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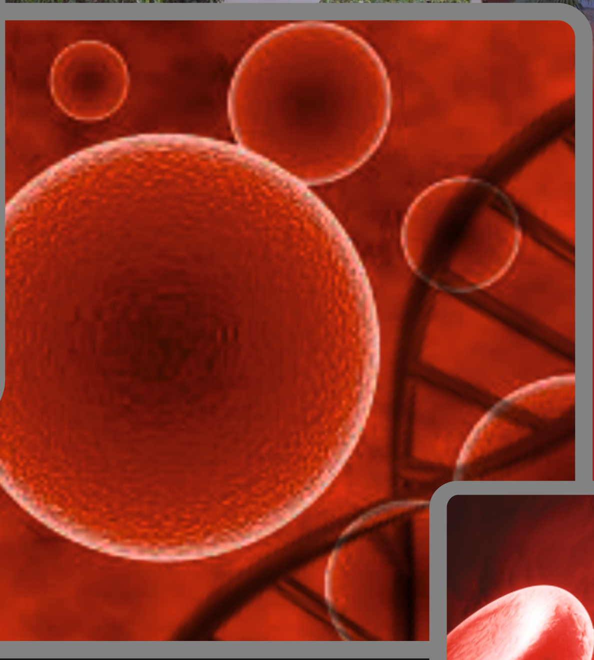

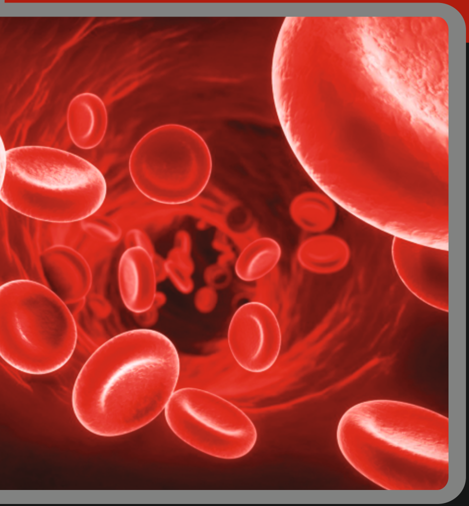

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Original Article

Hemophilia Treatment Center: A Stratification Model for Developing Countries: A Pilot Study from India

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Abstract

Background: Hemophilia center, treatment center (TC), hemophilia TC (HTC), and Hemophilia Comprehensive Care Center (CCC) are terminologies used to describe centers caring for persons with hemophilia (PWH). These are based on their capability to provide multidisciplinary care and laboratory services. Widely described are the European HTCs (EHTCs) and the European Hemophilia CCCs (EHCCCs). However, most centers in developing countries providing care for PWH have variable clinical expertise and laboratory facilities, which do not qualify for the existing models. **Materials and Methods:** This cross-sectional study was done to evaluate the laboratory and clinical care facilities available in HTCs in India. The survey questionnaire was sent to 62 HTCs in India. Laboratory and clinical care facilities were categorized based on a predefined stratification model. Level IV being the minimum and Level I the maximum were used to define clinical and laboratory facilities. **Results:** Fifty-two (85%) centers responded representing 17 states in India. Only 28 HTCs had attached laboratory services. Although all the centers cared for acute bleeds, only half managed chronic joint disease (Level III) while one-sixth could perform surgeries (Level II). Only one-third of the laboratories had instituted quality control measures and performed factor assays. Only four centers qualified for EHTC criteria and two for the EHCCC criteria. **Conclusion:** This HTC stratification model provides assessment and differentiation of the clinical and laboratory services. It allows an individual HTC to identify the standard of care and provides a framework for objectively planning, implementing, and evaluating its services.

Keywords: *Comprehensive care, Hemophilia Treatment Center, India, model*

Introduction

Hemophilia is an X-linked disease with an estimated frequency of approximately 1:10000 births.[1] There are approximately 400,000 patients with hemophilia in the world according to the World Federation of Hemophilia (WFH) annual global survey.[2] In India, there are 17,470 registered patients affected with hemophilia. However, this is only <15% of the estimated number of persons with hemophilia (PWH). This reflects the low awareness, poor diagnostic facilities, and limited available data registry. Only an estimated 1% of patients less than the age of 18 undergo prophylaxis in India.[3] Although there are many individual treatment centers (TCs), there are limited data on the actual number and facilities in hemophilia TCs (HTCs) in India.

The concept of comprehensive care evolved over the years to promote physical, psychosocial health, and quality of life of patients while reducing the morbidity and mortality.[4-7] Controversy exists as to the optimal structure in the levels of HTCs. For example, two to four levels of HTC have frequently been suggested depending on the number of patients in a geographic area and the resources available with up to six levels of HTC suggested in Thailand.[8-9] In 2008, the European principles of hemophilia care document were published by the European Association for Hemophilia and Associated Disorders and later proposed two levels of Hemophilia care: (i) European HTCs (EHTC) to provide local routine care and (ii) European Hemophilia Comprehensive Care Centers (EHCCCs) to provide specialized and multidisciplinary care and functioning as a tertiary referral center.[10,11]

This classification was based on the minimum number of severe hemophilia patients taken care of services rendered in the form of hemophilia medical cover, coagulation testing, turnaround time, and integrated approach to patient multidisciplinary comprehensive care.

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An adherence survey performed throughout Europe including 21 centers from 14 countries reported that 36% of patients were treated outside of centers meeting the definitions of HTCs or CCCs.[12]

Existing models of care have integrated laboratory and clinical care services which work best in the developed countries. In a majority of Indian centers, clinical and laboratory facilities do not coexist as hemophilia care is still evolving in the country. There still exists a significant lack of expertise, and most centers would not meet the criteria for the EHTC or EHCCCs.

Given this heterogeneity, a pilot study was conducted to assess the care available in different HTCs throughout the country aimed at dichotomous categorizations of laboratory and clinical care facilities.

Materials and Methods

A cross-sectional mail-out survey was given to 62 HTCs in India from July 2014 to January 2015 based on the list of centers registered for hemophilia update meetings as there is no comprehensive list of HTCs in India. An HTC was defined where there was factor availability with facility for factor infusion, a doctor, and/or a nurse who could administer factors irrespective of the patient number. The clinical care and laboratory facilities were categorized based on a predefined HTC novel stratification model [Tables 1 and 2]. There were four levels each from Level IV to Level I, where Level IV facility is the minimum and Level I facility is the maximum. As the patient accesses the clinical services first, a center was considered to be an HTC even without associated laboratory services within the premises. However, an HTC-associated laboratory was considered only if it had coexisted with a clinical service. Stand-alone molecular laboratories without coagulation laboratory facility were not included in this study.

Results

Completed questionnaires were received from 22 centers (85%) representing 17 of the 29 states in India. Government centers constituted the majority (49) as compared to the private sector.[3] Except for one stand-alone center which treated only hemophilia patients, all the other centers were multispecialty centers [Table 3].

The median number of patients managed in each center was 69 (range: 1–1900) patients. Forty-eight percent of the centers had 25–350 registered patients.

Clinical services

All centers were categorized based on their available clinical and laboratory services. Only 28 of the clinical services had attached laboratory services within the same institution, and the rest relied on an outsourced referral laboratory. Seventy percent (36/52) of centers were either Level IV or III being able to manage acute and chronic bleeds without surgical intervention while eight centers could care for PWH with inhibitors (Level 1) [Figure 1].

Laboratory services

Twenty-four of HTCs did not have an onsite laboratory. Of the rest, 8 performed manual clotting assays, 11 had semiautomated coagulometers, and 9 used fully automated coagulometers. Mixing studies using pooled normal plasma or commercial plasma were available in only seven laboratories.

Nineteen centers could perform factor assays, and only five centers could perform inhibitor titers or Bethesda assay. The availability of an automated coagulometer did not

Table 1: Levels of clinical services in the Hemophilia Treatment Centers

Levels of facility	Functionality	Facility requirement
Level IV	Ability to manage acute bleeds Maintain an in-house database and make efforts in working toward sending data to the National Hemophilia Registry	Doctor trained in basic hemophilia care Availability and expertise to use factor concentrates (CFC) Dedicated/part time nurse who can administer CFC
Level III	In addition to Level IV, ability to support patients with chronic synovitis/arthropathy	Level IV + physiotherapist with or without facility for radioisotope synovectomy
Level II	In addition to Level III, ability to perform surgery for PWH, 24-h clinical facility, and facility to initiate continuous or intermittent prophylaxis. Ability to use bypassing agents Submit data to the National Hemophilia Registry	Level III + hematologist/MD physician or pediatrician who is trained in hemophilia surgical care. Backup surgical team, 24-h emergency services. Ability to manage other rare bleeding disorders, dedicated nurse coordinator, PMR doctor, occupational therapist, social worker, dentist, psychiatrist (multidisciplinary care). Provides advisory service, including genetic counseling, to patients and health-care professionals
Level I	Ability to conduct ITI treatment. Work in close association with the National Hemophilia Registry	Level II + physician/hematologist trained in ITI

ITI: Immune tolerance induction, CFC: Clotting factor concentrate, PMR: Physical medicine and rehabilitation, PWH: Persons with hemophilia, MD: Doctor of Medicine

Table 2: Levels of laboratory services in the Hemophilia Treatment Centers

Levels of facility	Functionality	Facility requirement
Level IV	PT, aPTT, TT, Mixing studies/correction studies, daily use of quality controls (PNP or commercial plasma)	Manual/semiautomated/automated instruments Trained workforce
Level III	Factor VIII and IX assay, time-dependent Inhibitor screen*,#	Level IV + Trained workforce to perform these tests
Level II	Inhibitor titer/Bethesda assay. Other rare factor assays. vWF assays (quantitative and functional), platelet function tests**	Level III + platelet aggregometer
Level I	Facility or for mutation studies and ability to perform antenatal testing through CVS	Level II + molecular lab

#The inhibitor screen is an aPTT-based test that evaluates the effect of mixing the test plasma with the control plasma after incubation for 1-2 h. A positive inhibitor screen points to the presence of an inhibitor and necessitates an inhibitor assay (Bethesda or Nijmegen modification), *All routine assays should be performed at least once in 2 weeks, **Should be able to perform in case of emergency whenever required. PNP: Pooled normal plasma, CVS: Chorionic villus sampling, vWF: Von Willebrand Factor, aPTT: Activated partial thromboplastin time, TT: Thrombin time, PT: Prothrombin time

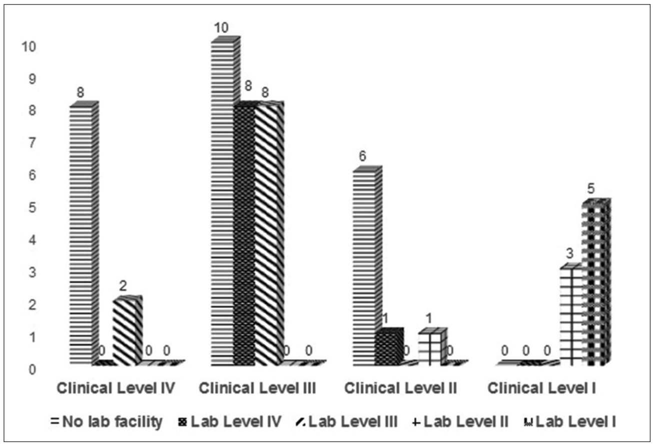

Figure 1: Levels of clinical and laboratory care in the Hemophilia Treatment Centers (*n* = 52)

always translate to the ability to perform factor assay due to lack of expertise.

Internal quality control was undertaken by only five laboratories, and of those, four took part in national or international external quality assurance programs.

Multidisciplinary care availability

All centers were able to provide day care facility for PWH, and 93% of centers were able to provide inpatient services. The availability of different disciplines involved at center level is shown in Figure 2. Staffing of all centers included doctors either full time (71.2%) or part time (28.8%). Seventy-three percent of centers had full-time nurses, and 38.5% of centers had full-time physiotherapist. Although many centers had access to an orthopedic and general surgeon, they did not perform surgeries in PWH.

Space allocation

Twelve centers had dedicated outpatient department space and rest managed the patients in shared space collaborating with other facilities within their institutions. Shared inpatient department space was utilized by 45 centers, and three centers had exclusive hemophilia inpatient facility [Table 3]. One center existed as a stand-alone HTC of clinical Level III and laboratory Level II with facility for admissions related to acute and chronic joint complications. They had a full-time doctor, nurse, and a physiotherapist, and patients were referred to another tertiary care center for surgical management.

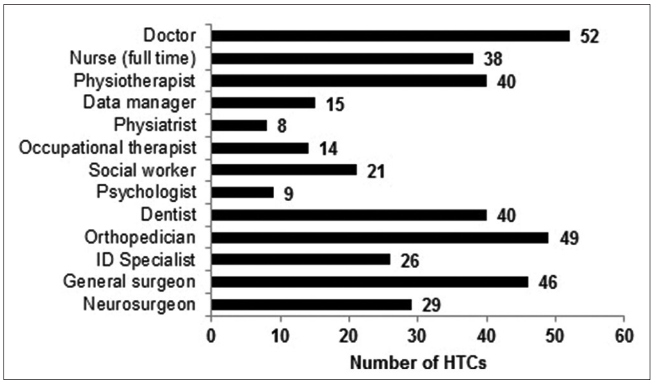

Figure 2: Access to various disciplines in the Hemophilia Treatment Centers (*n* = 52)

Surgical support

Twenty-six centers offered no surgical support to PWH. Thirteen centers offered only minor surgeries, and 13 centers offered both major and minor surgeries. Of the 26 centers offering surgery, only half could perform factor assays.

Outcome assessment

Of the 52 responding centers, 16 offered some form of outcome assessment. Missing school documentation (10) and annual bleeding rate (8) were the most commonly performed outcome assessment measures. HJHS, dental health status, FISH, and Hemo-QoL were performed in 6, 5, 3, and 2 centers, respectively.

Table 3: Characteristics of the Hemophilia Treatment Centers with regards to infrastructure (*n*=52)

Characteristic	*n* (%)
Type of center	
Government sector	49 (94.2)
Private sector	3 (5.8)
Tertiary care center	29 (55.8)
Secondary care center	15 (28.8)
Primary care center	8 (15.4)
Outpatient space allocation	
Dedicated space	12 (23.1)
Sharing with general OPD	22 (42.3)
Sharing with thalassemia unit	8 (15.4)
General OPD and thalassemia unit	3 (5.8)
Chemotherapy area/day care center	1 (1.9)
Other areas (not specified)	6 (11.5)
Inpatient space allocation	
No IPD services	4 (7.7)
Dedicated IPD space	3 (5.8)
Shared space	45 (86.5)
Pediatrics ward	15 (28.8)
Internal medicine ward	11 (21.2)
Clinical hematology ward	4 (7.7)
Emergency ward	1 (1.9)
Pediatrics and Internal medicine ward	10 (19.2)
PMR	1 (1.9)
Oncology ward	2 (3.8)
Not specified	2 (3.8)

PMR: Physical medicine and rehabilitation, IPD: Inpatient department, OPD: Outpatient department

Discussion

This study has shown a wide variation in the clinical and laboratory services within the HTCs in India. Almost half of the HTCs did not have laboratory facility. Of all the HTCs which cared for PWH, only 6 qualified for the EHTC criteria and/or EHCCC criteria.

The terminologies Hemophilia Center (HC), HTC, Hemophilia Care Center (HCC), and Hemophilia CCC (HCCC) have been used internationally for referencing centers caring for PWH. Although there have been attempts to define each of these, there exists ambiguity, especially in developing countries with limited resources.

It is imperative to have an inclusive stratification model to define hemophilia care, especially for regions, where the support systems are evolving. This will also help in planning the delivery of care and evaluating the center for its role and responsibilities. Such a system also provides a framework for future center development.

Over the past 20 years, many models have been proposed in different parts of the world [Table 4]. All of them have tried to incorporate both the clinical and laboratory services, but this poses difficulty in categorizing a center where discrepancy in the ability to deliver each element of care exists. Among all the categorization models, the most clearly defined and standardized is the European Hemophilia Network project, HTCs, and CCCs based on parameters mentioned above.[11]

If one was to apply the EHTC/EHCCC parameters in India, only four centers qualified for EHTC criteria and two centers for the EHCCC criteria leaving out more than 88% of centers. Thus, the utility in assessing centers and guiding development need to be evaluated further. Based on the varied socioeconomic status in a country, there is a limitation in laboratory expertise and facility.

The concept of components of an HTC is still evolving in India. The focus on hemophilia has improved in the past 10 years because of allocation of funding for free factors by the state governments. Almost 75% of states in India now provide free factors to PWH which will suffice for at least on demand use.[17]

Multidisciplinary care for PWH entails bringing together a team of caregivers across different specialties. While the concept of dedicated space and stand-alone HTCs are possible designs, HTC is a virtual concept which interlaces different departments with a common cause of keeping the welfare of the PWH as the unifying goal. This is best possible in a multispecialty hospital where the facilities already exist. The challenges in these settings are limited clinical and laboratory expertise. As shown in our study, some of the clinical Level II centers were doing surgeries in PWH without an in-house laboratory by sending the samples to external laboratories. This practice can result in untoward complications. Capacity building for hemophilia care with available workforce with restructuring and improving the facilities would be the best way forward in establishing HTCs at different levels.

The stratification model used in our study dichotomizes both clinical and laboratory services and gives room for HTCs to have different levels of clinical and laboratory services. This also serves as an inclusive model inspite of the wide range of disparity in the services across a nation.[18] These criteria may require to be further modified to include patient numbers served by an HTC and another substratification of Level 1 to Level 1 plus could be added to recognize the centers that are recognized by the WFH as regional or International HTCs.

Conclusion

This HTC stratification model shows marked variation in the levels of clinical care and laboratory services. This model can also assist planning and implementation of services in a given state/province or a country in a top-down approach and provides objectivity in the functionality and facility requirement. This is an aspirational model where new centers can adopt policies and request the government for support to fulfill its basic

Table 4: Previously defined hemophilia center stratification models

Study	Types of categorization	Parameters considered	Difference from the current HTC stratification model
Peak *et al*., 1995[13] (UK and Israel)	Types of laboratories CL CCL Reference coagulation laboratory RCL	Types and number of tests vWAg assay and platelet aggregation studies Multimer analysis and carrier detection	Meant only for the laboratory Minimum requirement includes factor assay even for CL
Srivastava *et al*., 1998[14] (India)	Primary HCC Secondary HCC Tertiary HCC Comprehensive HCC	Number of beds Various laboratory tests including venous clotting time, diagnosis of carrier status, prenatal diagnosis	Number of beds, laboratory tests is combined Clinical services are not defined
Isarangkura P, 2002[9] (Thailand)	Level 1: No treatment (no MD) Level 2: MD for hemophilia treatment Level 3: 10 hemophilia care Level 4: 20 hemophilia care Level 5: Comprehensive hemophilia care Level 6: Reference center for hemostatic disorders	Clinical care and treatment Laboratory services Therapeutic products (FFP, CPP, and CF, patient–parent organization)	All the services mentioned are combined, and blood products and patient–parent organization also determine the stratification
Chuansumrit, 2003[15] (Thailand)	Hemophilia primary care center Hemophilia Treatment Center Comprehensive care center Reference center for hemostatic disorders	Type of hospital (health stations, provincial hospitals, regional hospitals, and university hospitals) Number of beds Clinical services Laboratory tests Prevention	Number of beds, laboratory and clinical services are combined
Calizzani *et al*., 2013[16] (Italy)	Level 1 HC Level 2 HC	Level 1 based on 23 different criteria combining both clinical and laboratory requirements Level 2 additional parameters	
Giangrande, *et al*., 2014[11] (European)	EHTCs, providing local routine care EHCCCs	Minimum number of severe hemophilia patients Expert hemophilia medical cover Coagulation tests and related “turnaround time” of the laboratories Integrated approach to patient multidisciplinary Comprehensive care	Clinical and laboratory services are combined Outliers who do not fit into any of these criteria will be high

CL: Coagulation laboratory, CCL: Comprehensive coagulation laboratory, FFP: Fresh frozen plasma, CF: Clotting factor, CPP: Cryoprecipitate-poor plasma, HC: Hemophilia center, EHTCs: European Hemophilia Treatment Centers, EHCCCs: European Hemophilia Comprehensive Care Centers, RCL: Reference coagulation laboratory, vWAg: von Willebrand Antigen, MD: Doctor of Medicine

requirements. It can also help in fund allocation and future planning based on levels of care. Self-assessment, auditing, certification, and accreditation can be derived from this model. Larger studies and validation in other countries with similar socioeconomic profile are required to assess its applicability.

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Conflicts of interest

There are no conflicts of interest.

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