without excessive bleeding.
Al-Ansari et al. (2023) [5]	39/F	69 seconds	1.10%	44%	None; the patient was asymptomatic. The condition was an incidental finding due to prolonged aPTT discovered during routine screening. She had no history of bruising, petechiae, or ecchymosis.	Familial Multiple Coagulation Factor Deficiency (FMCFD) involving Factor XI and Factor XII.	No specific treatment was required. She had previously undergone an appendectomy, tonsillectomy, cholecystectomy, and three vaginal deliveries without complications, blood transfusions, or factor replacement.
Singer et al. (2005) [14]	29/F	Prolonged. (Note: The exact numerical value in seconds or a ratio is not specified in the paper).	35%	37%	None; the patient was asymptomatic. The coagulopathy was discovered incidentally during a routine pre-operative screening for a planned surgical procedure.	FXI and FXII deficiency identified as an incidental finding in the context of an underlying Williams-Beuren syndrome and caudal regression syndrome.	No specific factor replacement or hematological treatment was required for the coagulopathy. The patient underwent surgery for her underlying conditions without any bleeding complications.
Hellstern et al. (1985) [15]	12/F	106–117 seconds	0.02–0.06U/ml	0.24–0.50 U/ml	Lifelong hemorrhagic episodes, which culminated in severe bleeding following dental surgery.	Combined dys-form of homozygous Factor XI deficiency and heterozygous Factor XII deficiency	Replacement therapy and local measures, including the application of fibrin glue. The authors highlight that the most effective ongoing management requires the transfusion of sufficient amounts of fresh frozen plasma (FFP) until at least the 5th postoperative day.
Okamoto et al. (1993)						Co-inheritance of Carbohydrate-	None

Studies	Age/Sex	APTT	FXI Activity	FXII activity	First Sign of bleeding	Diagnosis	Treatment
[16]	7 year, 8 month, 10year/M 1 month, 1 year 7 months, and 4 years 5 months/F	> 100seconds > 100 seconds	44%, 35%, and 37% 29%, 45%, and 44%	< 10% < 10%	Asymptomatic Asymptomatic	Deficient Glycoprotein (CDG) syndrome and congenital homozygous Factor XII deficiency.	
Sugar et al. (1994) [17]	22/M	62 seconds (normal: 43 seconds)	49%	37%	None prior to major surgery (asymptomatic history).	Noonan's syndrome associated with mild/borderline Factor XI and Factor XII deficiencies and a moderate reduction of plasma fibrinogen (1.25\text{g/L}).	FFP, Cryoprecipitate, tranexamic acid, Carotid Ligation

Limitations

Factor XIII was assessed only qualitatively, and a formal quantitative FXIII activity assay could not be performed. Molecular genetic analysis was not performed, precluding genotype–phenotype correlation. Family screening of first-degree relatives was also not conducted, preventing assessment of the familial versus de novo nature of both deficiencies. Finally, the approximately 12-year diagnostic interval reflects the limited availability of targeted coagulation factor assessment at referral centres in Bangladesh, exhibiting a significant healthcare resource limitation relevant to this case.

Image Credit :

The coagulation pathway diagram (Fig. 5) was created de novo by the authors using Canva Software. Pathway components, directional arrows, and color-coded boxes representing normal and deficient coagulation factors were drawn and arranged manually with reference to established descriptions of the intrinsic, extrinsic, and common coagulation cascades. No previously published figures were traced, copied, or reproduced. Annotations including factor activity percentages, pathway labels, and color-coded legends were added to highlight the sites of concurrent FXI, FXII, and FXIII deficiency relevant to this case. All clinical investigation documents (Figs. 1–4) are original patient records reproduced with written informed consent. Because all artwork and documentation represent original author-generated or patient-consented material, no publisher permission was required.

Reporting Guidelines :

This manuscript was prepared in accordance with CARE (CAse REport) guidelines to ensure transparent, complete, and Standardized reporting of the case.

Conclusions

We report a rare case of concurrent congenital FXI and FXII deficiency with qualitatively diminished FXIII activity in a 23-year-old Bangladeshi male confirmed after nearly two decades of evaluation. The case emphasises that a persistently prolonged isolated aPTT with a mild provoked bleeding phenotype should prompt a thorough and stepwise evaluation of all intrinsic pathway factors, including the frequently underrecognized contact activation factors FXI and FXII. Combined factor deficiencies, though rare, must be included in the differential diagnosis, especially when a single-factor deficiency cannot fully explain the laboratory findings or clinical presentation. This report contributes to the limited world literature on concurrent FXI and FXII deficiency highlighting the necessity for greater awareness of this atypical coagulopathy among haematologists and clinicians in resource-limited settings.

Declarations

A. Ethics and Consent to Participate :

Institutional Review Board (IRB) approval is not required at our institution for the publication of a single retrospective case report.

B. Consent to publish :

Written informed consent was obtained from the patient for publication of this case report and accompanying images. The consent form was reviewed and updated to ensure consistency with the final manuscript title, and all identifying and descriptive elements correspond to the present submission. The consent form is available for review by the journal editor upon request.

C. Availability of Data and Materials :

The data and materials that support the findings of this study are available from the corresponding author upon reasonable request.

D. Competing interest :

The authors declare that they have no competing interests as defined by BMC, or other interests that might be perceived to influence the results and/or discussion reported in this paper.

E. Funding Statement :

The authors have nothing to report.

F. Author contributions :

01. Md. Nazmul Hasan: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing – original draft, writing – review and editing.

02. Dr. Iftekhar Ahmed Sakib : conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, validation, writing – original draft, writing – review and editing.

03. Fardin Shariar: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, writing – original draft, writing – review and editing.

04. Sanjida Islam Shuma: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, writing – original draft, writing – review and editing.

05. Erfat Jahan Lubna: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, writing – original draft, writing – review.

06. Sudeshna Paul Tultul: data curation, formal analysis, project administration, resources, software, writing – original draft, writing – review and editing.

G. Acknowledgments

The authors are sincerely thankful to the patient for providing written informed consent for publication of this case report and accompanying data. The authors also acknowledge the Armed Forces Institute of Pathology (AFIP), Dhaka Cantonment, Dhaka Shishu Hospital, and Apollo Hospitals Dhaka for providing the laboratory documentation and clinical records necessary for this report. The authors further show gratitude to Dr. Saki Mohammad Abdul Baki, Assistant Professor, Department of Haematology, Comilla Medical College and Hospital, Cumilla, Bangladesh, and Dr. Joydeep Chowdhury, Resident Physician, USA, for their expert review and supervision of this manuscript.

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Figures

A

TEL : 8750011 6600, 6602
6612, 6614
6622, 6626
6632, 6636
6640, 6648
6616 (Reception)

Civ : 8754600, 8754602
Fax : 88-02-8754604
E-mail : afip@bttb.net.bd
Website : http://www.bangladesharmy.mil.bd/afip.htm

DHAKA CANTONMENT, DHAKA, BANGLADESH
(RECIPIENT OF INDEPENDENCE DAY AWARD-1987)

Reference No.			
Name of the patient			
Age	03 Yrs	06 Months	Sex: M
Referred by	Dr L E Fatmi		
Nature of the specimen	Blood		
Examination required	As under		

APTT

Patient	35	Second
Control	28	Second

Factor VIII activity : 70 %
(Normal : 60-150 %)

Comments : Factor VIII activity is within normal limit

Bleeding time	: 06	Minute	2—7 Minute
Coagulation time	: 13	Minute	5—11 Minute

MBBS, MCPS (BD), FCPS (Haematology)
Lt Col
Classified Specialist in Pathology
Dept. of Haematology
AFIP, Dhaka Cantt.

MBBS (Dhaka) MCPS, FCPS (BD)
Classified Specialist in Pathology
Commandant

B

TEL : 8750011 6600, 6602
6612, 6614
6622, 6626
6632, 6636
6640, 6648
6616 (Reception)

Civ : 8754600, 8754602
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DHAKA CANTONMENT, DHAKA, BANGLADESH
(RECIPIENT OF INDEPENDENCE DAY AWARD-1987)

Reference No.			
Name of the patient			
Age	03 Yrs	- Months	Sex: M
Referred by	DMCH		
Nature of the specimen	Blood		
Examination required	As under		

APTT

Patient	50	Second
Control	28	Second

Factor IX activity : 110 %
(Normal : 60-150 %)

Comments : Factor IX activities is within normal limit.

MBBS, MCPS (BD), FCPS (Haematology)
Classified Specialist in Pathology
Department of Haematology
For Commandant

MBBS (Dhaka) MCPS, FCPS (BD)
Classified Specialist in Pathology
Commandant

* NB : This institute remains open round the clock including holidays. *

Figure 1

Coagulation factor assay results. **(A)** Activated partial thromboplastin time (APTT) assay showing a patient value of 35 seconds (control: 28 seconds) with Factor VIII activity of 70% (reference range: 60–150%), interpreted as within normal limits. Bleeding time was 6 minutes (reference range: 2–7 minutes) and coagulation time was 13 minutes (reference range: 5–11 minutes). **(B)** Activated partial thromboplastin time (APTT) assay showing a patient value of 50 seconds (control: 28 seconds) with Factor IX activity of 110% (reference range: 60–150%), interpreted as within normal limits.

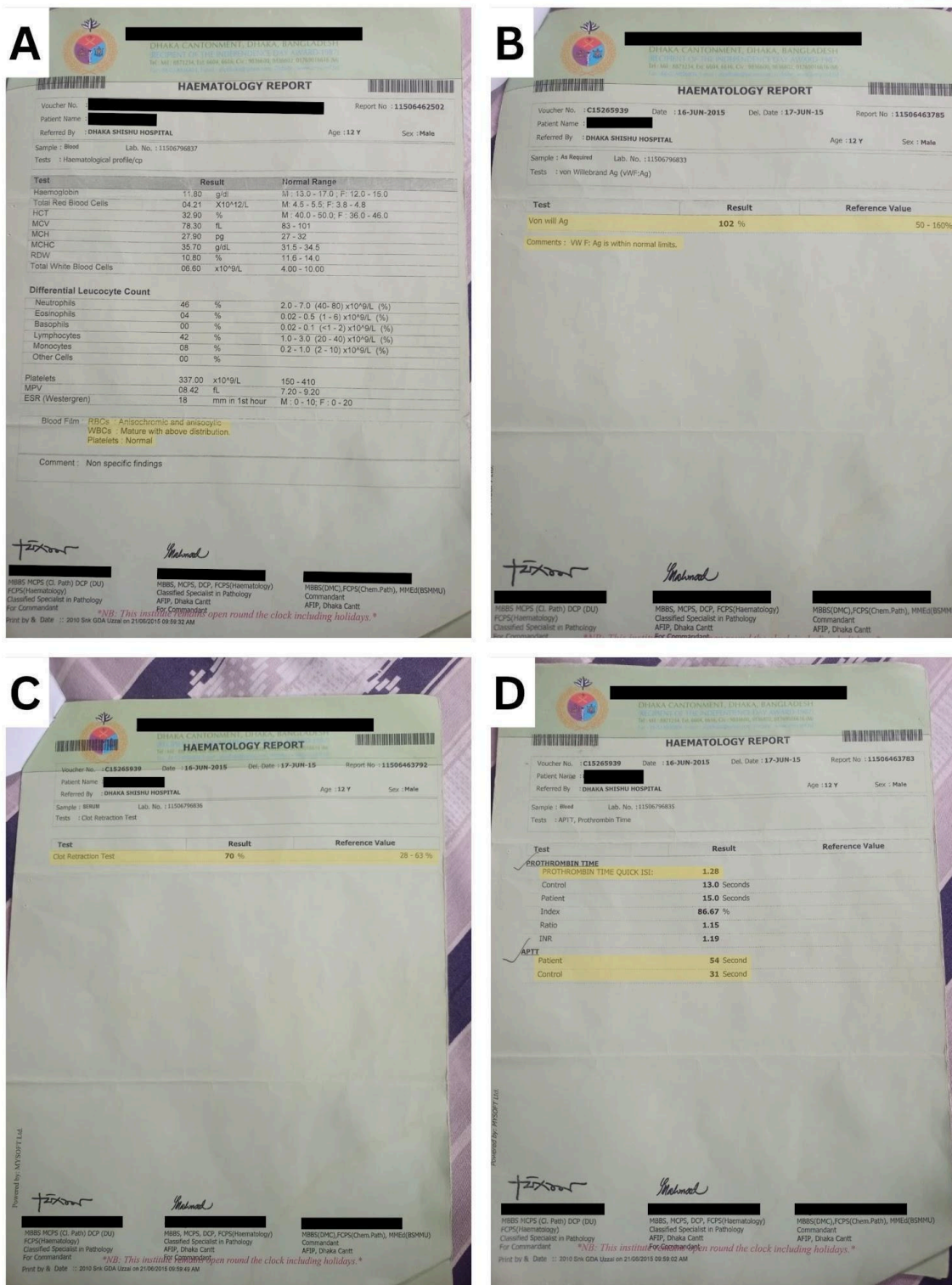


Figure 2

Blood film showed anisochromic and anisocytic red blood cells with mature white blood cells and normal platelets, reported as non-specific findings. The persistently prolonged aPTT with a normal PT, normal VWF antigen, and normal bleeding time effectively excluded Von Willebrand Disease. Factor VIII activity (70%) and Factor IX activity (110%) were within normal limits, ruling out Haemophilia A and B respectively. No inhibitor was identified in mixing studies.

A

INVESTIGATION REPORT

Lab Id. : [REDACTED] Receipt No. : [REDACTED]
 Name : [REDACTED] UHID No. : BD1/886297
 Referred by : [REDACTED] Age / Sex : 12 Yrs / Male
 Clinical Note : [REDACTED] Sample Date : 24/07/2017
 Result Date : 24/07/2017

HAEMATOLOGY

Test Name	Result	units	Reference range
FACTOR XI, FUNCTIONAL (Photo optical clot detection)	23.20	%	70.00-120.00

Interpretation
 Parameter: Factor XI activity in %
 Result: Severe deficiency <20, Mild deficiency 20-70

Note
 1. Results should be clinically correlated
 2. Test conducted on citrated plasma

Comments
 Factor XI / plasma thromboplastin antecedent deficiency is commonly seen in Ashkenazi Jews with a frequency of 8% in heterozygotes. These patients have spontaneous hemorrhages and bleeding following injury or surgery. Women experience menorrhagia and post partum hemorrhage. The development of inhibitors is rarely seen in patients with factor XI deficiency. It is the most common of the rare bleeding disorders and the second most common bleeding disorder affecting women after von Willebrand disease.

B

INVESTIGATION REPORT

Id. : [REDACTED] Receipt No. : [REDACTED]
 Name : [REDACTED] UHID No. : [REDACTED]
 Referred by : [REDACTED] Age / Sex : [REDACTED]
 Clinical Note : [REDACTED] Sample Date : [REDACTED]
 Result Date : [REDACTED]

HAEMATOLOGY

Test Name	Result	units	Reference range
FACTOR XII, FUNCTIONAL (Photo optical clot detection)	31.20	%	70.00-120.00

Note
 1. Results should be clinically correlated
 2. Test conducted on citrated plasma

Comments
 Factor XI / Hageman factor deficiency is most common, occurring in all racial & ethnic backgrounds. It is associated with prolonged APTT without risk of bleeding. It is important to recognize deficiency of factor XII in all cases with prolonged APTT to prevent unnecessary transfusion. Deficiency of Factor XII may be associated with increased risk of thrombosis.

Decreased levels
 * Inherited deficiency
 * Acquired due to liver disease, vitamin K deficiency or anticoagulant therapy.

C

INVESTIGATION REPORT

Id. : [REDACTED] Receipt No. : [REDACTED]
 Name : [REDACTED] UHID No. : [REDACTED]
 Referred by : [REDACTED] Age / Sex : [REDACTED]
 Clinical Note : [REDACTED] Sample Date : [REDACTED]
 Result Date : [REDACTED]

HAEMATOLOGY

Test Name	Result	units	Reference range
FACTOR XIII, FUNCTIONAL QUALITATIVE (clot dissolution with 5M Urea)	Factor XIII Activity Diminished		

Note
 1. Results should be clinically correlated
 2. Test conducted on citrated plasma

Comments
 Factor XIII / Fibrin stabilizing factor deficiency is suspected in individuals with a positive bleeding history, but normal PT & PTT. If prophylactic therapy has not been initiated, 30% of severely deficient patients die of spontaneous intra cranial hemorrhage in middle age. Factor VIII deficiency usually results in bleeding from umbilical stump & miscarriages.

Decreased levels
 * Inherited deficiency
 * Acquired due to Acute Myeloid Leukemia, Liver disease, association with hypofibrinogenemia in Obstetric complications & presence of circulating inhibitors.

D

CONSULTATION SUMMARY

UHID : BD1/886297 Patient Name : [REDACTED]
 Age / Sex : 12 Y- 11 M- 26 D/M Consultant : [REDACTED]
 Visit No : 2 Visit Date : [REDACTED]
 Blood Group : [REDACTED] Referred By : [REDACTED]
 Telephone : [REDACTED]
 Address : [REDACTED]

PATIENT HISTORY:

PRESENTING COMPLAINTS:

Remarks : S/O prolonged bleeding from cut injury since 3 years of age. Repeated testing of PT/APTT/FVIII, FIX/VWF - all normal except prolonged APTT (40 to 50 seconds). So far managed with FFP transfusion. Came for further opinion. No family HISTORY of bleeding disorder. 27/7/2017: C/C: pain both LIs. **FACTOR XI - 23.20%, FACTOR XIII : Diminished, FACTOR XII - 31.20%**
Impression : likely FXI deficiency

PHYSICAL EXAMINATION:

VITAL SIGN:
 Date : 27/07/2017 10:01 AM
 BP : 110/60
 PULSE : 92
 TEMPERATURE : 98
 RESPIRATION : 20
 HEIGHT : 157
 WEIGHT : 49.5

MANAGEMENT PLAN:
 Instruction : 1. Medicine as advised. 2. Follow up with reports.

E

INVESTIGATION REPORT

Id. : [REDACTED] Receipt No. : [REDACTED]
 Name : [REDACTED] UHID No. : [REDACTED]
 Referred by : [REDACTED] Age / Sex : [REDACTED]
 Clinical Note : [REDACTED] Sample Date : [REDACTED]
 Result Date : [REDACTED]

HAEMATOLOGY

Test Name	Result	units	Reference range
FACTOR XIII, FUNCTIONAL QUALITATIVE (clot dissolution with 5M Urea)	Factor XIII Activity Diminished		

Note
 1. Results should be clinically correlated
 2. Test conducted on citrated plasma

Comments
 Factor XIII / Fibrin stabilizing factor deficiency is suspected in individuals with a positive bleeding history, but normal PT & PTT. If prophylactic therapy has not been initiated, 30% of severely deficient patients die of spontaneous intra cranial hemorrhage in middle age. Factor VIII deficiency usually results in bleeding from umbilical stump & miscarriages.

Decreased levels
 * Inherited deficiency
 * Acquired due to Acute Myeloid Leukemia, Liver disease, association with hypofibrinogenemia in Obstetric complications & presence of circulating inhibitors.

Figure 3

The consultant's impression, documented in the follow-up consultation summary of 27 July 2017, recorded: "Factor XI 23.20%; Factor XIII: Diminished; Factor XII 31.20%" shows in A,B,C,D respectively.

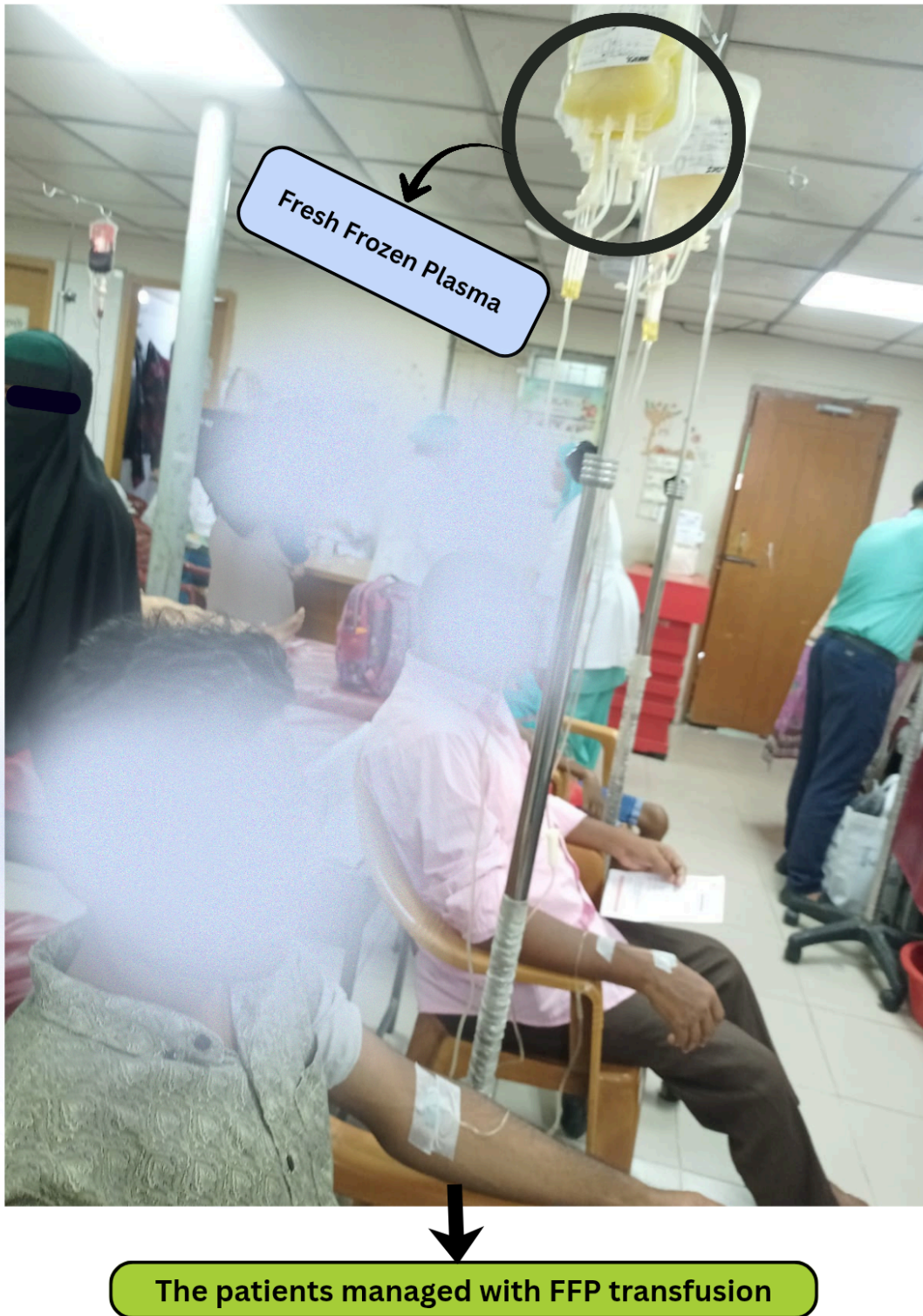


Figure 4

Patient has been taken Fresh Frozen Plasma (FFP)

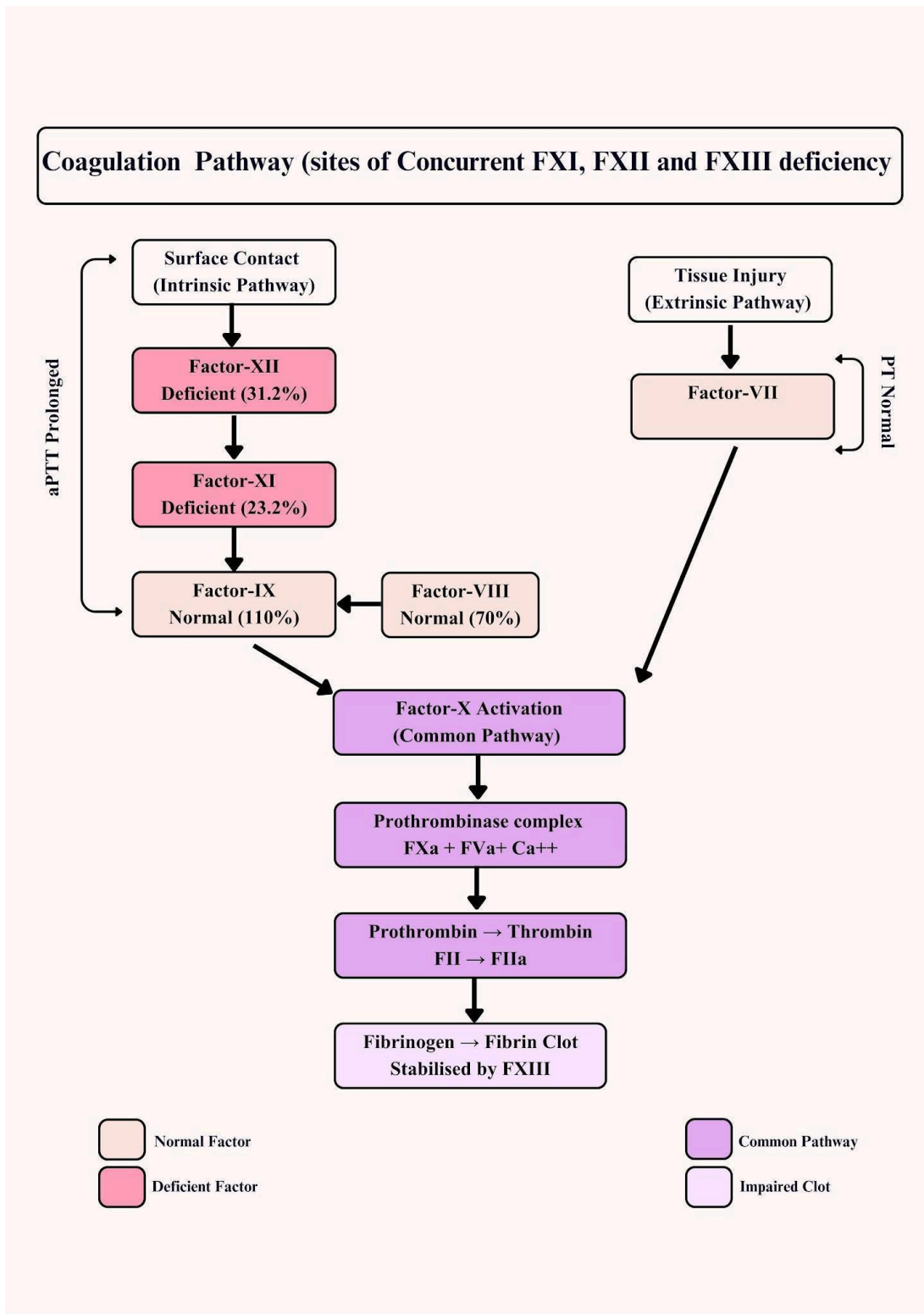


Figure 5

Coagulation pathway (Intrinsic and Extrinsic)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [2.SupplementaryMaterials.docx](#)

- [CAREChecklist2.docx](#)