Portal hypertension at high altitude:
more questions than answers

Venous thrombosis is being increasingly recognized as a major cause of morbidity and mortality at a relatively young age in populations at risk. A subset of patients developing venous thrombosis with or without apparent predisposing cause carry genetic polymorphisms of coagulant proteins, e.g., factor V, inhibitors of coagulation, e.g., proteins C and S, and antithrombin and fibrinolytic proteins. Such hereditary predispositions to thrombosis have been termed thrombophilia. The episodes of venous thrombosis in such individuals are often precipitated by a wide range of physiological and pathological conditions that either cause stasis of blood in the veins, e.g., postoperative state and immobilization, or alter the balance between the procoagulant and anticoagulant forces in blood, e.g., pregnancy, trauma, and oral contraceptives. Factor V Leiden gene mutation, prothrombin G20210A gene mutation, high level of factor VIII and hyperhomocysteinemia seem to be the four most common inherited risk factors for venous thrombosis in the Western population. In contrast, the prevalence of factor V Leiden gene mutation and of prothrombin G20210A appears to be very low among Indians.

Thrombosis of the hepatic portal venous system and hepatic veins are important clinical problems presenting as portal hypertension, veno-occlusive disease, and Budd-Chiari syndrome. Thrombophilia is one of the important predisposing causes for such clinical conditions. There are few Indian studies on thrombophilia in general and thrombophilia in relation to portal venous thrombosis and Budd-Chiari syndrome in particular. A notable finding is a high incidence of factor V Leiden mutation in Budd-Chiari syndrome (19%-26%) and 3-4 times higher incidence (26%) in portal venous thrombosis.

In this issue of the Journal, Anand et al. from the Armed Forces Medical Service, describe another interesting subset of patients presenting with portal venous thrombosis after reaching high (3000-5000 meters) or very high (>5000 meters) altitudes above mean sea level. These patients were young healthy recruits for the arduous task of high-altitude policing and warfare. Their findings suggest that, as compared to recruits who work at low altitudes, personnel working at high altitude have almost 100 times more risk of developing portal venous thrombosis. The authors had earlier described higher incidences of venous thrombosis in different areas of the circulation in persons recruited for high-altitude duty.

In addition to gene-gene interactions, interaction between acquired and congenital risk factors leading to several-fold increase in the incidence of venous thrombosis is a well-documented fact. Among the acquired risk factors, prolonged immobilization, pregnancy, and use of oral contraceptives appear to be significantly associated with venous thrombosis in individuals with inherited predisposition.

Although the study by Anand et al. is commendable and involves work that could have been done only by the Armed Forces in India, it lacks in-depth analysis. The authors have, for example, emphasized the possibility that polycythemia produced thrombosis at high altitude, but have not provided data on hematocrit determination. A majority of personnel at high altitude also consume hard liquor quite regularly. Only 5 of 9 patients had some work-up done for thrombophilia, with negative results. In these five cases factor V Leiden has not been done. How many of these nine patients had clinical and/or biochemical markers of chronic liver disease? Though proteins C and S cannot be tested properly when the patient is on oral anticoagulants, other biochemical parameters like fibrinogen level, C-reactive protein level, VWF level, and factor VIII could have been measured in these cases.

Certain unusual clinical features in these patients have also been described by the authors, like early development of collateral circulation. We do not know whether the problem existed before the patient went to high altitude. Presence of ascites is also distinctly unusual and again raises the question of whether these patients had underlying liver disease or other clinical conditions. The ascitic fluid needed to be examined in detail.

Finally the investigations that mattered most in these patients, i.e., factor V Leiden and APC resistance test, are missing. Though the latter cannot be done properly in anticoagulated patients, factor V Leiden could have been tested by using DNA-based technique.

We in this country have little data on the incidence of antithrombin III, protein C and protein S deficiency in our population mainly because the kits for testing these are costly. The gap in the knowledge in this area can be filled by the Armed Forces Medical Service if they do a thrombophilia work-up on their recruits before sending them to high altitudes, and subsequently following up the cohort. Hemoglobin electrophoresis to demonstrate HbS should also be part of such an exercise.

Future studies on this subject should be undertaken with some planning so that we not only uncover new
References