Profile of suspected women carriers for Haemophilia-A in a new haemophilia centre

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OBJECTIVES

Haemophilia A is X-linked recessive inherited bleeding disorder, with resultant deficiency of procoagulant Factor VIII. Women are the carriers of this disease- classified as obligate or possible carriers. Clinical, haemostatic and genetic profile of the suspected women carriers from families of haemophilia cases attending our Haemophilia Centre in New Delhi, India was studied.

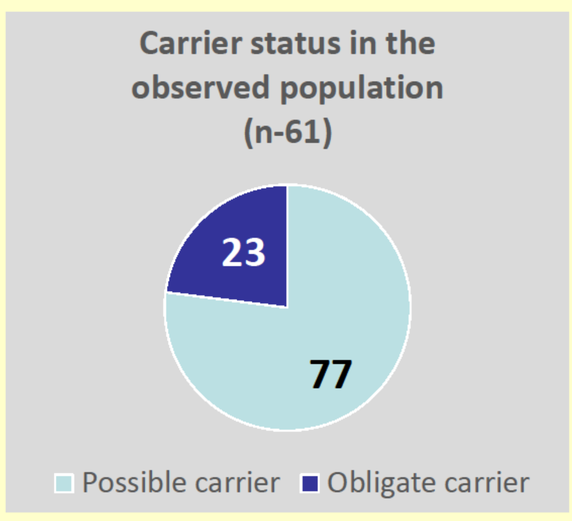
METHODS

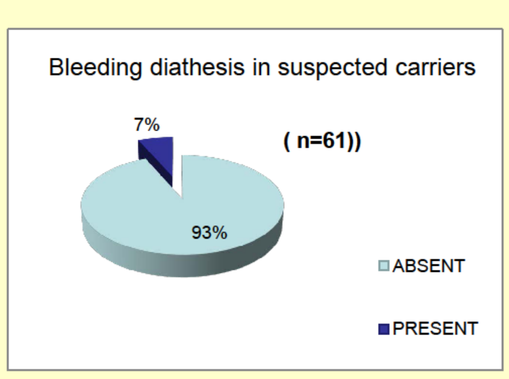
Amongst 25 families of haemophilic attending our Haemophilia Centre, 61 suspected women carriers were identified and subjected to pedigree analysis, haematological investigations including prothrombin time (PT), activated partial thromboplastin time (APTT) and Factor VIIIc assay. Molecular genetic analysis by linkage analysis using marker bcl1 for Intron 18 was done in 31 suspected carriers.

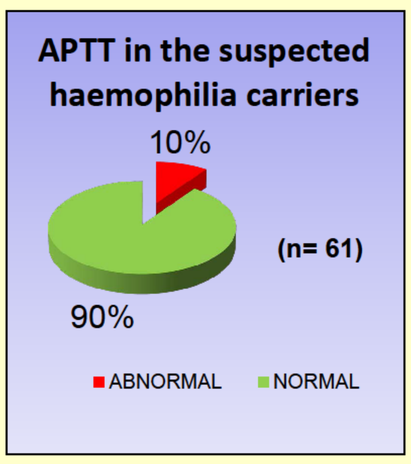
OBSERVATION AND RESULTS

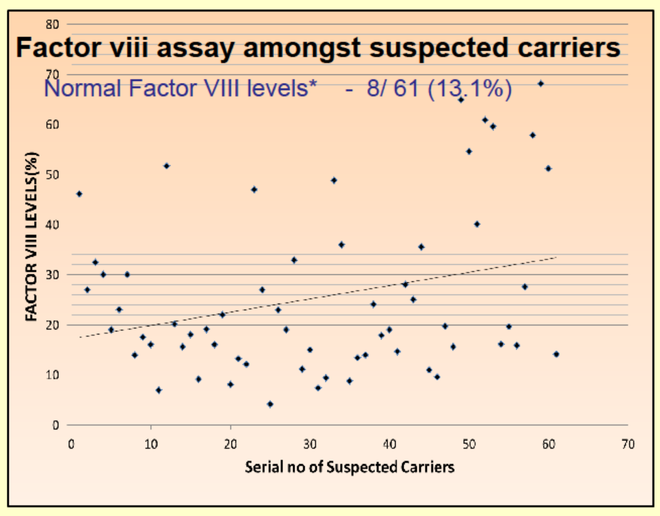
Amongst the total suspected carriers, there were 47 (77%) possible carriers and 14 (23 %) obligate carriers. No bleeding history was recorded in 57 (93.45%).

Mean Factor VIII level amongst suspected women carriers with positive family history (inherited case) was significantly lower at 22.6%± 8.8% compared to 26.9%± 19.1% for without positive family history(sporadic case), p value=0.04.









Haemoglobin was normal in 24 out of 61 suspected carriers (39.4%), mild (Hb 10-12) and moderately severe (Hb 7-10) anemia were found in 33 (54.1%) in 4 (6.55%) cases respectively.

Abnormal APTT was seen in 6/61 (10%) of suspected carriers. Mean Factor VIIIc level in these suspected carriers was 25.47 ± 16.3%. Eighty seven percent (53/61) of carriers had abnormally low Factor VIIIc level and only 8/61 had normal levels.

Out of 25 families, ten families (10 confirmed patients and 31 suspected carriers) were selected for molecular genetic profiling by RFLP linkage analysis using BCL1 (Intron 18) and HINDIII (Intron 19) markers which gave non informative results.

CONCLUSIONS

1. Whereas the male subjects in haemophilia are affected clinically, the asymptomatic females with a single mutated gene are the carriers of disease.

2. Even a clinical and basic haematological evaluation of the suspected women carriers can be pretty informative prior to the molecular genetic analysis to assess the carrier status.

REFERENCES:

1. Shetty S, Ghosh K, Bhide A, Mohanty D (2001). Carrier detection and prenatal diagnosis in families with Hemophilia , Natl . Med J India; 14(2): 81-83
2. Prenatal diagnosis in hemophilia A using factor VIII gene polymorphism—Indian experience . M. R. Chowdhury, M. Tiwari, M. Kabra, P. S. N. Menon. Annals of Hematology July 2003, Volume 82, Issue 7, pp 427-430
3. Factor VIII and IX gene polymorphisms and carrier analysis in Indian population. Shrimati Shetty, Kanjaksha Ghosh, Anil Pathare, Roshan Colah, Suresh Badakare and Dipika Mohanty. 1998 DOI:10.1002/(SICI)10968652(199704)54:4<271::AID-AJH2>3.0.CO;2-S

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