Future of Haemophilia Research in India

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Haemophilia represents a high-cost, low-volume disease [1]. Hence, in developing countries where 90% of haemophilia patients of the world live, it puts the government of the day in a conundrum, i.e. the limited resources of that country earmarked for health need to be distributed amongst management and prevention of various diseases which optimally helps the population of the country. Hence, there is a need for developing research protocols suitable for that country in an evidence-based manner. Haemophilia research in India is one of the examples of need-based research, often driven by patient organizations like the Haemophilia Federation of India [2]. In the last 30 years, a large number of research papers in haemophilia have contributed materially to our diagnostics, management and training of manpower in the country [3].

However, till recently, NIIH, Mumbai, AIIMS, New Delhi and CMC Vellore were the three Institutions which spearheaded major areas of research in haemophilia i.e. management, diagnosis, complications, prenatal diagnosis, molecular pathology etc. [4]. Recently many more institutions are taking part in haemophilia research. One of the major areas in which it is happening are the international clinical trials of many new products that are already in the market or on the horizon. The SIPPET trial is one of the best examples of that Indian collaboration with the international community [5]. The Haemophilia Federation of India did establish a haemophilia patient registry which has

stimulated ICMR to take up this registry and introduce similar registries in common genetic disorders.

Registries often not only drive significant amount of research in that disorder [6] with important implications for health planners in resource redistribution, strengthen diagnosis and management in areas where it is most required, allow comparisons of wellbeing and prevalence of various complications within that disorder with other countries' registry data [7, 8], they also stimulate well-balanced clinical trials which are statistically robust and many such trials allow patients to receive expensive therapeutic interventions free-of-cost.

At present, the Indian haemophilia (Bleeding Disorder) registry has close to 20,000 haemophilia patients from all over the country, though we expect this number to swell near 85,000–100,000 when investigative techniques i.e. coagulation laboratories become available across 750 districts in the country. This project is under consideration by National Rural Health Mission. When that happens, the number of research efforts, individual case reports etc. in haemophilia will increase manifold.

CMC Vellore for last few years has been making grounds [9] for gene therapy in the disease and that will be one of the big areas of research. Our seminal findings showing that deficiency of procoagulant proteins or coinheritance of thrombotic genes substantially reduce the clinical severity of bleeding [10] have now been translated into products [11]. At NIIH in Mumbai, efforts are being made to use clinical modulation of protein C levels to obtain similar results. Development of plasma-based and recombinant-based factor concentrate industry in India in the near future will be another area of operational research which will benefit a large number of haemophilia patients. Our study of mutations in haemophilia already gave some direction to develop factor VIII concentrates with

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supernormal activity [12]. Recombinant proteins incorporating those mutations in our own country will be a reality.

India already has a strong prenatal disease diagnostic capability in haemophilia using a combination of techniques [13, 14]. This area can be further improved by non-invasive mode using maternal blood or using in vitro fertilization techniques, in which our country has immense expertise. Further trials on low dose prophylaxis [15] and long-acting concentrates which could be produced in this country will be interesting to observe. We should not forget carrier state in mothers, sisters and daughters. We are sure quite a few research programmes involving this group will emerge in future.

Pain relief is an important component of disease management, so also behavioral problem in this condition, research in complementary therapy can significantly contribute in this area [16]. Studies at the National Institute of Immunology using an animal model has shown that bone marrow-derived allogeneic stem cell could be used to improve bleeding in haemophilic mice with regeneration and differentiation of allogenic stem cells into liver cells, this study also could be taken further to see if it can reach clinical trial stage [17]. Allogenic liver transplantation does cure haemophilia [18], though I am not advocating it yet seeing the vast improvement in the expertise technique and outcome in live donor transplantation in our country, who knows that some research will not take place in this direction. We already have a vast number of hepatitis C and/or B positive haemophilia patients, a proportion of them will eventually develop end-stage liver disease when such transplantations will be eminently justified.

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