PREVALENCE OF CARDIOVASCULAR DISEASE OR ITS EQUIVALENTS IN PATIENTS WITH INHERITED COAGULOPATHIES

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BACKGROUND

Cardiovascular disease (CVD) and its risk equivalents (diabetes mellitus and non-coronary atherosclerotic disease including peripheral arterial disease, abdominal aortic aneurysm, carotid artery disease, transient ischaemic attack and stroke are among the leading causes of morbidity and mortality in ageing patients throughout the world. Thanks to the therapeutic advances and availability of factor concentrates the life expectancy of people with inherited coagulopathies (PWIC) is approaching that of general population in developed countries. Current data suggest that hypocoagulable states do not provide complete protection from ischemic heart diseases (IHD), as once thought. There is growing evidence showing that PWIC are not exempt from ischemic vascular complications. Data on cardiovascular status of PWIC from developing countries with limited access to factor replacement therapies are lacking.

AIM OF THE STUDY

The aim of this study was to assess the prevalence of CVD and/or its equivalents in adult PWIC followed and treated at a single institution in Turkey.

MATERIALS AND METHODS

All severe type PWIC ≥ 30 years old, followed at the Adult Haematology Department of the Cerrahpasa Medical Faculty, Istanbul University were included. Demographic information, type and severity of bleeding disorder, data on CVD risk factors (hypertension, dyslipidaemia, diabetes, obesity, and smoking) and family and drug history were collected.

RESULTS

A total of 41 PWIC (4 females, 37 males) were included. Median age was 45 years (31 – 80). Five patients had von Willebrand disease (vWD; 2 females, 3 males), 1 female patient had long-lasting, acquired (?) FII, VII, IX, X deficiency, 1 female patient was diagnosed with FXI deficiency, and there were 4 haemophilia B (HB) and 30 haemophilia A (HA) patients. Twenty-six patients were severe haemophiliacs. None of the patients had inhibitor. Biochemical characteristics of the study population were listed in Table 1.

Hypertension and hyperlipidaemia were identified in 10/41 (24%), and in 14/41 (34%) patients, respectively. There were nine patients with HDL levels ≤ 40 mg/dl. Diabetes was found in 2/41 (5%), and obesity (defined as having a BMI ≥ 30) in 5/41 (12%) patients. Twenty-nine patients (78%) were smokers. Risk factor profile of the patients were summarised in Table 2. More than one third of patients had a family history of either IHD or its equivalents. There were nine patients with 4 or more CVD risk factors. Four of those nine patients (2 vWD, 2 HA) had IHD confirmed by angiography. One of those patients underwent percutaneous coronary intervention, the other three had coronary by-pass grafting..

The mean and median age of the four patients at the diagnosis of confirmed IHD were 61.5 and 57 years (range, 52-80 years), which is almost 20 years more than the rest of the patients mean age at study entrance (43.8 years). All the study patients were negative for HIV, which could be an additional risk factor for CVD.

Table 1. Laboratory characteristics of the study population

Parameter	Value (mean± SD)
Total Cholesterol (mg/dl)	191.13±30.70
HDL-Cholesterol (mg/dl)	46.94±15.44
LDL-Cholesterol (mg/dl)	127.59±33.60
Triglyceride (mg/dl)	117.21±54.40
Fasting glucose (mg/dl)	92.59±25.76
$HbA1_C$ (%)	5.53±0.94
ALT (U/l)	28.05±20.51
AST (U/l)	22.78±8.67
Urea (mg/dl)	30.21±8.32
Creatinine (mg/dl)	0.85±0.17

Table 2. Patient characteristics

Parameter	PWIC	General Population
Age (years, mean±SD)	43.18±9.47	
BMI (kg/m^2, mean ± SD)	24.96±3.71	
Severe haemophilia (n [%])	24 [63] (all HA)	
Moderate/mild haemophilia (n [%])	9 [27](5HA/4HB)	
vWD (n [%])	5 [12]	
RBD (FII,VII,IX,X def. and FXI def.) (n [%])	2 [5]	
Obesity (n [%])	5 [12]	18%
Smokers (n [%])	29 [78]	65%
Hypertension (n [%])	9 [24]	41%
Family history of IHD (n [%])	11 [27]	26%
Family history of CVD equivalent (n [%])	16 [39]	
Hyperlipidemia (n [%])	14 [34]	58%
Diabetes Mellitus (n [%])	2 [5]	20%
IHD (n [%])	4[10]	3.8%

BMI, body mass index; HA, haemophilia A; HB, haemophilia B; RBD, rare bleeding disorders; SD, standard deviation; vWD, von Willebrand's disease

DISCUSSION AND CONCLUSION

Through the availability of factor concentrates and establishment of prophylactic factor replacement therapy as the standard of care in coagulopathies a considerable number of PWIC worldwide live longer and begin to face with age-related comorbidities. Despite its limitations (single referral centre study, low subject number, heterogeneous study population) our study demonstrated that the frequency of CVD risk factors and age-related morbidities such as, hypertension, hyperlipidaemia, ischemic vascular disease in PWIC are not much different from that of general population (Table 2). Thus, bleeding disorders do not seem to protect PWIC from the development of risk factors and ischaemic diseases completely as once thought. Therefore CVD risk factors should be checked and the risk for IHD should be determined in PWIC. Patients at risk should be given the same treatment for CVD as their non-coagulopathic counterparts and be kept on prophylactic factor replacement.

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