

The potential significance of two coagulation defects: Prekallikrein Deficiency and Arg304Gln (FVII Padua) frequently found among African-Americans

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Dear Sir,

Sporadic observations have suggested that Prekallikrein (PK) deficiency occurs frequently among African-Americans [1,2].

A recent comparative study on reported cases has confirmed the prevalence of PK deficiency among African-Americans as compared to the general American population [3].

It is interesting to note that other contact phase defects have been described in African-Americans namely, High Molecular Weight Kininogen (HMWK) deficiency or Fitzgerald trait [4]. Total KN (Williams defect) defect has been described instead in Caucasians [5].

As far as FXII deficiency is concerned no information about ethnic preference is available. Mr Hageman was Caucasian [6]. Patients with PK deficiency show no bleeding tendency but seem to be frequently associated with hypertension and hypertension related disorders [7].

The role of this defect on the frequent increase of CVD found among African-Americans is unknown.

It is interesting to note that no increased prevalence of FXII deficiency is present among African-Americans.

The evaluation of the cases with total kininogen (KN) or HMWK deficiency is still unclear due to the rarity of the defects [8].

As far as FVII deficiency, is concerned, it has been demonstrated that the Arg304Gln mutation in exon 8, originally described in Padua, is frequent among African-Americans [9-12]. No other FVII defect has a similar behavior. Incidentally, the index patient with FVII deficiency described by Alexander et al in 1950 was Caucasian and showed a different mutation [13].

PK and, perhaps, the HMWK deficiencies are or seem more frequent among African-Americans [1,2]. Factor VII Padua, a Type 2 variant, due to Arg304Gln mutation in exon 8, seems also frequent among African-Americans [9-12].

PK and FVII are controlled by different genes, on different chromosomes.

Interestingly, there is no report of patient with both defects at the homozygote or at the heterozygote level.

However, due to the fact that PK deficient patients do not bleed and that patients with the FVII Arg304Gln mutation have only a mild bleeding tendency or are also asymptomatic, we cannot exclude that patients with a combined defect of these two disorders do exist. Because

of the lack or paucity of symptoms they could go undetected [14].

If one takes into account the other side of the homeostatic balance, namely thrombosis, it may be, at least on theoretical grounds, more likely that PK deficiency is associated with hypertension related disorders [15,16] while FVII Padua has been demonstrated to show an increased risk of venous thrombosis [17]. On the contrary, these seem rare in PK deficiency [16].

The rarity of the conditions has prevented long term observational studies and therefore no sure conclusion can be drawn.

Tentatively it may be stated that PK deficiency is associated with arterial disorders whereas the FVII Arg304Gln mutation is mainly associated with venous thrombosis [3,17].

The African American population is known to present frequent cardiovascular disorders [18-20]. The potential role of these two mutations has never been thoroughly investigated.

Sporadic reports and limited series of case studies indicate that both defects are frequent among African-Americans [1,2,9,12].

It would be useful to progress in this investigation in order to ascertain whether these defects are responsible, at least in part, for the increased prevalence of cardiovascular disorders seen among this population.

Conflicts of interest

The authors declare that they have no conflict of interest.

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Received: December 06, 2019; Accepted: January 10, 2020; Published: January 13, 2020

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