

# Status of Thalassemia and Haemophilia Services in Existing Health Care Delivery System of the Punjab

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This study was conducted to evaluate current diagnostic, therapeutic, transfusion Services and their mutual liaison for Thalassemia and Haemophilia disorders in existing health care system of the Punjab. A sample field survey of health facilities providing care for thalassemia and Haemophilia patients or with its potential capability was conducted, involving 75 units (including paediatric units, diagnostic laboratories, blood banks/transfusion services, Thalassemia /Haemophilia Centres) of 27 health institutes/facilities scattered in 12 districts of Punjab. The survey revealed that the number and qualification of staff; capacity of buildings; and equipment for routine tests are sufficient with few exceptions to establish Thalassemia /Haemophilia Services networks all over the Punjab. However there are major deficiencies in staff's knowledge and skills in the management of Thalassemia /Haemophilia patients; equipment and kits for specific diagnostic tests; blood component and other therapeutic supplies; transport facilities for distribution of delicate blood components to peripheral health facilities and Information system for Thalassemia /Haemophilia. The most important problem identified is the very weak inter/intra institution co-ordination/referral linkage and absence of standardised protocols for case management and laboratory diagnosis.

**Keywords:** Thalassemia, Haemophilia. Services, Health delivery, Punjab

The hemoglobinopathies are probably the world's most common genetic diseases: The World Health Organization has estimated that at least 5% of the population is carrier for one or other of the most serious forms, the alpha- and beta-thalassemias and the structural variant hemoglobins S, C, and E, which are found at polymorphic frequencies in many countries.<sup>4</sup> Because of increased population mobility, the disease is found today throughout the world, even in places far from the tropical areas in which it arose<sup>5</sup>. Thalassemia is the most common inherited disorder in Pakistan and there are inadequate treatment facilities for over 4000 homozygotes born each year. Prevention of these disorders therefore forms an essential part of the management of this enormous health problem. There have been characterized 1216 beta-thalassaemia alleles from the five major ethnic groups of Pakistan. The complete spectrum comprised 19 different mutations. There are important ethnic and regional differences in the prevalence of mutations.<sup>6</sup> In Pakistan, the estimated carrier status is about 7%. The estimated number of patients in Pakistan are 14000, 50% of them reside in Punjab. The number of registered patients with various organizations is about 4000 in Punjab<sup>7</sup>.

Hemophilia is a bleeding disorder with X-linked recessive pattern of inheritance with only manifestation in the males. The genetic basis leads to deficiency of vital blood clotting protein, either factor VIII or factor IX. The deficiency of factor VIII is known as "Hemophilia A" or "Classical Hemophilia". The deficiency of factor IX is known as "Hemophilia B" which is also named as "Christmas Disease."<sup>8</sup> Both conditions are characterized by episodes of prolonged bleeding especially in to the muscles, joints or internal organs of the body. Hemophilia A affects approximately 1 in 7500 males, while

Hemophilia B is less common, accounting for only 15-20% of cases of hemophilia.<sup>9</sup> Although the local estimates are not available but the incidence of these congenital disorders would be higher as compared to western estimates of disease due to traditional trends of consanguineous marriages in our country. Therapy of thalassemia has in the past been confined to transfusion and chelation. Recently, novel modes of therapy have been developed for thalassemia, based on the pathophysiology and molecular pathology of the disease, both of which have been extensively studied<sup>10</sup>.

There are problems with management of thalassemia and hemophilia in developing countries due to lack of awareness, inadequate diagnostic facilities and scarce blood product preparation, their preservation and transport facilities. The priorities in establishing services for thalassemia and hemophilia include training care providers, setting up care centers, initiating a registry, educating affected people and their families about the condition, providing low-cost factor concentrates, improving social awareness and developing a comprehensive care team.<sup>11</sup> A hematology laboratory capable of reliably performing clotting times with correction studies using normal pooled, FVIII and FIX deficient patients plasma and factor assay is most essential for diagnosis. More advanced centralized laboratories are also needed. Molecular biology techniques for mutation detection and gene tracking should be established in each country for accurate carrier detection and antenatal diagnosis<sup>12</sup>.

Different models of thalassemia hemophilia care exist in the developing and developed countries. In Pakistan and India, there is no support from the government. Services, Blood, factor concentrates, blood

products and chelating medicine are organized mostly by the Non-government Organizations<sup>13</sup>. Haemophilia is managed with minimal replacement therapy (about 2000 i.u./PWH/year). In Malaysia, where the system is fully supported by the government, facilities are available at all public hospitals and moderate levels of factor concentrates can be made available 'on-demand' (about 11,000 i.u./PWH/year) at the hospitals. Haemophilia care in South Africa is provided through major public hospitals. Intermediate purity factor concentrates are locally produced (about 12,000 i.u./PWH/year) at low cost. The combined experience in the developing world in providing haemophilia services should be used to define standards for care and set achievable goals<sup>11,13</sup>.

The use of blood product transfusions and antibiotics has improved the premature deaths and disabilities among children with thalassemia major. Unfortunately repeated transfusion leads to build-up iron in the body, which can damage heart, liver and other organs in the body. Iron chelators are required to decrease the iron load in the body. Children with thalassemia major treated with frequent blood transfusions and iron chelation live 20 to 30 years longer<sup>14</sup>.

The disease are present in the genetic material and can not be treated at the time of its manifestation, however the disorder can be prevented among the future generation with full medical information about the testing of trait, prenatal diagnosis, genetic counseling, health education and family planning<sup>15</sup>.

#### Objectives of the study

1. To evaluate the current diagnostic, therapeutic and transfusion facilities for Thalassemia and Hemophilia in Punjab.
2. To assess the deficiencies in terms of physical/human resources, supplies and equipment's in the existing health delivery system to establish these services
3. To make recommendation for the establishment of Thalassemia/Hemophilia services network in Punjab.

#### Methodology

It was a cross-sectional descriptive study based on the primary data collection from the sampled Health Facilities. For the estimation of disease burden the secondary data from the literature was utilised. After the literature review, a field survey was conducted to perform situation analysis of health facilities/institutions currently providing diagnostic/therapeutic services related to Thalassemia and Haemophilia, with special emphasis on their potential capabilities for upgradation and linkage with the other facilities proposed for Thalassemia and Haemophilia Services.

For purpose of this situation analysis, Punjab was stratified in three regions Northern region (Rawalpindi, Sargodha, Faisalabad Divisions) Central region (Lahore and Gujranwala Divisions) and Southern region (Bahawalpur, Multan and Dera Ghazi Khan Divisions).

Out of each region 4 districts were selected, to provide adequate regional representation while ensuring a mix of big and smaller district headquarter cities which can participate in the proposed network. By contacting the relevant departments and NGOs; and visiting the concerned cities a list of all the health facilities providing the diagnostics and therapeutic facilities for Thalassemia and Haemophilia, in each city was prepared. In the meantime, data collection instruments including interview schedule and data extraction forms were designed and pre-tested to collect information for the variables of interest. The main areas covered were adequacy of building and furniture, organisational structure, staff availability and training need, equipment availability and functioning status, regularity of laboratory and therapeutic supplies, clinical case load, information system, community support mechanism, availability and adequacy of case management protocols.

#### Results

In the institutions studied total 5129 children were registered. Out of those only 462 (9.00%) with 95% CI (8.23-9.86) were registered with the government institutions and 4002(78.03%) with 95% CI (76.9-79.15) were registered by NGO's while 665 (12.97%) 95% CI (12.1-13.9) were registered by the institutions with collaboration of government and NGO's.

Out of total registered cases, 4026(78.5%) were suffering from Beta Thalassemia and 725(14.14%) were suffering from Haemophilia A, while no specific information was available for Alpha Thalassemia or Haemophilia B. However 378(7.37%) cases were registered for other haematological disorders. From all the registered cases, 1628 patients visits were made during the month prior to the study period i.e. May 2000; while 22570 patient visits were made during the preceding year i.e. Calendar year 1999. Out of total visits, 90.63% visits during last year were by the patients suffering from beta thalassemia while Haemophilia A shared 6.32% visits during last year.

#### Paediatrics units services profile

As part of this study, 21 Paediatrics units were assessed in 27 institutions, for various services related to thalassemia and haemophilia. Only 4(19.05%) out of 21 facilities were having registration services with liaison with the other related services in the institution and 1(4.76%) having registration without internal liaison. Clinical assessment and consultation were present in 19(90.47%) facilities, while only 5(23.81%) of them had liaison with other related services. Facilities for *blood* Transfusion/ treatment services were available in 20(90.90%) units, while only 5(23.81%) units were providing services with internal liaison and co-ordination. One facility had these services, which were not utilized. Follow-up services were available in 5(23.81%) units with reasonable liaison with other units in the institution, while 16(76.19%) units had no follow up

services. HMIS tools were available in 4(19.05%) units, while 17(80.95%) had no HMIS tools. Health Education Services were not available in 16(76.19%) units. Only four units had this facility, while only one of them had this facility with liaison with other related services.

#### *Services Profile at Thalassaemia / Haemophilia Centre*

As part of this study six thalassaemia/haemophilia Centres were evaluated for various services. Registration services for thalassaemia were available in all the facilities. Referral liaison for consultation and clinical assessment was available in 3(50.0%) facilities. Specific diagnostic services for thalassaemia or haemophilia were not available in any Centre.

The patients were referred for diagnosis but there was no liaison for these referrals. Transfusion and follow up services were available in all facilities. HMIS tools for record keeping were available in all facilities but were inadequate for the establishment of referral/reporting mechanism. Health education services were available in all Centers but the services were without the coordination with the related services like prenatal diagnosis, genetic testing and genetic counseling.

#### *Laboratory Services reference to Thalassaemia and Haemophilia*

In 27 institutes studied 22 had diagnostic laboratories, which were evaluated for various diagnostic services related to thalassaemia or haemophilia. Consultation services were available in 20(90.90%) laboratories. Out of them, formal co-ordination or liaison with the other thalassaemia / haemophilia related services in the institute, was present in 5 (27.73%) facilities only.

Routine diagnostic services were available in all the facilities including Hb, TLC, DLC, RBC morphology and Reticulocyte Count for thalassaemia and Bleeding time, clotting time, platelet count, for haemophilia. While in the liaison with other related services was present only in 5(27.73%) laboratories. 95% CI for routine diagnostic availability was (84.5-100) Specific diagnostic tests for thalassaemia, like Foetal haemoglobin estimation, Hb Electrophoresis, serum iron, serum ferritin and iron binding capacity were available in 3(13.41%) laboratories, and out of them two had a liaison with related services in the institute.

Specific diagnostic tests for haemophilia like Factor assays, PT, APTT, Thromboplastin generation, Test Fibrinogen level and Platelet function Test were available in 2 (09.09%) laboratories and only one of these laboratories had a liaison with other related services. 95% CI for specific diagnostic availability was (2.9-34.9) Blood screening services for HIV and Hepatitis B were available in 14(63.63%) facilities, but without any liaison with other related services. 95% CI for screening services availability was (40.6-82.8)

#### *Laboratory Equipment*

The equipment for routine diagnosis was available in all 22(100%) laboratories, but was found non-functional in 1

(4.55%) of them. 95% CI for routine functional equipment was (77.1-99.7) Specific diagnostic equipment for thalassaemia and haemophilia was available in 5(12.75%) laboratories, while it was found functional in 3(13.64%) laboratories only. 95% CI for specific diagnostic equipment was (2.9-34.9)

#### *Supply of Reagents and kits etc. for Laboratories*

The routine diagnostic supplies were generally available in all 22(100%) laboratories but the supplies were irregular in 4(18.18%) of these laboratories. 95% for regular routine diagnostic supplies was (59.7-94.9)

Out of 14 laboratories with services for screening tests, kits for blood screening were regular only in 3 (13.64%) laboratories. In other laboratories it was irregular in 9(40.91%) while permanently out of stock in 2(9.09%) laboratories. 95% CI for regular supply of screening kits was (2.9-34.9). The kits for Hb electrophoresis were regularly available only in 1 laboratory while it was irregularly available in 2 other laboratories. The specific reagents for factor assay were regularly available only in 1 of the laboratories and irregularly available in 1 laboratory. 95% CI for the regular supply of specific diagnostic kits was (0.11-22.8)

#### *Services Profile in the blood Banks*

In 27 institute evaluated, transfusion services in the form of blood banks were present in 26 institutes. The consultation services were available in 23(88.46) facilities, while among those it was available and utilised with liaison in 9(34.62%) facilities, only. The blood screening, bleeding and storage services were available in all 26 (100%) facilities. But only 10(38.46%) of these facilities, these services were utilised with liaison with the related services Blood transfusion facility within the blood bank was available only in the 6(23.08%) Blood Banks attached with Thalassaemia/Haemophilia Centres. Blood component preparation and storage services were available in 6(23.08%) facilities only, while among them 5(19.23%) have liaison to related services.

#### *Thalassaemia Haemophilia related equipment in the Blood Banks*

Blood grouping, cross matching and storing equipment was available in all 26(100%) of the blood banks. 95% CI for functional Grouping Cross Matching equipment was (86.7-100.00). Equipment required for preparation of blood products was available in 7 facilities only. Among them it was found non-functional in one facility. 95% CI for functional blood product equipment was (8.9-43.6). Apheresis (Cell Separator) equipment was available in 3 facilities, and all of them were functional.

#### **Discussion**

The study was aimed at the assessment of existing clinical load shared by thalassaemia and haemophilia and potentials in the existing health services for the establishment of thalassaemia and haemophilia services in Punjab. Due to number of technical reasons and resource limitation, it was

not feasible to conduct a burden of disease survey, as part of this situational analysis. In the absence of the primary data, the estimates of disease prevalence were based on the available secondary data collected as part of literature review and discussions with the experts working in the field.

Out of total 27 facilities studied a total of 4,000 patients have been registered in all the facilities combined. The study was conducted in only 12 sampled districts instead of a total of 34 districts, so the total number of registered patients could be less than 50.0% of actual number. However while interpreting these figures it has to be kept in mind that this registration includes multiple registration with no mechanism of removal from register in case of death or lost to follow up.

The secondary data from the literature review has shown that the Thalassemia is the most common inherited disorder in Pakistan and there are very inadequate treatment facilities for over 4000 homozygotes born each year.<sup>6</sup> According to WHO estimate 5% of the world population have Alpha or Beta Thalassemia Genes. In the light of this estimate, 2,250,000 people in Punjab have the genes. According to another estimate 7% of Pakistan's population is carrier of the disease, which gives a carrier estimate of 5,250,000 for Punjab.<sup>7</sup> The disease has been noted to be more common in people of Italian, Greek, Middle East, South Asian and African ancestry. As large groups of people living in Punjab are descendants of races from Greece and Middle East, overall risk of disease is likely to be higher in Punjab as compared to general world. Regarding incidence of disease over 300,000 infants with major syndromes are born every year and the majority die undiagnosed, untreated or under-treated an estimated birth of 1250 children in Punjab suffering from severe thalassemia. According to another estimate Pakistan has a total of 14,000 patients of thalassemia, which give Punjab an approximate share of 7,000 patients, ignoring any racial variation within the country.<sup>7</sup>

According to a global estimate, Haemophilia A affects one male in every 7,500 males, so in Punjab approximately 5,200 males would be effected by Haemophilia A.<sup>9</sup> Haemophilia B is considered to be 15-20% of total cases of Haemophilia thus Punjab is estimated to have approximately 1,000 - 1,300 cases of Haemophilia B. The consanguineous marriages are very common in Pakistan, due to this cultural practice the risk of Haemophilia should be much higher in this country as compared to the western races where consanguineous marriages are not common.

As the management of both of these diseases involves the contribution of many disciplines of health care system, therefore the various health institutions in the Punjab were critically evaluated for different issues related to thalassemia or haemophilia services. The existing health

care system has the following strengths and weaknesses that can help to establish a network of Thalassemia/ Haemophilia Centers in the Province.

### Conclusion

As described in the results section, in the existing health care system there is adequate infrastructure in terms of buildings, equipment and manpower available all over the Punjab which can provide a strong base for development of integrated comprehensive services. In the public sector there is an organised network of hospitals at district/divisional headquarters along with a number of teaching hospitals in five major cities; all of which have variable capability of providing diagnostic and clinical care to the thalassaemia/ haemophilia patients. Attached to these hospitals, there is also well organised network of transfusion services (Blood Banks) with separate directorates at the Divisional and Provincial Level. Therefore, the main pillars for the establishment of Thalassemia and Haemophilia are available at the District Level in the existing health care settings. In order to establish the integrated Thalassemia and Haemophilia Care in Punjab the only requirement is the organisation of network with clear lines of co-ordination and communication, to utilise various disciplines available in the existing health care system with some additional resource inputs in terms of equipment, supplies and training of staff.

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