

LAB DIAGNOSIS OF BLEEDING DISORDERS

Sunil Kumar Godara

Assistant Professor, Dept. of Rognidana evam Vikriti Vigyana, National College of Ayurveda, Barwala, Hisar, Haryana, India

Email: skgodara4382@gmail.com

ABSTRACT

Blood is an integral part of life as life depends on it. All the cells, tissues and organ system depend on blood for their normal functioning. Sometimes the stores of this precious thing depleted in the body due to various pathological states of human body. The oozing out of blood from body surface or inside an organ is termed as bleeding and if it persists for a long term then it is called as bleeding disorder. Bleeding disorder is life threatening as loss of significant amount of blood definitively will put hazardous health effects. Coagulation defects are responsible majorly for bleeding disorders. Haemorrhage is another term used for bleeding also. Bleeding disorders can be diagnosed by means of laboratory test methods. Present article will help to understand bleeding disorders, their basic pathology and various laboratory tests which help to diagnose this particular state.

Keywords: Blood, Bleeding disorder, Haemorrhage, Lab diagnosis

INTRODUCTION

The meaning of bleeding is given in 2 ways

1. Emitting blood as from an injured vessel
2. The process of emitting blood as a hemorrhage or the operation of letting blood

Bleeding disorders or hemorrhagic diathesis are a group of disorders characterised by defective haemostasis with abnormal bleeding^[1]. The tendency to bleeding may be spontaneous in the form of small hemorrhages into the skin and mucus membranes (e.g. petechiae, purpura etc.) or there may be excessive or internal bleeding following trauma and surgical procedure (e.g. hematoma, haemarthrosis etc.)^[2]. Bleeding disorder is the outcome of coagulation defect. Coagulation system checks the oozing of blood and stops it by its action and thus prevents more

blood loss but various diseases are there like hereditary bleeding disorders etc. which prolongs coagulation of blood.

AIM:

Bleeding tendencies or bleeding diathesis is life threatening conditions. They should be diagnosed as early as possible. Present article is written to elaborate different Laboratory tests to diagnose bleeding disorders.

SOURCE OF DATA:

The data for the present article is collected from relevant textual sources given under Reference section

BASIC THEORY OF COAGULATION:^[3]

There are substances that cause or affect blood coagulation in the blood and in the tissues – some that promote coagulation are called procoagulants, and others that inhibit coagulation are called anticoagulants. Whether blood will coagulate depends on the balance between these two groups of substances. In the blood stream, the anti coagulants normally predominate, so that the blood does not coagulate while it is circulating in the blood vessels. But when a vessel is ruptured, procoagulants from the area of tissue damage become activated and override the anti coagulants, and then a clot does develop.

COAGULATION SYSTEM:

The coagulation system includes a mechanism of formation of clot, necessary to secure the repair of the damaged blood vessel. This is done by cascades or sequence of steps of three pathways

e.g. Intrinsic, Extrinsic and Common pathways ^[4]

Where the plasma coagulation proteins take part and there is formation of thrombin

The fibrin then

- ✓ Activates platelets and helps further hemostasis
- ✓ Forms a stable fibrin network from circulating fibrinogen
- ✓ Stimulates the coagulation inactivating mechanism, thereby limiting the process of coagulation in the vicinity of injury

COMPONENTS OF COAGULATION SYSTEM:

- The plasma protein coagulation factors, calcium, platelets, all of which are present in circulatory blood
- Certain surface which is not normally in contact with the circulating blood. E.g. damaged vessel wall, extravascular connective tissue, contact with the test tube or syringe wall
- Lipo protein derived from the injured tissue cells termed tissue factor

CLOTTING FACTORS:^[5]

1. Fibrinogen
2. Prothrombin

3. Tissue factor (thromboplastin)
4. Calcium
5. Labile factor, proaccelerin,
6. Ac- globulin
7. Stable factor, proconvertin
8. Antihæmophilic globulin (AHG), antihæmophilic factor A
9. Christmas factor, plasma thromboplastin component (PTA), antihæmophilic factor B
10. Stuart prower factor
11. Plasma thromboplastin antecedent (PTA), antihæmophilic factor C
12. Hageman factor
13. Fibrin stabilizing factor

ROOT LEVEL CAUSE OF BLEEDING DISORDERS:^[6]

A patient with hemorrhagic tendency may bleed due to the following reasons:

1. Local pathological lesion
2. Hemorrhagic disorders due to vascular abnormalities, platelet abnormalities, fibrinolytic defects
3. Disorders of coagulation factors
4. Combination of all these as occurs in disseminated intravascular coagulation (DIC)

CLINICAL PATTERNS OF BLEEDING:

Severe coagulation factor deficiency as in hemophilia tends to produce joint bleeding (haemarthrosis), intramuscular bleeds and deeper tissue bleeds, where as platelet defects or deficiencies tend to produce mucocutaneous bleeding. Von Willebrand disease where there is low levels of circulating factor 8 and platelet dysfunction due to absence of Von Willebrand factor produces a clinical picture which is a combination of platelet defect (mucocutaneous bleeding) as well as severe factor 8 deficiency.

HISTORY OF BLEEDING DISORDER IN A PATIENT WITH CAUSES:^[7]

- Congenital bleeding tendency: (x linked, autosomal, recessive or dominant inheritance disorder) H/o spontaneous bleeding, minor traumatic bleeding, bleeding during falling of deciduous

teeth, severe post operative bleeding, minor bleeding requiring transfusion

- Wound healing and blood coagulation are closely related. Congenital defects like afibrinogenaemia/ dysfibrinogenaemia and factor 12 deficiency may be associated with delayed wound healing
- Physical examination in the patient may show haemarthrosis, Ch. Sinusitis, muscle haematoma or volkman's ischaemic contracture due to compartment syndrome following a bleed, compressive neuropathy, petechiae, purpura, ecchymoses, nasal bleed, bleeding gums, bleeding from urogenital, gastrointestinal tract etc.
- Acquired cause of bleeding involves chronic diseases involving liver, kidneys, obstructive jaundice, ac. Liver failure, use of anticoagulants, antiplatelet drugs like aspirin and clopidogrel
- Haematological disorders like aplastic anaemia , ac. Leukaemias may be associated with bleeding
- Auto immune disorders and various vasculitides can cause bleeding tendency either by producing severe thrombocytopenia, inhibitors to coagulation factors, immune complexes or leucocytoclastic vasculitis or by a combination of all the causes
- Generally antiphospholipid antibodies associated with SLE can cause thrombotic tendency but occasionally it may lead to severe hypoprothrombinaemia causing severe bleeding

TESTS OF IMPORTANCE IN BLEEDING DISORDERS:^[8]

There is no single test which will evaluate the integrity of the complex haemostasis mechanism of blood. Tests used to diagnose bleeding disorders are as follows:

1. Bleeding time(Duke method)
2. Capillary fragility test (HESS test)
3. Clotting time (Lee & White method)
4. Platelet count
5. Prothrombin time
6. Activated partial thromboplastin time (APTT)
7. D- dimer

1. BLEEDING TIME:

It is the time to arrest bleeding after puncture is made on the skin surface allowing free flowing of blood

Normal Range: 2-7 minutes

Indications of increased bleeding time are as follows:

- a) Inadequate platelet activity in sealing the puncture
- b) Failure of vascular contraction
- c) Or both

Bleeding time is increased in following conditions:

- a) Severe thrombocytopenia
- b) Defective platelet functions
- c) Von Willebrand's disease
- d) Certain drugs

2. CAPILLARY FRAGILITY TEST (HESS TEST):

This test is also k/a Tourniquet test. This test is done by tying sphygmomanometer cuff to the upper arm and raising the pressure in it between diastolic and systolic for 5 minutes. After deflation the no. of petechiae appearing in the next 5 minutes in 3 cm. Square area over the cubital fossa are counted.

Interpretation of the test:

- 1) Presence of more than 20 petechiae is considered a positive test

Indications of this test are as:

- a) Increased capillary fragility
- b) Thrombocytopenia

3. CLOTTING TIME:

Time taken by blood to clot is the clotting time

Normal Range: 4-9 minutes

Causes of increased clotting time are as follows:

- a) Haemophilias, e.g. Factors 8 & 9 deficiency
- b) Significantly prolonged in severe deficiency of various factors involved in intrinsic and common pathways
- c) Prolonged when circulating anticoagulant e.g. Heparin is present in excess

4. PLATELET COUNT:

Platelet count involves the testing of the platelets quantitatively as well as qualitatively. Platelets are non nucleated round or oval, flattened disc shaped structure. Platelet activity is necessary for blood clotting, vascular integrity and vasoconstriction. Life span of a platelet is 7.5 days. 70% of all the body platelets are found in circulating blood and 30% in the spleen. Factors such as stress, epinephrine and exercise stimulate platelet production.

Normal Range: 1.5-4 lakh/cu.mm

Causes of Thrombocytosis are as follows:

- a) Polycythemia Vera
- b) Splenectomy
- c) Iron deficiency anaemia
- d) Rapid blood regeneration caused by acute blood loss
- e) Malignancies
- f) Renal failure
- g) Recovery from bone marrow suppression

Causes of Thrombocytopenia are as follows:

- a) Idiopathic thrombocytopenic purpura (ITP)
- b) Pernicious, aplastic and hemolytic anaemia
- c) Viral, bacterial infections
- d) Thrombopoietin deficiency
- e) During cancer therapy and radiation, exposure to certain chemicals like DDT
- f) Anti platelet antibody
- g) Alcohol toxicity
- h) After massive blood transfusion (dilution effect)

5. PROTHROMBINE TIME (PT):

It is the time taken to clot citrated plasma sample in presence of thromboplastin (tissue factor) and calcium ions and reflects the integrity of the extrinsic and common pathways of coagulation system

Normal range: 11-15 seconds

Causes of elevated PT are as follows:

- a) Oral anticoagulant therapy
- b) Liver diseases
- c) Haemorrhagic disease of the newborn
- d) Disseminated intravascular coagulation
- e) Congenital deficiency of coagulation factors 2, 5, 9 and 10 either singly or in combination

INR: International normalized ratio (INR) is the ratio of patient's Prothrombin time to a normal (control) sample

Normal Range: For healthy individual is 0.8-1.2 and target value for patients on anticoagulant therapy like warfarin is 2.0-3.0

Use of INR: Typically used to monitor patients on anticoagulant therapy

Test Interpretation indications: High INR – high risk of bleeding

Low INR – high risk of developing a clot

6. ACTIVATED PARTIAL THROMBOPLASTIN TIME (APTT):

The time taken by the plasma for the formation of thrombin and fibrin clot by intrinsic coagulation pathway. This test measures the intrinsic procoagulant activity of plasma

Normal Range: 35-43 seconds

Causes of prolonged APTT are as follows:

- a) Deficiency of coagulation factors 8 and 9
- b) Administration of heparin therapy
- c) Circulating anticoagulants
- d) Liver diseases
- e) DIC (Disseminated intravascular coagulation)
- f) Massive blood transfusion
- g) Antibodies to factors 8 and 9

7. D- dimer:

D-dimer is produced by the action of plasmin on cross linked fibrin and not on unclotted Fibrinogen or FDP'S (Fibrin degradation products)

Normal Range: <250 mg/ml (0.25 mg/ litre)

Conditions for increased D- dimer values are as follows:

- a) DIC (Secondary embolism, late pregnancy and postpartum)
- b) Sickle cell crisis
- c) Malignancy
- d) tPA anticoagulant therapy

TERMINOLOGIES RELATED WITH BLEEDING DISORDERS:^{19]}

1. Petechiae: bleeding spots (1-2 mm/pin head size) in the skin

2. Purpura: macular (flat and small lesions with altered texture and colour (<2cm) or papular Solid elevated area of skin (<0.5-1 cm) collection of blood in the skin (>3mm size)
3. Ecchymoses: large area of bleeding in the skin
4. Hematoma: collection of blood in the skin with elevation

DISCUSSION

Human life depends on health and health is considered with appropriate body systems in all aspects. Blood is life as it serves lot of functions in human body, but this blood should move freely inside blood vessels and it should not leak out from its territories but certain type of pathological states are there which forces this precious element to come out easily from the body surfaces. Coming out of blood from body surfaces is termed as bleeding disorders or bleeding diathesis. Bleeding diathesis is a clinical term used to denote bleeding disorders. Oozing out of blood from body surface is termed as haemorrhage. Bleeding from a body surface should be minimized properly in a normal healthy individual. Coagulation system helps to arrest the bleeding sites inside human body and thus prevents body from getting into a state of decreased blood volume. Bleeding disorders puts strain on the body system that causes bleeding from minor to major haemorrhagic states. Bleeding disorder is life threatening. Bleeding disorders can be diagnosed by various laboratory test methods and patient's life can be prevented from falling into a state of life danger. Lab diagnosis of bleeding disorders is well understood with this present article as various factors are discussed here regarding bleeding disorders and various investigations are also dealt for the diagnosis of bleeding disorders.

CONCLUSION

Bleeding is a term given to oozing out of blood from outside the blood vessel. Bleeding disorders are a result of faulty coagulation mechanism especially the cascade system. Bleeding disorders can affect the

individual minor as well as at major level. Various investigations are explained to find out the defective pattern of bleeding disorders. Bleeding disorder should be ruled out by means of different laboratory tests.

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