University Journal of Pre and Para Clinical Sciences

ISSN 2455– 2879 Volume 2 Issue 6 2016

ANALYSIS OF APPROACH TO THE INTERPRETATION OF SCREENING TESTS OF THE COAGULATION SYSTEM

YOGALAKSHMI SENGODAGOUNDER
Department of Pathology,
COIMBATORE MEDICAL COLLEGE

Abstract :
To analyse the approach to a patient with bleeding disorder.To document the utility of screening tests such as bleeding time, platelet count, PT, APTT in patients with acquired and congenital bleeding disorder.To improvise the system of factor assay in individual cases. MATERIALS AND METHODSThis study was carried out in clinical pathology laboratory, department of pathology, Coimbatore. A total of 100 cases from all age groups of both genders with various bleeding disorders were selected and investigations carried out by standard procedures. In each case a detailed history including age ,sex, occupation, personal and family history were taken.RESULTSAmong 100 cases studied 82 were due to acquired bleeding disorder, In remaining 18 cases 8 were due to congenital bleeding disorder and 10 cases of unknown etiology with abnormal coagulation profile which may be due to other factor deficiency.
Keyword :APPROACH TO COAGULATION SYSTEM SCREENING TESTS INTERPRETATION

ANALYSIS OF APPROACH TO THE INTERPRETATION OF SCREENING TESTS OF THE COAGULATION SYSTEM

ABSTRACT:
OBJECTIVE: To analyse the approach to a patient with bleeding disorder.To document the utility of screening tests such as bleeding time, platelet count, PT, APTT in patients with acquired and congenital bleeding disorder.To improvise the system of factor assay in individual cases. MATERIALS AND METHODS: This study was carried out in clinical pathology laboratory, department of pathology, Coimbatore. A total of 100 cases from all age groups of both genders with various bleeding disorders were selected and investigations carried out by standard procedures. In each case a detailed history including age ,sex, occupation, personal and family history were taken.RESULTS:Among 100 cases studied 82 were due to acquired bleeding disorder, In remaining 18 cases 8 were due to congenital bleeding disorder

and 10 cases of unknown etiology with abnormal coagulation profile which may be due to other factor deficiency.

INTRODUCTION:

It is important to go in stepwise approach to diagnose spectrum of bleeding disorders,so that minimum tests are undertaken to make a definitive diagnosis and to avoid unnecessary laboratory tests. Depending on the abnormalities observed in short screening ,extended screening tests can be performed followed by specialized diagnostic testCoagulation profiles are useful in bleeding disorders(acquired,hereditary),therapy related coagulopathies, acquired thrombophilia/hypercoagulable states and hereditary thrombophilia/hypercoagulopathies. In diagnosis of hemostatic disorders,it is important to have relevant clinical information before interpreting the results.Hereditary disorders start early in life,recurrent in nature and may have positive family history. Acquired disorders occur at any age, have an underlying predisposing cause. History of medications should be noted.

MATERIALS AND METHODS:

This study was carried out in clinical pathology laboratory, department of pathology,Coimbatore.A total of 100 cases from all age groups of both genders with various bleeding disorders from january 2011 to june 2011 were selected and investigations carried out by standard procedures.In each case a detailed history including age,sex,personal and family history were taken.

Inclusion criteria:

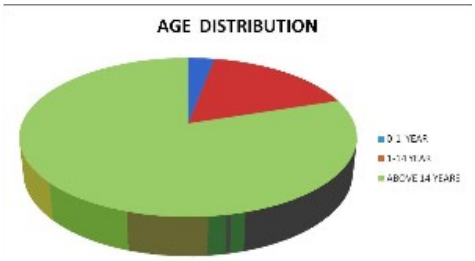
Clinical presentations of bleeding disorders like sspetechiae,ecchymosis,bleeding from oral,nasal,gastrointestinal,genitourinary tract,hemarthrosis , spontaneous soft tissue intramuscular hemorrhage and sudden bleeding from multiple sites.H/O of anticoagulants administration.

laboratory investigations

1.Bleeding time 2.Prothrombin time and controls 3.Activated partial thromboplastin time and controls 4.Platelet count

OBSERVATION:

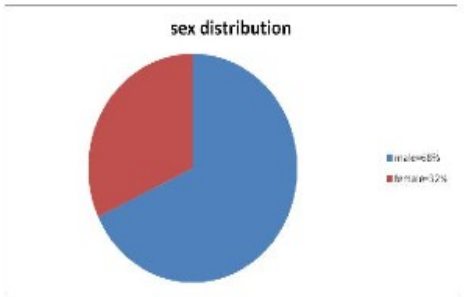
Age distribution *of patients -among 100 cases 3 cases are infants ,17 cases belong to 1-14 years and 80 cases belong to >14years.*



Age Distribution

Sex distribution

Among 100 cases 68 cases were males and 32 cases were females.



Sex Distribution

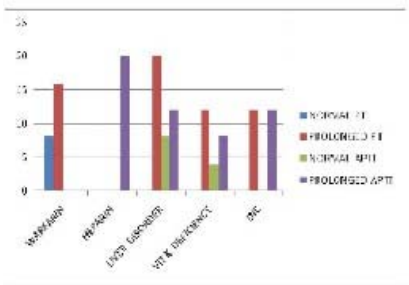
Short Screening Test[1]

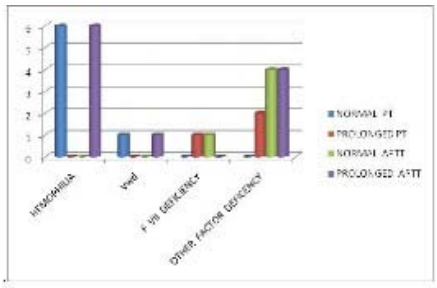
Screening Test	Normal	Defective
Platelet count (PC)	150-450/cumm	•increase/decrease.
Bleeding time (BT)	205'	• Platelet function • Vascular function
Prothrombin time (PT)	12-14s	• Extrinsic pathway • (FVII def.) • Common Path. (FX, V, II, I def.
Activated Partial Thromboplastin time (APTT)	35-45s	• Intrinsic • Common path (FX, V, II, I def)

Clinical findings-

The frequency of clinical findings in 100 cases is given

Diseases	No of cases
Hematomas	7
Ecchymosis	12
Purpura	8
Jaundice	20
Cardiac patients on anticoagulants	22
H/O cerebrovascular disorders on anticoagulant	16
H/O pregnancy with thrombosis on anticoagulant	6
Bleeding from nasal,GIT tract	9





Acquired bleeding disorders **Hereditary bleeding disorders**

Fig (2). Acquired bleeding disorders. X-axis showing number of cases & Y -axis showing normal & prolonged PT & APTT in various disorders.

Laboratory investigations

CLINICAL DIAGNOSIS	NO OF CASES	PT		APTT		BLEEDING TIME		PLATELET COUNT	
		normal	prolonged	normal	prolonged	normal	prolonged	normal	Decreased
HEPARIN THERAPY	20	-	-	-	20	18	2	16	2
WARFARIN THERAPY	24	8	16	-	-	24	-	24	-
LIVER DISEASES	20	-	20	8	12	20	-	14	6
VIT K DEFICIENCY	12	-	12	4	8	12	-	12	-
DIC	12	-	12	-	12	-	12	-	12
HEMOPHILIA	6	6	-	-	6	6	-	6	-
vWD	1	1	-	-	1	-	1	1	-
F VII DEFICIENCY	1	-	1	1	-	1	-	1	-
OTHER FACTOR DEFICIENCY	10	-	2	4	4	10	-	10	-

Fig (3). Hereditary bleeding disorders. X-axis showing number of cases & Y -axis showing normal & prolonged PT & APTT in various bleeding disorders.

Discussion Abnormal PT and PTT – causes[2]

Prolonged PT alone observed in F VII deficiency,warfarin ingestion,liver dysfunction,vit K deficiency,DIC, lupus anticoagulant.Prolonged APTT alone observed in heparin,FXII,FXI,FIX,VIII,X,V,II deficiency,lupus anticoagulant,specific inhibitor (FVIIIinhibitors),warfarin,liver dysfunction,DIC. PT,APTT both prolonged in deficiency of common pathway factors fibrinogen,prothrombin,F VorF X , or multiple factor deficiencies.

Disorders with normal screening tests

Mild clotting factor deficiency/Mild Platelet functional defects[3]

Simple purpura

Senile purpura

Henoch schonlein purpura

Scurvy

Hereditary hemorrhagic telengiectasia
Mild Von Willebrands Disease

Most common hereditary bleeding disorder, affecting 1-2% [4]of population. It prolongs bleeding time, APTT.In our study 1 case with vWD disease shows prolonged bleeding time and APTT. **Hemophilia** Hemophilia is an X-linked inherited bleeding disorder transmitted from female carriers to their male children. Laboratory findings include a markedly prolonged PTT (>100 seconds)[5] and a decreased factor VIII or IX activity. Other screening tests (PT, platelet count and bleeding time) should be normal. In our study 6 cases of hemoplilia showed prolonged APTT. VII Factor deficiency-one case showed prolonged PT with normal APTT,Bleeding time . 6 cases showed abnormal and 4 cases showed normal coagulation profile with bleeding manifestations without any clinical disorders.they may be due to other factor deficiency.normal profile maybe due to mild deficiency.

Used to determine if etiology of prolonged PT or PTT is due to a factor deficiency or an inhibitor[8] .Laboratory should be notified of presence of therapeutic anticoagulant.

Prolonged PTT becomes normal after mixing study and stays normal after 2 hours: indicates factor deficiency; perform assays for factors VIII, IX, XI and XII; if PT also prolonged, consider assays for common pathway factors

Prolonged PTT remains prolonged after mixing study: indicates inhibitor; most common is lupus anticoagulant; also therapeutic anticoagulant; rarely due to inhibitors to factors IX, XI or XII.

Prolonged PTT becomes normal after mixing study but prolonged after 1-2 hour incubation: indicates factor VIII inhibitor, rarely factor V inhibitor **Acquired Defects of Secondary Hemostasis** WARFARINTherapeutic anticoagulant to prevent thromboembolism by impairing regeneration of active vitamin K .Therapeutic warfarin or Vitamin K deficiency cause decreased activity of these proteins, which prolongs the PT.APTT may be normal if low warfarin levels.Takes 4-5 days for complete therapeutic effect due to long half-life of factors II and X.Therapeutic effect is measured by INR - goal is often INR between 2 and 3[5].In our study 24 patients were on warfarin with 16 cases showing prolonged PT &8 cases showing normal PT.

Also called unfractionated heparin.Works by markedly enhancing activity of antithrombin, which inhibits activated factors II, IX, X, XI, XII, kallikrein .heparin is administered to raise APTT to 1.5-2 times the patients preheparin APTT.

Has more predictable anticoagulant effect than standard heparin does not substantially prolong PT and PTT.Unlike regular heparin, does not inhibit thrombin or factor I.

In our study20 cases were on heparin who showed prolonged APTT.2cases showed increased bleeding time and decreased platelet count

Venous and arterial thrombosis embolism are common medical disorders.although risk factors like atherosclerotic vascular disease,congestive heart failure,malignancy,immobility predispose patients to thrombosis,specific coagulation defects have not been identified in most patients with thromboembolism.

Liver disorders:

Prothrombin time is commonly increased in liver diseases . Factor VII has the greatest influence on the prothrombin time[6]. Fall of factor VII which has shortest half life (6 hours) has bad prognosis. As the liver function worsens, theAPTT may become abnormal, the reason being that factors IX, XI and XII and fibrin stabilizing factors are also

produced by the liver.some degree of vit K deficiency may be seen.In our study 20 cases of liver diseases , 20cases showed prolonged PT,8 cases showed normal APTT ,12 cases showed prolonged APTT.6 cases showing decreased platelet count.

VITAMIN K DEFICIENCY:

The most common circumstance in which vitamin K deficiency leads to bleeding is hemorrhagic disease of the newborn. Because of rapid fall in F VII and protein c,mild vit K deficiency may have prolonged PT, normal APTT[5].later ,as the levels of factors fall,the PTT also will become prolonged.In our study 12 cases with vit K deficiency all showed prolonged PT,4 caes showed normal APTT, 8 cases showed prolonged APTT. DISEMINATED INTRA VASCULAR COAGULATION:

In DIC petechiae, purpura, and oozing from wounds and venipuncture sites may develop. Microvascular and large vessel thrombosis may occur. The platelet count is typically decreased due to consumption and platelet destruction. The PT and PTT are prolonged from depletion of factors V, VIII, IX, and XI. Fibrinogen is decreased. Fibrin degradation products and the D-dimer assay are increased[6].In our study 12 cases with DIC all showed prolonged PT ,APTT with decreased platelet count and increased bleeding time.

Circulating inhibitors such as heparin and the lupus anticoagulant (antiphospholipid antibody) often lead to abnormalities in screening coagulation laboratory values. These cause a prolonged PTT which is not corrected with 1:1 dilution with normal plasma (the PTT mixing study). If the patient has a factor deficiency such as hemophilia, adding normal plasma to the patient's plasma, will partially correct the factor deficiency and the PTT will normalize. If the PTT does not normalize by adding normal plasma, this implies that an anticoagulant is present in the patient's plasma

Conclusion:

Among the 100 cases studied 82cases were due to acquired bleeding disorder, In remaining 18 cases 8 were due to congenital bleeding disorder and 10 cases of unknown etiology with abnormal coagulation profile which may be due to other factor deficiency.This cannot be diagnosed only using short screening tests.Hence further factor assay is required.However owing to cost factor, the factor assay analysis can be limited to certain selected factor by the application of mixing studies.

References:

1. Renu Saxena, Meganathan Kannan and Ved P Choudhry. Laboratory Studies in CoagulationDisorders *Department of Hematology, All India Institute of Medical Sciences, New Delhi, IndiaIndian J Pediatr 2007; 74 (7) : 649-655.*

2 Richard A Mcpherson,Mathew R pinkus.coagulation and fibrinolysis.Henry's clinical diagnosis and management by laboratory methods 21st edn.Elsevier 2007;38:729-746.

3.Sirridge M. Laboratory evaluation of the bleeding patient. *Clin Lab Med 1984 Jun;4(2) : 285-301*

4. Lillicrap D, Dean J, Blanchette VS. Chapter 30 - von Willebrand Disease. In: Lilleyman J, Hann I, Blanchette V (eds). Pediatric Hematology, second edition. 1999, London: Churchill Livingstone Inc., pp 601-610.

5.Desiree Medeiros, MD .Bleeding disorders. Case Based Pediatrics For Medical Students and Residents, Department of Pediatrics, University of Hawaii John A. Burns School of Medicine 2003 ;11(6).E:/ Biomedica/Biomedica Vol.22 Jan-Jun 2006/Bio-11

6 Medeiros D, Buchanan GR. Chapter 47 - Disseminated Intravascular Coagulation and Other Acquired Bleeding Disorders. In: Levin DL, Morriss FC (eds). Essentials of Pediatric Intensive Care, second edition. 1997, New York: Churchill Livingstone Inc., pp. 473-482

7 Kendall Crookston, Lizabeth Rosenbaum, Julie Gober-Wilcox et al , University of New Mexico 24 July2001, PathologyOutlines.com, Inc.