Building blocks of hematology in the last 3 decades in Pakistan

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Background

The discipline of hematology is a new field in Pakistan. Pakistan is one of 57 countries facing shortages of health professionals below the threshold level defined by the World Health Organization. Hematologic disorders, especially hemoglobinopathies and bleeding disorders, are more prevalent in our population than in some others as a result of consanguinity. The environment may also be a contributory factor in bone marrow failure and malignant disorders. Before 1990, hematology (diagnostics and therapeutics) and blood transfusion services were almost nonexistent in Pakistan. The team of the National Institute of Blood Diseases and Bone Marrow Transplantation started the awareness and training drive in Pakistan.

Objectives

The National Institute of Blood Diseases & Bone Marrow Transplantation (NIBD & BMT) has established the following 8 goals:

1. Establish hospital-based hematology diagnostic services.
2. Establish hospital-based safe blood transfusion services capable of providing all required blood components.
3. Develop qualified human resources to provide these services.
4. Establish clinical hematology services.
5. Train hematologists, nursing staff, apheresis technologists, clinical pharmacists, clinical scientists, and genetic counselors.
6. Develop national, regional, and international collaborations for training and research in subspecialties of hematology.
7. Establish research facilities.
8. Expand the above-listed facilities to other cities in Pakistan.

Hypothesis

We will be able to provide cost-effective diagnosis and treatments with short turnaround times. We will use collaborative research-based investigations of locally important health conditions because they are an effective method of capacity building with sustainable goals.

Capacity building

Tahir S. Shamsi, MD, received training in hematology and specialized in bone marrow transplantation (BMT) under the mentorship of Steve Schey, MD, at Guy’s Hospital in London (United Kingdom) in the early 1990s. He also provided guidance in the initial years of the BMT program in Pakistan. He has written 119 articles, 6 books, and 22 chapters in various books, and he has trained 34 family care practitioners (MDs) in hematology, 9 transplant physicians, and 9 doctor of philosophy (PhD) scholars. He is Pakistan’s advisor in hematology for the Royal College of Pathologists (RCPath) in the United Kingdom. He is also a fellow of the Royal College of Pathologists, a member of the American Society of Hematology (ASH), International Society on Thrombosis and Haemostasis (ISTH), World Federation of
Hemophilia (WFH), European Hematology Association (EHA), Center for International Blood & Marrow Transplant Research (CIBMTR), Asia Pacific Blood and Marrow Transplantation (APBMT) group, Pakistan Society of Hematology, Pakistan Pediatrics Association, Pakistan Society of Clinical Oncology, and the Pakistan Bone Marrow Transplant Group.

Human resources

- Two transplant physicians received training at Guy’s Hospital, London, United Kingdom.
- Two nurses received training at Guy’s Hospital, London, United Kingdom.
- Five clinicians were trained in the subspecialties of thrombosis, hemostasis, blood cancer management, hemoglobinopathies, and women’s hematologic issues at various locations in the United Kingdom, Europe, and the United States.
- Six paramedics/apheresis specialists received training locally and in Malaysia.
- Four researchers/clinical scientists received training in London (United Kingdom), Germany, China, and the United States.
- Three pharmacists were trained locally.
- Two infection control nurses were trained locally.
- Two media marketing specialists were trained locally.

Transfer of knowledge

The NIBD team used various modes of communication such as workshops, online sessions, conferences and seminars, short courses, social media, outreach clinics in peripheral areas, placement of personnel building blocks in underdeveloped hospitals, and in-house training throughout Pakistan.

Timeline for the establishment of hematology institutions and organizations in Pakistan by specialty

**Bone marrow transplantation offered for the first time.**

- 1995: Dr. Ziauddin Hospitals, Karachi.
- 2000: Bismillah Taqi Blood Diseases Centre, Karachi.
- 2003: Bismillah Taqi Institute of Health Sciences, Karachi.
- 2009: Shifa International Hospital, Islamabad.
- 2016: National Centre for Blood Diseases, National Hospital, Lahore.
- 2017: Children’s Hospital, Lahore.
- 2019: Bahawal Victoria Hospital, Bahawalpur.

**Hemoglobinopathies.**

- 2001: Sindh Institute of Urology and Transplantation, Karachi.
- 2004: Bismillah Taqi Institute of Health Sciences, Karachi.
- 2010: Omair Sana Foundation, Karachi.
- 2012: Outreach clinics for teaching and awareness throughout Pakistan.
- 2019: Children’s Hospital, Karachi.

**Thrombosis and hemostasis.**

- 1996: Dr. Ziauddin Hospitals, Karachi.
- 1997: Fatimid Foundation and Hussaini Laboratory and Blood Bank (management of hemophilia).
- 1999: Sindh Institute of Urology and Transplantation (secondary screening).
- 2001: Bismillah Taqi Institute of Health Sciences Karachi (management of hemophilia).
- 2004: Collaboration with Civil Hospital (issues of women with blood disorders), Karachi.
- 2007: Novo Nordisk Haemophilia Foundation (NNHF) Pakistan, PK-1 capacity building for hemophilia in Karachi.
- 2010: NNHF Pakistan, PK-4 capacity building for the diagnosis and management of bleeding disorders for patients throughout Pakistan (Lahore, Rawalpindi, Peshawar, Quetta, Muzaffarabad, and Multan).
- 2011-2013: Established a laboratory to study genetics of bleeding disorders in NIBD.
- 2013-2019: Established a reference laboratory in NIBD that provided consultancy, prenatal testing, and genetics testing for blood disorders in patients throughout Pakistan.

**Blood cancer management.**

- 1996: Dr. Ziauddin Hospitals, Karachi.
- 1999: Sindh Institute of Urology and Transplantation, Karachi.
- 2001-2007: Bismillah Taqi Institute of Health Sciences, Karachi.
- 2008-2019: Established a reference laboratory in NIBD that provided consultancy, prenatal testing, and genentic testing for blood disorders in patients throughout Pakistan.

**Diagnostic laboratory services**

Approximately 34 MDs, 9 PhDs, and more than 100 clinical scientists and laboratory technologists were trained. The Diagnostic Division of NIBD had a fully equipped advanced hematology laboratory that could perform:

- Routine hematology tests such as complete blood count, detailed bone marrow examination with trephine biopsy, and special cytogenetic staining for leukemia diagnosis;
- Flow cytometry for markers of leukemia and lymphoma, red blood cell and platelet disorders, stem cell analysis, and lymphocyte subset analysis;
- Molecular medicine (HLA class I and II low and high resolution, chimerism, chorionic villus sampling (CVS) and patient screening for hemoglobinopaties by polymerase chain reaction (PCR), XmnI polymorphism-158 (computed tomography), BCL2 gene polymorphism by PCR, HLA DQ2 and DQ8, myeloproliferative neoplasm profile, qualitative and quantitative detection of infectious markers such as BCR-ABL, PML-RARA, MLL, FLT3, JAK2, and CALR; and
- Cytogenetics and fluorescence in situ hybridization (FISH) assays for conventional karyotyping. FISH probes for PML-RARA, MLL, PDGFRα and PDGFRβ gene rearrangement, BCR-ABL 4;14, 8;21, and 16;16 translocations; 20q, 5q, 7q, and 17p53 deletions; and trisomies 13, 18, 21, X, and Y;
• Primary and secondary screening for acquired and congenital coagulopathies was performed by thrombosis and hemostasis specialists, who also tested for clotting factors, thrombophilia markers, menorrhagia profile, and platelet aggregation;
• Genomics experts helped with sequencing of clotting factors and performed assays for platelets, thrombophilia, thalassemia, selected cancer genes, and myeloid and inherited panels of next-generation sequencing;
• Apheresis and transfusion medicine specialists encouraged volunteers to donate blood through blood camps, and they performed blood collection, screening, preparation of quality blood products, peripheral blood stem cell collection, stem cell cryopreservation, transfusion of mega unit platelets, and therapeutic apheresis of plasma, platelets, leukocytes, and red cells; and
• Experts are on board to perform histopathology, immunology, clinical chemistry, microbiology, and parasitology tests.

Clinical development

• Twenty-four clinics with different subspecialties such as hematology, 34 FCPs, 22 postdoctoral fellows, more than 50 nurses, 5 infection control nurses, more than 30 nurses aids, and more than 20 pharmacists. Clinics are located in the NIBD and different cities of Pakistan.

Research and development

• More than 10 clinical research associates are involved in multiple clinical trials and managing the resulting data.

Administration

• NIBD & BMT has more than 500 employees, including those in housekeeping, finance, human resources, media marketing, procurement, and maintenance.

Coaching

The fourth generation is involved in research and coaching under the supervision of senior practitioners for in-house and countrywide trainings. These students came to the NIBD and passed their exams.

Further progress by the next generation

• Pioneer in BMT: more than 600 BMTs were performed. Thalassemia and aplastic anemia were the most common indications. Approximately 13 publications were prepared, and several practitioners registered with CIBMTR and the Human Organ Transplant Act (HOTA). The HOTA is the regulatory body whose permission is needed before any center starts organ transplantation in Pakistan. Its team visits the site physically, evaluates the facilities in the center and hospital where the transplants are intended to be done, and evaluates the credentials of the transplant team and support services staff and planned SOPs of the center. Approved centers have to follow the legal framework of the authority. Success rate for BMTs in aplastic anemia is higher compared with other hematological disorders. Six fellows were trained internationally.

• Pioneer in prenatal testing of bleeding disorders; 6 scholars earned their PhD degrees, 50 people became master trainers, and 5 fellows were trained internationally. By collaborating with 10 international experts, we were able to publish more than 40 articles in journals with good impact factors. More than 3000 patients were screened. von Willebrand disease type 3 and platelet disorders are the most prevalent bleeding disorders among our patients. More than 50 novel mutations have been identified so far.

• Pioneer in blood cancer genetics and rare blood disorders. More than 10 articles have been published, and 6 scholars earned their PhDs. Jak2-v617f was reported in 26% of patients with chronic myelogenous leukemia.

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| Subspecialty                     | International organizations                                           | National organizations                            | Mentor and collaborators                        |
|----------------------------------|-----------------------------------------------------------------------|--------------------------------------------------|------------------------------------------------|
| Bone marrow transplant           | Guy’s Hospital, London, United Kingdom                                | Philanthropists: Zakat, Pakistan Bait-ul-mal      | Steve Schey, Majid Kazmi, Muzaffar H. Qazilbash, |
|                                  | MD Anderson Cancer Center, Houston, TX                                | Governments of Punjab, Balochistan, Sindh, Pakistan| Qaiser Bashir, Lawrence Faulkner                |
|                                  | Oncology, Deke Slayton Cancer Center                                  |                                                  |                                                 |
|                                  | Cure2Children Foundation                                              |                                                  |                                                 |
| Hemoglobinopathies               | Hammersmith Hospital, London National Blood Bank, Kuala Lumpur, Malaysia| PNS, Shifa                                       | Suhai Ahmed, Asad Usman, Yasmine Ayub          |
|                                   |                                                                       |                                                  |                                                 |
| Bleeding disorders               | Bonn, Germany; Milan, Italy; Sheffield, United Kingdom;              | Shehla Tariq Sohail and Masood Fareed Malik,      | Johannes Oldenburg, Flore Peyvand, Anne        |
|                                  | Geneva, Switzerland; Royal Free London, London, United Kingdom;       | Pakistan Hemophilia Patients Welfare Society      | Goodeve, Steve Kitchen, Peter Hans Kohler,     |
|                                  | Debrecen and Budapest, Hungary; Freiburg Germany; NNIF, WFH, ISTH, ASH|                                                  | Philippe de Moerloose, Keith Gomez, Laszlo      |
|                                  | and EHA                                                               |                                                  | Mubsbek, Barbara Zeiger                        |
| Cancer diagnosis and management  | Columbia University, Weill Cornell, New York                          |                                                  | Murty Vundavalli, Jorge Cortes, Ellen K Ritchie|
|                                  | Presbyterian Hospital                                                 |                                                  |                                                 |
Authorship

Conflict-of-interest disclosure: The authors declare no competing financial interests.

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