


Increased Prevalence of Reported Cases of Congenital Prekallikrein Deficiency Among African Americans as Compared With the General Population of the United States

Clinical and Applied
Thrombosis/Hemostasis
Volume 26: 1-3
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DOI: 10.1177/1076029620918301
journals.sagepub.com/home/cat


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Keywords

prekallikrein, prevalence, countries, differences

Date received: 27 November 2019; revised: 06 February 2020; accepted: 03 March 2020.

African Americans show an increased incidence of hypertension and hypertension-related morbid conditions.¹⁻³ Several causes, both congenital and acquired, have been implicated to explain the phenomenon. No information is available with regard to the prevalence of prekallikrein (PK) deficiency among African Americans.

Since PK deficiency has been reported to be associated with hypertension and hypertension-related cardiovascular disorders,⁴⁻⁶ it would be interesting to know whether the defect is common among this population. However, no specific report has ever been published so far on the subject. The purpose of this study was to evaluate all published papers on PK deficiency.

A total of 122 papers dealing with PK deficient patients have been evaluated. Such papers were obtained from 2 sources, namely (1) from personal files dealing with patients with PK deficiency, seen or studied in Padua during the past 20 years and (2) from two, time-unlimited PubMed searches carried out on March 2010 and March 2019. The keywords were Prekallikrein, deficiency, contact phase defects asymptomatic, coagulation disorders, Prekallikrein deficiency in African Americans in the USA population.

Side tables were also evaluated whenever available. Cross examination of the references listed at the end of each paper was carried out in order to avoid omissions. Only cases with severe PK deficiency (PK level of 1% of normal or of less than 1%) were taken into consideration.

Statistical analysis of results was carried out by means by the χ^2 and odd ratio tests using Microsoft Excel Software 365 (Richmond, Virginia). Value of *P* value less than .05 was considered significant. Twenty-two papers were eliminated because they did not deal with new cases of PK deficiency (Figure 1).

The total number of cases was 105 in 90 papers. The total number of papers reported in the United States was 25. Fourteen of these (15 patients) dealt with African Americans.⁷⁻²⁰ The remaining papers dealt with Caucasians or with patients with an unspecified ethnic group.

In addition, 3 Africans (one African-Caribbean, one African-European, and one African African) were found among the 65 papers that dealt with PK deficiency published outside the United States.²¹⁻²³

No patient, but two, showed a bleeding tendency. In one case, reported by Waddell et al¹⁹ PK deficiency was associated with chronic lymphocytic leukemia. The bleeding in this patient was attributed to thrombocytopenia and chemotherapy. Another patient presented mucosal bleeding which was not clarified.¹⁰

A thrombotic stroke was present in a woman with diabetes and hypertension.¹⁴ In another woman, recurrent cerebrovascular accidents were reported.⁹ On the contrary, no venous thrombosis has been noted.

Only one paper in the United States contained molecular biology investigations of the patient and this was found to be homozygote for Cys529Tyr.¹⁰

No paper about the prevalence of PK deficiency in the population of the United States has ever been published. However, an apparent, possible increase of the defect among the African

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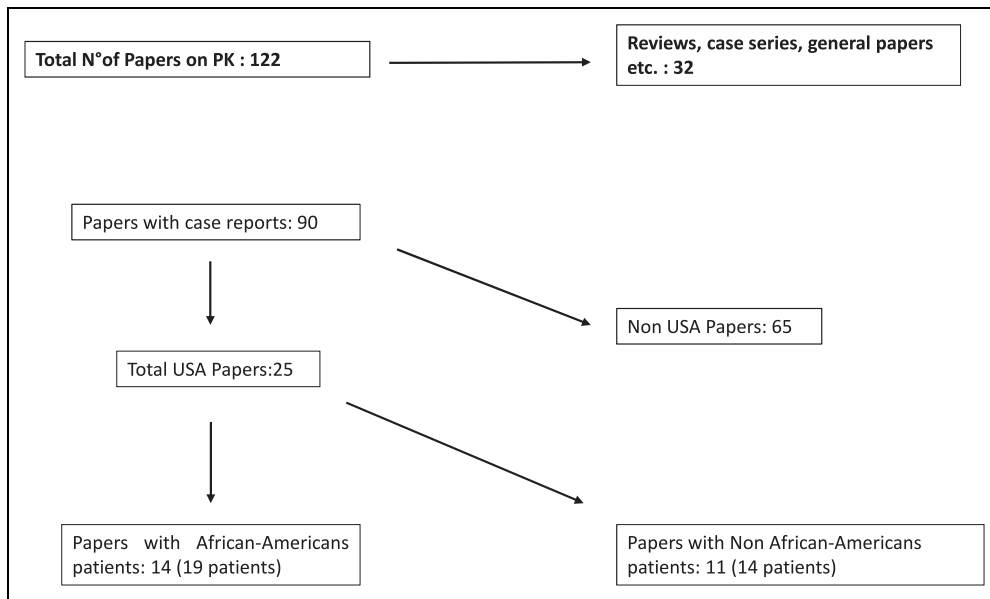


Figure 1. Evaluation and classification of 122 papers with prekallikrein (PK) deficiency. The papers examined were written in English, Spanish, Italian, Portuguese, French, German, Turkish, and Japanese.

Table 1. Estimated Prevalence of PK Deficiency Among the Non-African American and African American Populations in the United States.^a

		Reported Cases With PK Deficiency	Prevalence in 1,000,000
Non-African American population of US	289 millions	14	0.048
African American population of US	42 millions	19	0.452

Abbreviation: PK, prekallikrein.

^aEthnic background of African American as supplied in published paper on the subject. Data on population were supplied by *Encyclopedia Britannica*, supplement year 2018. The difference was statistically significant ($P < .05$).

American population of that country was noted in Sollo and Saleem in 1985.¹⁸

On the basis of this survey, it appears that PK deficiency is more frequent among African Americans as compared with Caucasians-Americans. The difference is statistically significant (Table 1).

The population of African Americans is estimated to about 13% of the total population of the United States, namely 324 million. This would indicate that the total population of African Americans is about 42 million.²⁴ The discrepancy is evident. There are more African Americans affected by PK deficiency than the rest of the US population. Needless to say that further studies on the African American and the entire US population are needed before sure conclusions are reached.

The role played by PK deficiency in cardiovascular diseases (CVD) is still ill defined. However, hypertension has been frequently reported in patients with PK deficiency.⁴⁻⁶

The exact role played by the increased prevalence of PK deficiency found among African-Americans in the pathogenesis of CVD is unclear. The association between CVD and prevalence of PK deficiency is suggestive for a link between the 2 events.

It should be noted that in the index family, reported in 1965 by Hathaway et al,²⁵ the father of the propositus was a mulatto (half African American) and a silent heterozygote whereas the


mother was Caucasian but was also a silent heterozygote.²⁵ Partial Thromboplastin Time can be normal in heterozygotes for PK deficiency or only borderline.⁵ This explains the fact that some of their children were homozygotes. The hereditary pattern is confirmed by the observation that the son that the mother had from a first marriage was normal.²⁵

The non-African Americans cases seen in the United States can be subdivided in cases for whom it was stated that they are Caucasians and in a group with no ethnic specification. It could be surmised that at least some of the latter group could also be African Americans. This is a limitation of the study between it could further spread the discrepancy and increase the value of the results. There is no difference in the clinical behavior of the disease in the 2 ethnic groups. There is no bleeding tendency safe for occasional bleeding, of unknown origin.^{10,19} Hypertension and hypertension-related conditions (myocardial infarction, atherosclerosis, heart failure, etc) seems more frequent among the African Americans. Nobody knows the exact prevalence of PK deficiency in the African Americans population versus that seen in the rest of the US population. The present study based on the analysis of all reported patients indicates that a difference may exist. The suspected higher prevalence of PK deficiency could be one of the causes of the known increased incidence of cardiovascular disorders seen in African Americans.¹⁻³

Authors' Note

This study was supported in part by the “Associazione Emofilia ed altre coagulopatie delle Tre Venezie.”

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