PREVALENCE OF INHIBITORS IN INDIAN HAEMOPHILIA PATIENTS

Shrimati Shetty, *Kanjaksha Ghosh, Patricia Pinto, Tejashree Shelar, Vidhya Nawadkar, Darshana Mirgal, Alfiya Mukaddam*

Dept. of Haemostasis & Thrombosis,National Institute of Immunohaematology (ICMR), Mumbai, India.

OBJECTIVES

- A serious complication of replacement therapy in patients with bleeding disorders, is the development of specific antibodies or 'inhibitors' to the deficient coagulation factors, particularly in Haemophilia A (HA) patients.
- This leads to an increase in the management cost, morbidity and mortality, especially post-operatively in case of FVIII inhibitors.
- The mechanism of FVIII inhibitor development is quite complex and it is difficult to predict their development, but a prompt and accurate diagnosis is critical as early therapy can save lives.
- **The aim of this study was to screen patients with bleeding disorders for inhibitors, and analyse the incidence of inhibitors in different regions in India, as well as the patient and treatment-related characteristics.**

Prompt recognition of inhibitors is critical, since early therapy can be life-saving!

METHODS

After Ethics Committee approval, patient details were recorded in a clinical proforma.

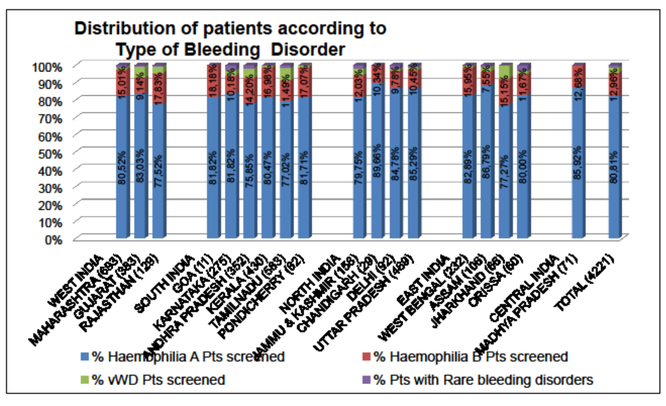
Blood samples were collected in 3.18% trisodium citrate vacutainers, and centrifuged at 4000 rpm /15 min/ 4 C to obtain Platelet Poor Plasma (PPP), aliquoted & transported to the NIIH, the testing centre in Mumbai on dry ice.

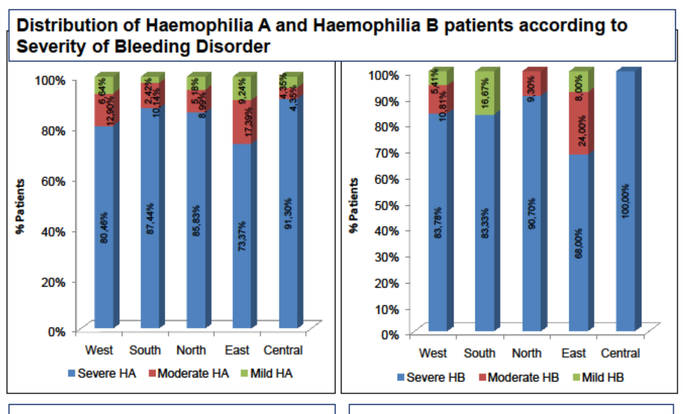
Coagulation screening tests [PT, APTT, Mixing studies], Factor assays, vWF:Ag assays etc. were performed.

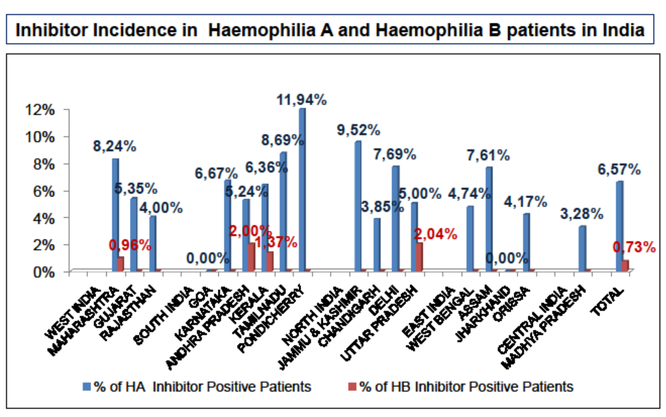
Inhibitor screening assays were performed & Inhibitor titres were quantitated in positive samples by the Nijmegen-Bethesda Assay.

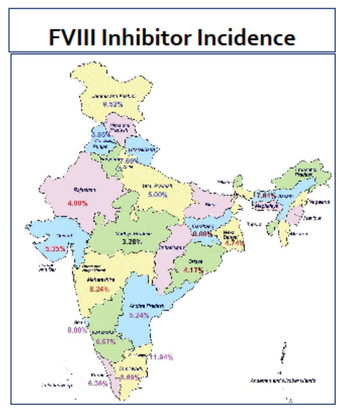
RESULTS

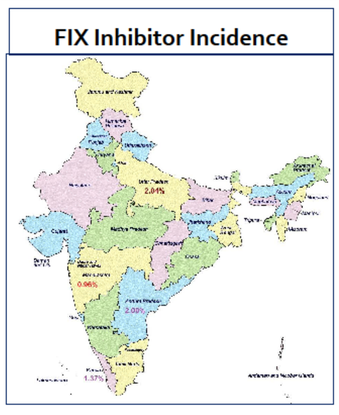
Bleeding Disorder	No of Patients (%)	No. of Inhibitor Positive Patients (%)
Haemophilia A	3411 (80.81%)	224 (6.57%)
Haemophilia B	547 (12.96%)	4 (0.73%)
von Willebrand Disease (vWD)	139 (3.29%)	-
Rare Bleeding Disorders	50 (1.18%)	-





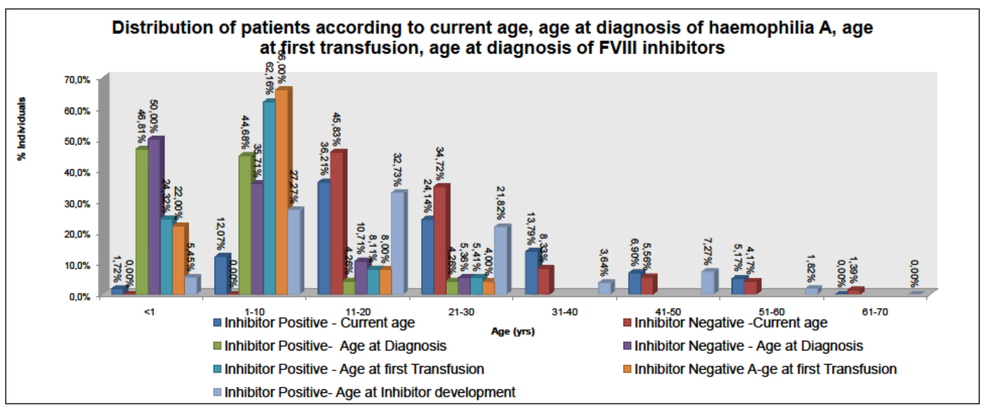


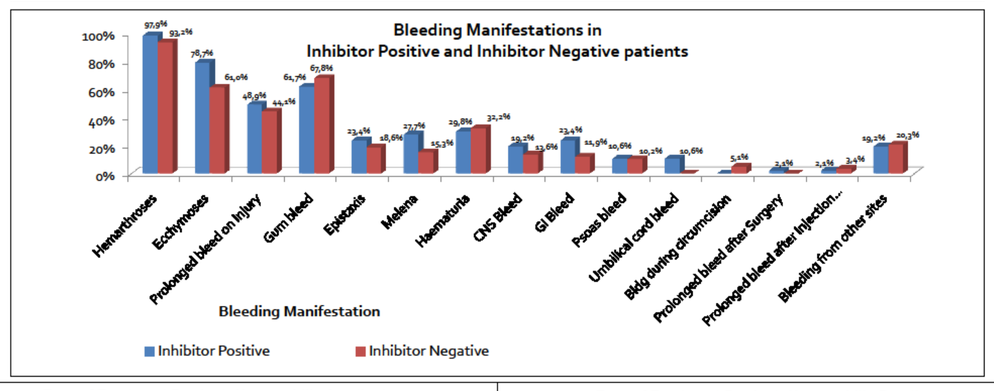


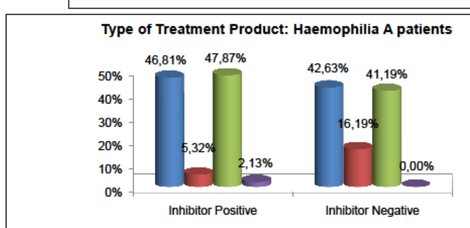


FVIII Inhibitor Positive Patients	High-responders (>5 BU/ml)	Low-responders (≤ 5 BU/ml)
No. (%) of Patients	(137/224) 61.16 %	(87/224) 38.84%
Mean Inhibitor Titre (BU/ml)	59.66 (5.1-416)	2.93 (2.0-4.95)

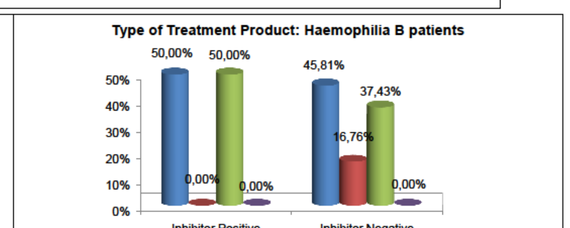
FIX Inhibitor Positive Patients	High-responders (>5 BU/ml)	Low-responders (≤ 5 BU/ml)
No. (%) of Patients	(3/4) 75.00 %	(1/4) 25.00%
Mean Inhibitor Titre (BU/ml)	8.53 (6-10)	2.9 (2.9-2.9)







Use of Blood Products : Fisher's exact test P-value: 0.0028, Odds Ratio: 0.2909, 95% confidence Interval: 0.1166 – 0.7258 (using Woolfs approx.)



CONCLUSIONS

- Out of the 4221 samples screened,
  3411 (80.81%) were Haemophilia A patients, 224 (6.57%) FVIII Inhibitor Positive
  547 (12.96%) were Haemophilia B patients, 4 (0.73%) FIX Inhibitor Positive.
- The highest incidence of FVIII Inhibitors i.e. 11.94% was seen in the Pondicherry samples (11.94%), followed by Jammu & Kashmir (9.52%), Tamil Nadu (8.69%) and Maharashtra (8.24%) w.r.t. the samples analysed.
- The other regions showed FVIII inhibitor incidences varying from 7.69% to 3.28%.
- FIX:C inhibitors were detected in samples from Maharashtra (0.96%), Andhra Pradesh (2.00%), Kerala (1.37%), and Uttar Pradesh (2.04%).
- None of the other rare bleeding disorder patients screened were found to have specific inhibitors.

- Of the 224 FVIII Inhibitor Positive patients, 137 (61.16%) were high responders, and 87 (38.84%) were low-responders.
- The age group between 11-20 yrs showed the highest incidence of FVIII inhibitors (32.73%) in this study.
- Majority of the pts were diagnosed to have HA before 1 yr of age, and majority (>60%) were transfused for the first time between 1-10 yrs of age.
- Indian haemophilia patients are generally treated 'on-demand' in case of bleeding episodes, rather than prophylactically.
- The number of inhibitor negative HA patients treated with only blood products was significantly higher than the inhibitor positive patients, thus suggesting a protective association w.r.t inhibitors, but must be interpreted with caution because of the risk of transfusion-transmitted diseases.

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Approaches to inhibitors

Shrimati Shetty

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