FIBRINOGEN LEVEL IN HEALTH AND DISEASE

S S Tsang, R S C Szeto, C S Feng

ABSTRACT

The plasma fibrinogen concentration of 47 healthy individuals was measured in order to determine the reference range for our laboratory, which was calculated to be 1.75 - 3.31 g/l.

The plasma fibrinogen concentration of 44 hospital patients was also measured for comparison. These patients were selected because they were free from bleeding tendency and liver disease. The distribution of their fibrinogen levels was Gaussian, but more wide-based than the distribution of our normal controls. The mean fibrinogen value of the patient group was 3.60 g/l, significantly higher than that of the healthy group, which was 2.53 g/l. The reasons why the fibrinogen distribution graph of patients assumed such a pattern and the role of fibrinogen in health and disease are discussed.

Keywords: Fibrinogen, Reference range

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INTRODUCTION

Plasma fibrinogen level is one of a battery of laboratory tests which constitute the "Coagulation Profile" of a bleeding patient. It is specifically used for diagnosing hypofibrinogenaemia which can be congenital, or secondary to numerous clinical conditions. In our laboratory, the more common indications for requesting plasma fibrinogen level are liver failure, disseminated intravascular coagulopathy (DIC), snake-bite, and thrombolytic therapy.

Since reference data on the local population were not available, we measured the plasma fibrinogen concentration in a group of healthy subjects for the purpose of establishing the normal reference range. For comparison, we also measured the fibrinogen level in a selected group of patients.

MATERIALS AND METHODS

Blood samples were collected in plastic vials containing 3.8% Trisodium Citrate. Fibrinogen level determination was carried out on platelet-poor plasma from 47 healthy individuals among the staff of the Clinical Pathology Unit at Prince of Wales Hospital, and 44 adult hospital patients. Patient selection was based on the criteria that both PT and APTT were within normal limits (10-14s for PT and 25-40s for APTT). Patients diagnosed as having liver disease were excluded from the study.

Fibrinogen concentration was determined by the chronometric method using the Fibrinomat Kit (bioMerieux, Charbonnieres des Bains, France). Thrombin was added to 1 in 10 dilution of citrated plasma and the clotting time determined. The concentration of fibrinogen was calculated from a standard curve after having been corrected for hematocrit and the dilution factor of liquid anticoagulant.

Statistical analysis employed the Student t test.

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RESULTS

It was interesting to find that the distribution graphs of both the healthy and patient populations were Gaussian (Fig 1). The mean value of fibrinogen level for the healthy controls was 2.53 g/l, based on which the reference range (mean ± 2 S.D.) was determined (1.75 - 3.31 g/l). The mean value of fibrinogen level for the patients was 3.60 g/l, which was significantly higher ($p < 0.001$) than the control population and was responsible for the right shift of the graph.

DISCUSSION

Fibrinogen is a large glycoprotein with a molecular weight of 340,000 daltons. It is synthesized in the liver and is present in both plasma and platelets (1). Being the precursor of fibrin, it plays an important role in the coagulation cascade and the fibrinolytic system. Hemostasis results in local fibrin deposition which serves to control infection as well as to arrest hemorrhage. The process of hemostasis also attracts white blood cells and alters local blood flow, facilitating host defense and tissue repair. Fibrinolysis functions as a feedback system in which clot is dissolved and fibrin formation is inhibited. Excessive host response to hemostasis can lead to excessive fibrinolysis and thus hemostatic imbalance (2).

Fibrinogen is also a reactive protein. As early as 1956, Malpighi experimentally proved that fibrinogen was markedly increased in many infectious diseases and inflammatory processes (2). It can be elevated to twice the resting level after 24 to 72 hours in response to inflammation or surgical trauma (3, 4), and stays elevated for several weeks even after the initial disease process has subsided. In the patient population we studied, the fibrinogen level distribution showed a right shift, i.e. most patients had fibrinogen concentration either at the upper limit of normal or beyond. Our study demonstrated the fact that if liver disease and diseases with prolonged PT and APTT were excluded, most other clonical conditions were associated with an increase in fibrinogen synthesis.

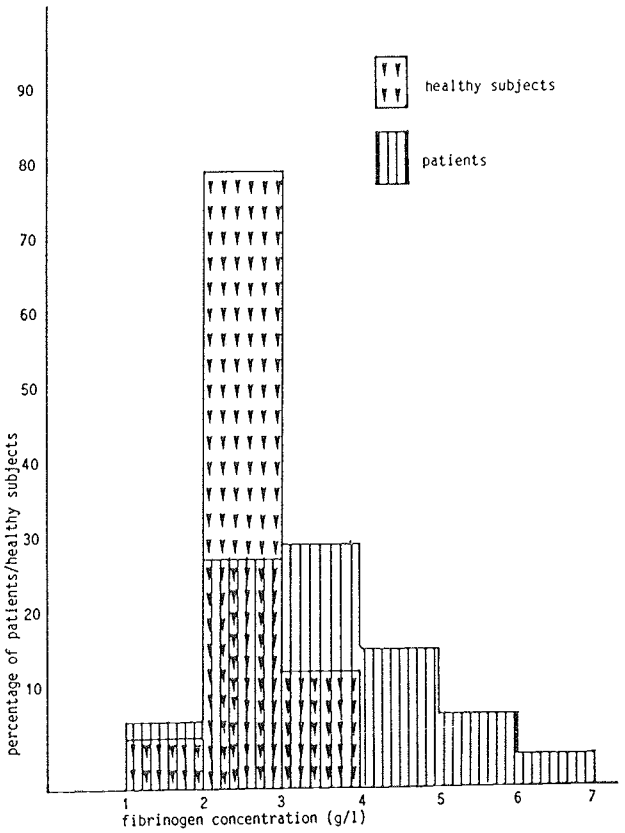

Fig 1
Distribution of fibrinogen levels of healthy subjects and a selected group of patients.

The Gaussian nature of distribution of fibrinogen levels among patients indicated the heterogeneity of patient response. Some were unaffected by these illnesses in terms of fibrinogen level, while in others, enhanced fibrinogen synthesis was elicited. A graded response to the elicitation would be one probable reason for the varying levels of fibrinogen among our patients.

There are clinical situations in which a "fibrinogen response" may not be apparent. An example of this is in disseminated intravascular coagulation (DIC) where the fibrinogen level usually falls due to consumption and secondary fibrinolysis. However, if a patient with DIC is also suffering from another condition associated with increased synthesis of fibrinogen, the hypofibrinogenaemia may be negated by an elevated baseline level of fibrinogen and hence becomes inapparent. This phenomenon is particularly prone in chronic compensated DIC often seen in cancer patients. In such a case, normal coagulation screening tests and fibrinogen level do not exclude the diagnosis of DIC (5).

Although fibrinogen is an acute phase reactant and an elevated level is most likely reactive, recent studies suggested that high fibrinogen level per se may be the cause of certain diseases (6). In one study, patients who had high plasma concentration of fibrinogen preoperatively were found to be more susceptible to venous thromboembolism postoperatively (7). Another study showed that high plasma fibrinogen concentration was strongly associated with ischaemic heart disease (8). It is noteworthy that in this study, subjects with high fibrinogen level developed heart disease within five years of their blood examination. In these instances, the elevation of fibrinogen level appeared to be pathological and causally related to thromboembolism, rather than an acute phase response to surgical trauma or myocardial infarction. Further studies are required to determine the exact role of fibrinogen in the pathogenesis of these diseases.

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