PATHWEL CENTER OF HEMATOLOGY
& BONE MARROW TRANSPLANT
A project of Pakistan Thalassaemia Welfare Society

PATHWEL times

BIMONTHLY NEWSLETTER
2025 | MAR - APR | VOL 2.2

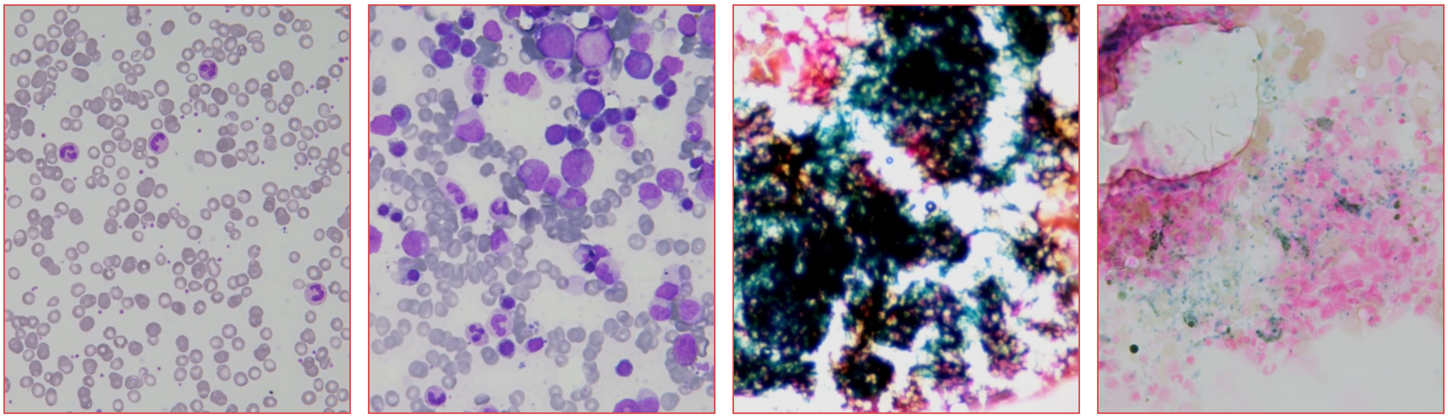
Transplant girl-Eman Bilal
Celebrating her birthday 2 days before transplant

Picture Quiz

by **Dr Sidra Barlas,** *Consultant Hematologist PATHWEL*

Answer on page :09

Eighty Seven years old female patient presented with transfusion dependent anemia for last 8 months. She was pale with no lymphadenopathy or visceromegaly. The complete blood picture showed Hb 7.3 g/dl, WBCs 6.6 x 10^3 /ul and platelet count 219 x 10^3 /ul. Look at the slides and give your diagnosis.



INSIDE THIS ISSUE

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#HealthcareHeroes (Page-06)

From healing hands to henna-adorned hands! Our PATHWEL doctors and staff enjoyed a well-deserved Mehndi celebration after another Ramadan of selfless service.

From Editor's Desk

In the global fight against blood diseases, especially blood cancers, medical science has made extraordinary progress. Yet, while patients in the US and Europe benefit from these advancements, Pakistani patients are left behind, forced to navigate a broken system where life-saving drugs remain out of reach. Many FDA/EMA-approved therapies have been standard of care abroad for years but remain unregistered in Pakistan.

A young ALL patient with a relapsed B-cell ALL could be saved by Blinatumomab, which has a 70-80% response rate. His survival depends on either importing the drug or travelling abroad to get it; this would cost somewhere around $50,000–$100,000—an impossible sum for most Pakistanis. Or take the case of a 60-year-old Myeloma patient who has progressed after first-line therapy. Daratumumab could extend her life by years, but since it's unregistered, she either buys smuggled, unverified versions or goes untreated.

With no legal access, desperate patients turn to unregulated suppliers – drugs smuggled in without proper storage (e.g., temperature-sensitive biologics like Rituximab biosimilars) may be ineffective or harmful. Moreover, counterfeit medicines - such as fake versions of Imatinib, Dasatinib, or Ibrutinib flood the market, putting lives at risk. Doctors, with all their expertise and know-how, can only put up a fragmented and compromised treatment plan offering not much hope to the already hapless patients. There is no recourse if smuggled drugs fail, and the government loses millions in potential tax revenue from legitimate sales.

Every day without these drugs means unnecessary deaths. Pakistan's patients deserve the same fighting chance as those in the US or Europe. At PATHWEL, we urge regulators, policymakers, and healthcare leaders to act now-because when it comes to cancer, delay is denial.

Memorandum of Understanding Between Pakistan Thalassemia Welfare Society and University of Wah

In a significant step toward advancing community welfare and healthcare initiatives, on February 27, 2025, the Pakistan Thalassemia Welfare Society entered into a formal Memorandum of Understanding (MoU) with the University of Wah (UW). This strategic partnership is designed to enhance collaborative efforts in critical areas of public health and social responsibility.

Key Objectives of the MoU. The agreement outlines the following shared goals:
1. Disseminating knowledge on thalassemia prevention and management.
2. Organizing blood donation camps & awareness campaigns.
3. Ensuring seamless blood availability and complimentary donor screening for the UW community.
4. Strengthening outreach programs for thalassemia patients through education and psychosocial support.

Signing Ceremony. The MoU was executed by Maj Gen (R) Dr Parvez Ahmed, MD, Pakistan Thalassemia Welfare Society & Brig (R) Haroon Abbas Khan, Registrar, UW.

Dr Parvez Ahmed expressed gratitude for the University's commitment to this noble cause. He further highlighted opportunities for UW students, especially in Biosciences and Psychology, to engage in internships, research projects, and community service. Brig (Retd) Haroon Abbas Khan reiterated UW's dedication to societal well-being, citing its consistent efforts in public health advocacy and collaborative research. He referenced the University's successful history of organizing blood donation drives and fostering community partnerships.

Present on the occasion were Ms. Nigar Shah, PRO, PATHWEL; Prof Dr Amjad Hassan, Director ORIC; Dr Shaukat Ali, Director QA&E; Ms. Sarah Khan, Acting Director Media; and Dr Bilal Ahmad, Director Student Affairs.

This landmark collaboration represents a transformative step in addressing critical healthcare challenges through strategic social partnership, while advancing the Pakistan Thalassemia Welfare Society's mission to promote accessible, high-quality healthcare services for blood disorders—with special emphasis on thalassemia prevention and care. By uniting academic institutions, medical organizations, and community stakeholders, this initiative exemplifies the power of collective action in fostering a healthier, more equitable society. The partnership not only strengthens public health outreach but also embodies a shared commitment to social responsibility.

Farewell

" Thank you for your efforts. We are grateful for everything you have done for the PATHWEL"

The PATHWEL Center of Hematology and Bone Marrow Transplant extends its sincere gratitude to **Col (R) Dr Kamran Mushtaq** on the conclusion of his tenure as Chief Operating Officer. Dr Kamran Mushtaq played a pivotal role during the formative phase of the center. His contributions were central to the initial structuring of the hospital, including the recruitment of key personnel and the development of foundational administrative frameworks. His enthusiasm and involvement were instrumental in setting the tone for the rapid progression of PATHWEL.

While personal and family commitments limited the extent of his long-term engagement, his early involvement provided essential momentum for the institution's growth. His service reflects a dedication to excellence and an enduring commitment to the mission of the center. On behalf of the entire PATHWEL team, we extend our best wishes to Dr Kamran Mushtaq in all his future pursuits and thank him for his valuable service to the organization.

Blood Camps' Diary

By Ms Nigar Shah
PRO & Camp Coordinator, PTWS

February was a very busy month for collection of blood donations as we had to prepare for the deficit that occur in the month of Ramazan each year. Alhamdulillah, our team put up a very good show and were able to collect sufficient number of donations which were enough to ensure that the children received their scheduled transfusions during the month of Ramazan.

Counter Terrorism Department, Islamabad Police
2 January 2025

PATHWEL arranged a blood donation camp in CTD with a kind approval of Inspector General Islamabad Police. Mr. Abdul Rauf and Ms. Sheeba (Dispensers CTD) and Irfan Kazmi, APS (Assistant Private Secretary) coordinated during the whole activity.

Security Division, Diplomatic Enclave, Islamabad Police
7 January 2025
Islamabad Police organized a blood donation camp in Security Division, Diplomatic Enclave, Islamabad. We greatly appreciate the support of IG Police (Islamabad) organizing back to back blood camps in all six departments/divisions Islamabad Police.

Mobile Van, Blood Donation Drive, Intercity
13, 16, 17, 18, 23, & 25 January 2025
Due to shortage of blood, PATHWEL arranged mobile van blood donation drive in Allama Iqbal Park, Commercial Market, Marir Chowk, and Lake View Park. We collected only 24 bags as public response was not favorable.

Steps College, Satellite Town, Rawalpindi
29 January 2025

PATHWEL arranged a blood donation camp in Steps College with the approval of Founder and Principal Muhammad Khalid. We collected 25 units in this camp. This was a first ever blood camp in Steps College history.

Punjab College, Morgah Campus, Rawalpindi (PGCAPC) | 6 February 2025
Chaudhry M Akram, Director Punjab Group of colleges, approved our request to arrange camps in different campuses of Punjab Colleges. The first blood camp was held in Morgah Campus, Rawalpindi. Principal Prof Ali Aqa Naqvi invited PRO PATHWEL to visit each classroom and give informative and motivational talks to students about the importance of blood donation.

NADRA Regional Head Office, G-10 / 4, Islamabad
11 February 2025

Ms Naz Shoeb, Director General, Regional Head Office, was kind enough to approve blood donation camp in NADRA Regioanl Head Office. The camp was organized by Assistant Director Admin S Azeem Hussain. Deputy Director Admin Fahim Khan, Deputy Director Operations M Khurshid, Deputy Director Projects Shahryar Achakzai and additional IG Motorway Police Islamabad M Zubair Hashmi.

Punjab College, D 9 Campus Satellite Town, Rawalpindi
13 February 2025

PATHWEL organized a second blood donation drive in Punjab College, D 9 Campus. Principal Prof. Tasleem Ashraf and Syed Zaigam Abbas (Student Affairs Officer) supported PRO PATHWEL to visit each classroom to deliver talks about the importance of blood donation.

Foundation University of Science & Technology (FUSST) Lala Zar Rawalpindi | 18 February 2025

We are thankful to Prof Dr Lubna Zafar and the students of Foundation University School of Health Sciences (FUSH) for their cooperation and support in organizing the camp.

Peshawar High Court, Peshawar | 20 February 2025

Advocate Aizaz Ali and Lead Council Osama Khalil (Khalil and Associates) organized this camp with the approval of Registrar Peshawar High Court. We appreciate the hospitality of Khalil & Associates.

Punjab College, D 9 Campus Satellite Town, (evening shift) Rawalpindi | 19 February 2025

This was our third camp in Punjab Colleges. Principal Prof. Tasleem Ashraf (D9 campus) and Syed Zaigam Abbas (Student Affairs Officer) supported our team during this evening drive.

Saifi Mosque (Saddar, Rawalpindi) | 23 February 2025

Executive Member PATHWEL, Mr. Murtaza Burhani organized a blood camp in Saifi Mosque, Saddar, Rawalpindi. His active participation in arranging blood donation camps is really appreciated. Mr. Burhani donated blood for 171st time, indeed a very commendable and noble act of kindness.

Asghar Mall, Govt Graduate College | 25 February 2025

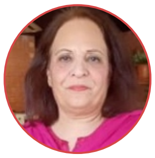
The camp was organized with the approval of Principal Prof Dr Abdul Kabeer Mohsin and VP Mr Aamir Zia. Prof Saima and PRO PATHWEL delivered valuable lectures in classes of Asghar Mall College.

University of Wah, Wah Cantt | 27 February 2025

PATHWEL organized a blood donation camp and an awareness seminar in University of Wah. The event featured Prof Dr Parvez Ahmed, MD PATHWEL as the guest speaker.

Courage & Colors: Smiles, Fun, and Care at PATHWEL

Report by Dr Zohra J Wazir, Chief Medical Officer Thalassemia Wing



A Special Eid Mehndi Event for PATHWEL's Dedicated Doctors & Staff

At PATHWEL, we know that behind every healthy smile of our thalassemia warriors stands an extraordinary team of doctors and staff—working tirelessly, often sacrificing their own celebrations to care for others.

On the last day of the holy month, we transformed the Thalassemia Ward into a festive Mehndi celebration, complete with sparkling bangles, intricate henna designs, and joyful moments of laughter. It was a moment of relaxation and joy for the doctors and staff, giving them a chance to unwind and celebrate before returning to their vital work.

At PATHWEL, we believe caregiving begins with caring for our caregivers too.

A Celebration of Hope & Joy: Eid Milan Party for Thalassemia

This Eid, the PATHWEL brought smiles and festive cheer to our brave patients with a heartwarming celebration on the 4th day of Eid. Dressed in colorful traditional attire, our young thalassemia heroes filled the room with infectious joy, transforming the center into a vibrant hub of happiness. The celebration held special significance for bone marrow transplant survivors, offering them—and all attendees—a powerful reminder of community, resilience, and hope.The event was graced by the presence of Mr. Rizwan Ahmed, President (North Punjab Region) of Al-Khidmat Foundation, along with his dedicated team, who distributed gifts and shared uplifting moments with patients and their families. A heartfelt thank you to Al-Khidmat Foundation, our staff, and everyone who made this day unforgettable!

Together, we're proving that even in the face of health challenges, joy and togetherness always shine through.

Ensuring Joyful Eid Celebrations for Our Thalassemia Heroes

At PATHWEL, we believe every child deserves to celebrate Eid with energy, happiness, and good health. This Ramadan, our team worked tirelessly to ensure that majority of our young thalassemia warriors received their life-saving blood transfusions in the final days of the holy month—helping them maintain hemoglobin levels above 10mg/dl so they could enjoy the festivities to the fullest. There were days when we transfused up to 50 children in a day.

We're proud to have kept the festive spirit alive, ensuring our brave little heroes could participate in the joy of the holiday—free from weakness or fatigue. Their smiles are our greatest reward! A heartfelt thank you to our incredible team, donors, and supporters for making this possible.

Together, we're turning challenges into moments of happiness.

PATHWEL Stars

An Inspiring Journey: Ahmad Faisal's Triumph Over Wiskott-Aldrich Syndrome

by ***Dr. Khalil ur Rehman****, Clinical Hematologist and BMT specialist, PATHWEL*

Before transplant

After transplant

Donor

Born to loving consanguineous parents Ahmad Faisal appeared to be a healthy baby—until the age of one month, when his health took an unexpected turn. He began experiencing frequent infections, recurrent bleeding, and eczema. What followed were countless hospital visits, intravenous antibiotics, and a heavy toll on Ahmad and his family.

Initially misdiagnosed as a case of ITP (Idiopathic Thrombocytopenic Purpura), he was given multiple courses of steroids, but his condition did not improve. Behind his innocent smile lay a rare and dangerous diagnosis that remained hidden until September 27, 2023, when whole exome sequencing confirmed that Ahmad had Wiskott-Aldrich Syndrome (WAS), caused by a C.91G>A (p.Glu31Lys) variant in the WAS gene on the X chromosome.

The diagnosis, while daunting, brought clarity and direction. In a heartening twist, his 8-year-old sister Sadhna was found to be a fully HLA-matched donor, and Ahmad was referred for bone marrow transplant (BMT)—his only chance at a cure.

By the time of his referral, Ahmad was battling peumonia and right eye cellulitis. With prompt treatment including IV meropenem and topical tobramycin, he recovered well and was prepared for the major step ahead.

On March 1, 2024, Ahmad underwent an allogeneic bone marrow transplant, powered by his sister's life-saving stem cells and the unwavering strength of his family. His post-transplant journey was tough—marked by grade III/IV mucositis, CSA-induced hypertension, transient liver dysfunction, and flu-like symptoms. Yet, with remarkable resilience and strong medical support, Ahmad overcame every hurdle.

Now, 410 days post-transplant, Ahmad is GVHD-free, infection-free, and thriving. His donor chimerism is over 95%, and his blood counts remain stable. With continued clinical monitoring and follow-up, he has entered the next critical phase of his recovery—his immunosuppressive medications are now being gradually tapered, and he has begun receiving age-appropriate vaccinations, marking his return to immune independence.

Ahmad's journey is a powerful testament to medical science, family support, and the enduring strength of a child's spirit. From misdiagnosis and suffering to a successful bone marrow transplant and new beginnings, he has emerged stronger, braver, & full of life.

Ahmad's story inspires not only those facing rare diseases but also every family fighting for their child's health. With love, timely care, and determination—recovery is not just possible, it is real.

PATHWEL Galaxy

Contributed by Dr Zohra J Wazir, Chief Medical Officer Thalassemia Wing

TransplantTidings TransplantTidings TransplantTidings

Current use of donor lymphocyte infusions after allogenic stem cell transplantation in Europe: a survey on behalf of the cellular therapy and immunobiology working party of the EBMT

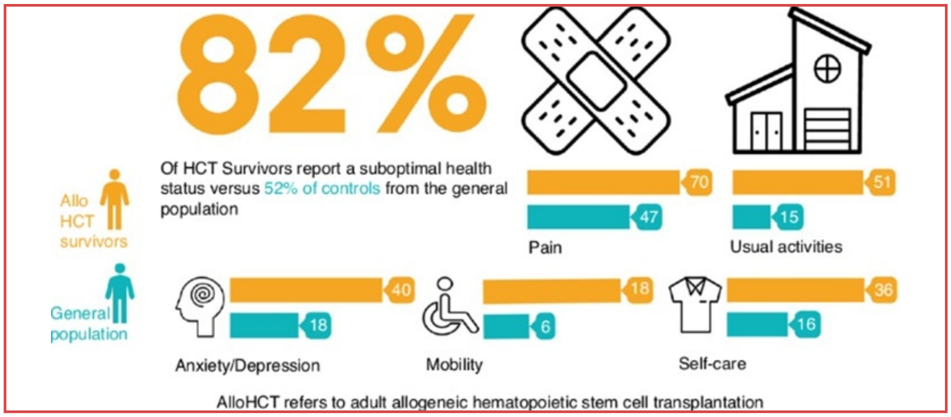
Santoro N, Schmid C, de Witte M et al; Bone Marrow Transplant (2025); https://doi.org/10.1038/s41409-025-02555-9

Unmanipulated donor lymphocyte infusions (DLI) are crucial for enhancing the graft versus tumor (GVT) effect in post-transplant settings. Practices regarding DLI use vary widely among centers, encompassing differences in indications, prerequisites, and application methods. To explore current DLI policies, we developed a comprehensive survey that garnered responses from 165 EBMT centers across 43 countries. Notably, 97% of respondents reported using DLI in their practices. Indications for DLI included preemptive use for minimal residual disease (MRD) positivity in 86.9% of centers and mixed chimerism in 73.1%; therapeutic use for hematological relapse in 73.1%; and prophylactic use for high-risk disease in 43.8%. Active graft-versus-host disease (GVHD) and active infections were deemed absolute contraindications by 85.6% and 57.5% of centers, respectively. 35% of centers did not consider a prior history of acute (a)GVHD as an exclusion criterion. The majority (71.9%) requested immunosuppression withdrawal before DLI. Most centers (71.3%) collected DLI post-transplant, with 78.1% utilizing unstimulated apheresis. The cell doses applied at the first DLI varied significantly, depending on indication, timing, and donor type. This survey provides the largest overview of current DLI practices, highlighting the need for high-quality data to assess the risks and benefits of different approaches.

Life 2.0: a comprehensive cross-sectional profiling of long-term allogeneic hematopoietic cell transplantation survivors compared to a matched general population cohort

Schoemans H, Goris K, Fieuws S et al; Bone Marrow Transplant 60, 507–518 (2025). https://doi.org/10.1038/s41409-025-02521-5

Long-term survivors after allogeneic cell transplantation (HCT) have unique needs. We performed a cross-sectional case-control study to describe the survivorship profile of 244 adult allogeneic transplantation recipients at a median of 8.4 years post-HCT and compared it to controls from the general population (matched 1:3 based on age, gender, and province of residence).



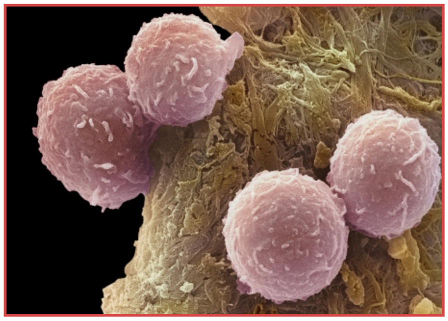
The most prevalent medical complications were graft versus host disease (46.7%), impaired kidney function (63.9%), and the presence of a metabolic syndrome (33.6%). Survivors were significantly more likely to report a sub-optimal perceived health status than controls (82.0% versus 52.1% respectively, OR 4.57, p < 0.0001). They also reported significantly lower employment rates (42.6% versus 55.6% respectively, OR 0.389, p < 0.0001) and more polypharmacy (32.0% versus 9.6% respectively, OR 5.0, p < 0.0001) than matched counterparts. Social support and mental health were generally preserved. Apart for a concerning tendency to medication non-adherence, low physical activity (54.5%), and inappropriate exposition to UV (44.7%), health-related behavior was adequate. Many survivors have a health status comparable to chronically ill patients and, if so, should be managed as such.

Novel patient-centered initiatives based on chronic care models could support survivors in preventing and dealing with long-term complications, regaining functionality, and returning to their role in society.

TransplantTidings TransplantTidings TransplantTidings

Outcomes of patients with multiple myeloma undergoing autologous transplant with suboptimal pretransplant response

Pasvolsky O, Abid MB, Milton DR, Tanner MR, Bashir Q, et al; Outcomes of patients with multiple myeloma undergoing autologous transplant with suboptimal pretransplant response. Br J Haematol. 2025; 00: 1–7. https://doi.org/10.1111/bjh.20062



There are scarce data in the literature focusing on newly diagnosed multiple myeloma (NDMM) patients who undergo autologous haematopoietic cell transplantation (autoHCT) after achieving suboptimal response to induction. To address this, we performed a retrospective, single-centre analysis of patients with NDMM who underwent upfront autoHCT between 2005 and 2021 with a pretransplant response of less than very good partial response (<VGPR). Primary outcomes were progression-free survival (PFS) and overall survival (OS). 1109 patients were included in our analysis. Median PFS and OS for the entire cohort were 38.6 (95% confidence interval [CI], 35.9–41.9) months and 103.8 (95% CI, 96.4–113.2) months, respectively. Patients with high-risk cytogenetic abnormalities (HRCA) had a median PFS and OS of 24.8 months and 69.9 months respectively. In multivariable analysis, the use of post-transplant maintenance (hazard ratio [HR] 0.75, p = 0.001 and HR 0.75, p = 0.008) and achieving complete response (CR) at best post-transplant response (HR 0.60, p < 0.001 and HR 0.51, p < 0.001) were associated with superior PFS and OS respectively. In conclusion, NDMM patients who received upfront autoHCT with a pretransplant response of <VGPR had a median PFS of >3 years and median OS of >8 years. Post-transplant maintenance further improved survival outcomes.

The 2023 EBMT report on hematopoietic cell transplantation and cellular therapies. Increased use of allogeneic HCT for myeloid malignancies and of CAR-T at the expense of autologous HCT

Passweg J, Baldomero H, Angelucci E at al; Bone Marrow Transplantation (2025) 60:519–528; https://doi.org/10.1038/s41409-025-02524-2

In 2023, 47,731 HCT (20,485 (42.9%) allogeneic and 27,246 (57.1%) autologous) in 43,902 patients were reported by 696 European centers. 6042 patients received advanced cellular therapies, 4888 of which were CAR-T. Compared to the previous year there was an increase in CAR-T (+52.5%), in allogeneic HCT (+7.8%) but none in autologous HCT (+0.4%). Main indications for allogeneic HCT were myeloid (11,748; 60.7%), lymphoid malignancies (4,850; 25.0%), and non-malignant disorders (2558; 13.2%). Use of allogeneic HCT increased for AML (+12.1%) and for NHL (+11.0%), particularly in T-NHL (+25.6%). Main indications for autologous HCT were lymphomas (7890; 32.2%), PCD (14,271; 58.2%), and solid tumors (1608; 6.6%) with recovering numbers for autoimmune diseases.

In patients with allogeneic HCT, the use of sibling donors increased by +1.0%, haploidentical donors by +11.7%, and unrelated donors by +11.1%. Cord blood HCT decreased again by −5.4%. Pediatric HCT activity increased slightly (5455; +0.1%) with differences between allogeneic (4111; −0.5%) and autologous HCT (1344: +1.7%). Use of CAR-T increased to a cumulative total of 13,927 patients including patients treated for autoimmune diseases.

Overall, numbers show a complete recovery from the pandemic dip with increased cellular therapy at the expense of autologous HCT. Allogeneic HCT activity focuses on myeloid malignancies.

Picture Quiz Answer

by ***Dr Sidra Barlas****. Consultant Hematologist PATHWEL*

Myelodysplastic syndrome with low blasts & ring sideroblasts (WHO 2022)

Peripheral film and bone marrow aspirate show dysplasia. Iron is markedly increased and there are more than 15 percent ring Sideroblasts.

Morphology Updates

Neutrophilic leukemoid reaction or chronic neutrophilic leukemia—not always so simple

Yorick Sandberg 1 | Leo M. Budel 2 | Barbara J. Bain 3
1. Department of Internal Medicine, Maasstad Hospital, Rotterdam, The Netherlands
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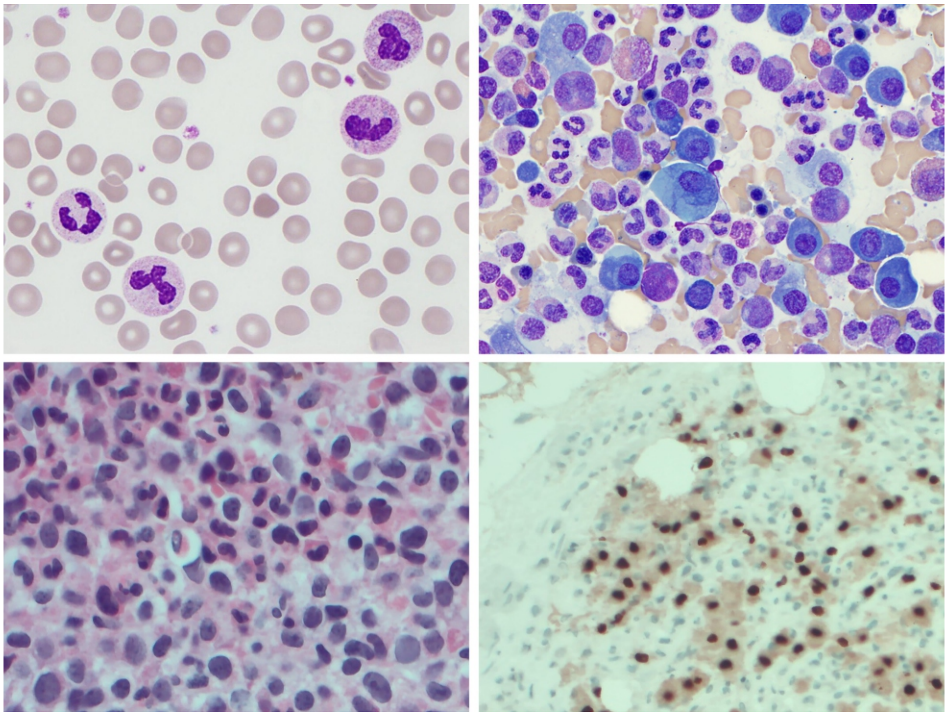
3. Department of Immunology and Inflammation, Imperial College Healthcare, St Mary's Hospital, London, UK.
https://doi.org/10.1002/ajh.27268



An 85-year-old man with a history of hypertension and cerebrovascular disease was admitted with anemia (hemoglobin concentration 100 g/L) and leukocytosis (white blood cell count 68.9 109/L; neutrophils 88%, 60.6 109 /L). Physical examination was unremarkable. His blood film showed toxic granulation and Döhle bodies, but no blast cells or neutrophil precursors (top left, May-Grünwald-Giemsa (MGG) 100 objective). A bone marrow aspirate was markedly hypercellular with neutrophilic proliferation and 24% cytologically abnormal plasma cells; the plasma cells were pleomorphic, sometimes with nucleoli and sometimes with the cytoplasm distended by weakly basophilic material (top right, MGG 100). A trephine biopsy section (bottom left, hematoxylin and eosin, 40) was markedly hypercellular (>90%) with marked neutrophilic proliferation and a clonal plasma cell population showing kappa light-chain restriction and expression of MUM1 (bottom right, immunoperoxidase, 20).

Flow cytometric immunophenotyping demonstrated an aberrant plasma cell population, positive for CD138, CD38, and CD56 and negative for CD19. Protein electrophoresis demonstrated an immunoglobulin A (IgA) kappa paraprotein. Computed tomography was performed and showed no hepatosplenomegaly or lytic bony lesions. A diagnosis of multiple myeloma/plasma cell myeloma was made.

It appeared likely that the patient had a neutrophilic leukemoid reaction, which is well recognized in myeloma. However, other possibilities were explored. Conventional cytogenetic analysis was normal. Molecular analysis showed no BCR::ABL1 or rearrangement of PDGFRA, PDGFRB, FGRF, or JAK2. Additional molecular analysis showed the presence of a CSF3R T618I mutation and concurrent pathogenic mutations in ASXL1 and SRSF2. Thes mutations were not present in the isolated clonal plasma cell population, ruling out acommon clonal origin. The final diagnosis was chronic neutrophilic leukemia (CNL) and a plasma cell neoplasm (PCN). It should be noted that the percentage of clonal plasma cells is lower than usually expected in myeloma because of the marked neutrophilic proliferation.

Concurrent CNL and PCN is rare, but the incidence of plasma cell neoplasms in association with CNL is disproportionately high, occurring in up to 32% of CNL cases.1 PCN-associated neutrophilic leukemoid reaction is also rare but well recognized, likely resulting from granulocyte colony-stimulating factor produced by neoplastic plasma cells.2 The diagnosis of CNL in a case with a coexisting plasma cell neoplasm can only be made if clonality of myeloid cells is demonstrated.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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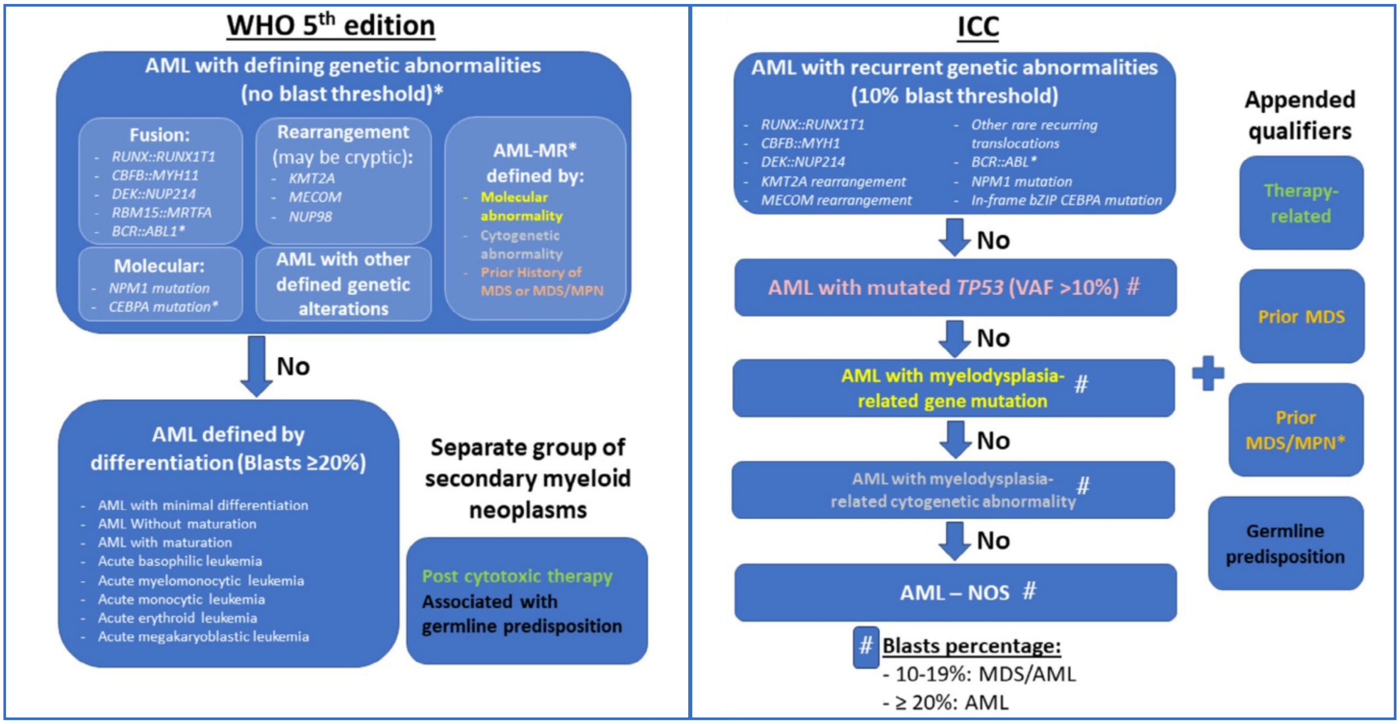
Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits

Comparison between WHO fifth versus ICC AML definitions

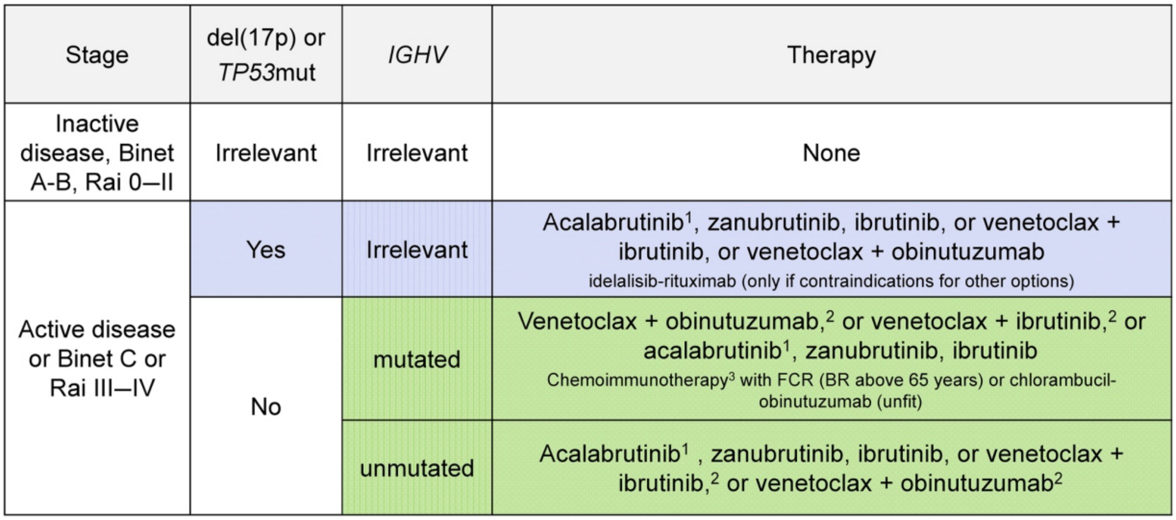
Acute Myeloid Leukemia: 2025 Update on Diagnosis, Risk-Stratification, and Management;
Shai Shimony, Maximilian Stahl, Richard M. Stone et al; AJH; https://doi.org/10.1002/ajh.27625



** ≥ 20% blasts are required for AML definition. Colors reflect similarsubgroups between classifications. AML—acute myeloid leukemia; ICC—international consensus classification; MDS—myelodysplastic syndrome; MPN—myelodysplastic neoplasm;*

Updated treatment algorithm for patients with CLL in first-line indications

Chronic Lymphocytic Leukemia: 2025 Update on theEpidemiology, Pathogenesis, Diagnosis, and Therapy
Michael Hallek; AJH; https://doi.org/10.1002/ajh.27546



Stage	del(17p) or *TP53*mut	*IGHV*	Therapy
Inactive disease, Binet A-B, Rai 0—II	Irrelevant	Irrelevant	None
Active disease or Binet C or Rai III—IV	Yes	Irrelevant	Acalabrutinib[1], zanubrutinib, ibrutinib, or venetoclax + ibrutinib, or venetoclax + obinutuzumab idelalisib-rituximab (only if contraindications for other options)
	No	mutated	Venetoclax + obinutuzumab,[2] or venetoclax + ibrutinib,[2] or acalabrutinib[1], zanubrutinib, ibrutinib Chemoimmunotherapy[3] with FCR (BR above 65 years) or chlorambucil-obinutuzumab (unfit)
		unmutated	Acalabrutinib[1] , zanubrutinib, ibrutinib, or venetoclax + ibrutinib,[2] or venetoclax + obinutuzumab[2]

(1) The addition of obinutuzumab to acalabrutinib may be considered.
(2) Consider and discuss with the patient: Continuous vs. fixed-duration therapy, specific side effects of drug classes (myelosuppression, infections, secondary malignancies for CIT; cardiovascular toxicity and bleeding for BTKi (Acalabrutinib < Ibrutinib); TLS and infections for Ven-Obi; autoimmune disease and opportunistic infections for Idelalisib.
(3) Chemoimmunotherapy in regions where other options are not available or approved.

Annual General Meeting 2024: A Commitment to Hemophilia Care and Community Support

HEMOPHILIA
PATIENTS WELFARE SOCIETY
RAWALPINDI CHAPTER

The Hemophilia Patient Welfare Society (HPWS) Rawalpindi held its Annual General Meeting (AGM) on 25 January 2025 at Pakistan Sweet Home, Islamabad. The event brought together over 100 participants, including doctors, patients, their families, donors, and healthcare providers, to review the achievements of 2024, and discuss future plans for improving hemophilia care.

The AGM commenced with the recitation of the Holy Quran and Naat-e-Rasul Maqbool. Dr Lubna Zafar, President of HPWS, presented the Annual Report, highlighting the society's accomplishments in 2024. These included legal registrations, financial updates, welfare projects, and awareness initiatives under the PACT program.

Dr. Tahira Zafar, Director of the Hemophilia Treatment Center (HTC), RWP, shared the HTC's progress, including the enrolment of 100 new patients, 11 successful surgeries, and extensive training programs for healthcare professionals and patients. She also emphasized international collaborations, such as the launch of the myWBDR application, which allows patients to track their bleeds and contribute to global research.

Inspiring patient interactions followed, Save One Life (SOL) scholarship recipients, and women who successfully established businesses through the Micro Enterprise Grant (MEG) program shared their experiences. HTC coordinator highlighted the transformative power of physiotherapy, encouraging patients to stay committed to their therapy.

The event also recognized the invaluable contributions of donors, including young philanthropist Hijara Bin-e-Shoaib, who actively supports HPWS.

Mr. Zamurd Khan, Founder of Pakistan Sweet Home, reaffirmed his unwavering support for the hemophilia community, promising to fund four outings for children and establish a Satellite Hemophilia Treatment Center at Fatima-tu-Zahra Hospital.

Dr. Tahira Zafar concluded the event with a vote of thanks, expressing gratitude to donors, supporters, and the dedicated HPWS staff for their continuous efforts. The AGM concluded with a group photo and a sumptuous lunch provided by Pakistan Sweet Home.

The HPWS remains committed to its mission of providing quality care and support to hemophilia patients, with plans to expand its reach and impact in 2025. Through collaboration and dedication, the society continues to make a lasting difference in the lives of those affected by bleeding disorders.

Case Report *By Ms. Hina Fatima*

Management of Severe Hemophilia A with Inhibitors and Post-Operative Multidrug-Resistant Escherichia coli Infection following Orthopedic Surgery

An 18-year-old male with severe Hemophilia A and high-titer factor VIII inhibitors presented after a traumatic accident, requiring ORIF for a distal femur fracture. Due to his inhibitor status, he received FEIBA (90 U/kg IV twice daily) preoperatively, with no major bleeding complications. Post-op, he was switched to FFP when FEIBA stocks ran out, prolonging healing due to a subsequent surgical site infection.

Microbial culture revealed ESBL- and CRE-producing E. coli, resistant to most antibiotics (including penicillins, cephalosporins, and carbapenems) but sensitive to doxycycline, polymyxin B, and tigecycline. Targeted therapy was initiated.

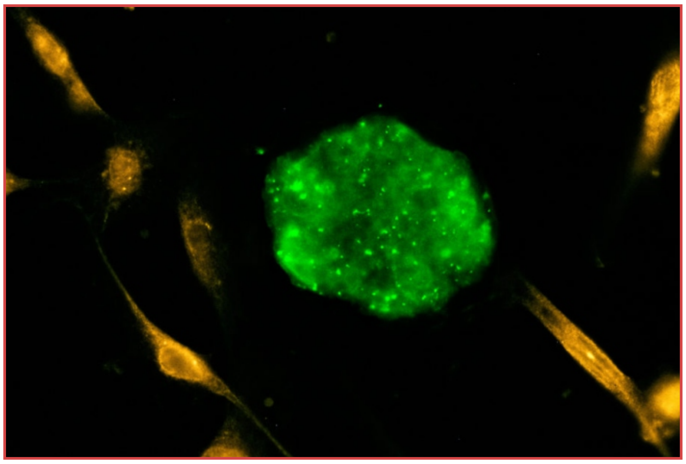
This case highlights:

- The challenges of managing hemophilia with inhibitors during surgery.
- The rising threat of multidrug-resistant infections in post-op care.
- The importance of multidisciplinary collaboration (hematology, infectious diseases, surgery) and tailored antimicrobial stewardship in high-risk patients.

Key Takeaways: Preemptive planning in hemophilia, vigilance for antimicrobial resistance, and precision diagnostics are critical in complex surgical cases.

Breakthrough in Gene Therapy: Lentiviral CD34+ Hematopoietic Cell Treatment Shows Promise for Hemophilia A

A Srivastava, F Aboobacker, G Singh et al; N Engl J Med 2025;392:450-457DOI: 10.1056/NEJMoa2410597VOL. 392 NO. 5



A recent study on Lentiviral Gene Therapy with CD34+ Hematopoietic Cells for Hemophilia A marks a significant advancement in the treatment of this rare bleeding disorder. Hemophilia A, caused by a deficiency of Factor VIII, leads to excessive bleeding and requires lifelong clotting factor replacement therapy.

Researchers have developed a lentiviral-based gene therapy approach that modifies CD34+ hematopoietic stem cells (HSCs) to express Factor VIII. This innovative method enables long-term correction of the disorder by integrating the therapeutic gene into the patient’s stem cells, potentially providing a permanent treatment.

Early preclinical results are promising, demonstrating sustained Factor VIII production and improved clotting function in treated subjects. If further trials confirm its safety and efficacy, this therapy could revolutionize hemophilia A management, reducing dependency on frequent infusions and improving patients' quality of life.

This groundbreaking approach brings hope for a one-time, durable treatment for hemophilia A, paving the way for future advancements in gene therapy.

ہوا کہ سوسائٹی میں وراثت نہیں بلکہ جمہوریت اور میرٹ چلتا ہے۔ جنرل صہیب کا نام ڈاکٹر قیوم اعوان نے تجویز کیا تھا۔ جنرل صہیب خوف خدا رکھنے والے ایک محنتی، لوگوں کا درد رکھنے والی دیانتدار اور خدمت انسانیت کے جذبے سے کام کرنے والی شخصیت ہیں۔ ان کے ساتھ ٹیم کے ایک اہم رکن جنرل پرویز ہیں جو کہ بون میروٹرانسپلانٹ کے ماہر ہیں ان کا پاکستان میں کوئی ثانی نہیں اور اس وقت پاکستان کے بہترین ہیماٹالوجسٹ ہیں۔ انہوں نے اس کام کا بیڑا لیا۔ جنرل فہیم کی وفات کے بعد ہم سب نے مل کر دوبارہ تھیلیسیمیا ہاؤس کو فعال کیا۔ ہم نے محسوس کیا کہ ماشاءاللہ جب اتنا کام ہو رہا ہے تو کیوں نہ ہم بھی اس میں اپنا بھرپور کردار ادا کریں جب کہ اتنے بڑے بڑے لوگ اس نیک کام میں ہمارے ساتھ وابستہ ہیں۔ آجکل اس کے صدر میجر جنرل (ر) ڈاکٹر صہیب احمد، نائب صدر ڈاکٹر جمال ناصر، سیکرٹری میجر جنرل (ر) صفوان مجید جنجوعہ، اور ایگزیکٹو کونسل میں میجر جنرل (ر) پروفیسر پرویز احمد، پروفیسر طاہرہ ظفر، مرتضی علی برہانی، کرنل لبنیٰ ظفر، شیخ سعید اختر ایڈووکیٹ اور بریگیڈیئر کامران محمود ہیں۔

ہم نے سوچا کہ کیوں نہ تھیلیسیمیا ہاؤس میں بون میروٹرانسپلانٹ شروع کیا جائے۔ اس کیلئے پہلے ممبران نے عطیات دیئے ماشاءاللہ ۲۳ دسمبر ۲۰۱۹ کو اس وقت کے صدر پاکستان سید عارف علوی نے اس کی پہلی اینٹ لگا کر اس کا سنگ بنیاد رکھا۔ اسی دوران کورونا آگیا اور فنڈز آنا بند ہوگئے۔ جنرل صہیب اور ہم مایوس ہوگئے کہ شائد بون میروٹرانسپلانٹ سنٹر کا خواب شرمندہ تعبیر نہ ہوسکے۔ لیکن اس وقت مجھے جنرل پرویز کی وہ بات یاد ہے کہ انہوں نے بڑے ایمان کے ساتھ کہا کہ جس اللہ تعالی نے اس کو شروع کرایا وہی اللہ تعالی اس ٹرانسپلانٹ سنٹر کو مکمل کرادے گا۔ اور ایسا ہی ہوا جنرل صہیب اور ٹیم کی کوششوں سے جیسے غیبی امداد آنا شروع ہوگئی اور بالآخر ۲۳ فروری ۲۰۲۲ء کو بون میروٹرانسپلانٹ سنٹر مکمل ہوگیا۔ اس کے مکمل ہونے پر افتتاح بھی صدر پاکستان جناب سید عارف علوی نے کیا۔ یہ پاکستان کا واحد ٹرانسپلانٹ سینٹر ہے جہاں بغیر کسی پیسے کے مستحق مریضوں کا علاج کیا جاتا ہے۔ میں اس وقت کے بیت المال کے ایم ڈی عامر فدا پراچہ جو کہ میرے چھوٹے بھائیوں کی طرح ہیں، ان سے ملا اور ان سے درخواست کی کہ اگر وہ ہماری مدد کریں اور ہر مریض کے لیے ہمیں ۱۰ سے ۱۵ لاکھ روپے دیں تو ہمارا خرچہ پورا ہو جائے گا۔ انہوں نے خصوصی دلچسپی لے کر ہمارے ساتھ ایم او یو سائن کیا اور خود تھیلاسیمیا ہاؤس تشریف لائے۔ اس کا فائدہ یہ ہوا کہ اب تقریباً ۱۰ سے ۱۵ لاکھ روپے بیت المال دیتا ہے اور باقی جو پیسوں کی کمی رہ جاتی ہے وہ یا تو مریض خود مہیا کرتا ہے یا ہم اپنے فنڈز سے کچھ نہ کچھ عطیات دے کر اس کی مدد کر دیتے ہیں۔ بون میروٹرانسپلانٹ پر تقریباً ۱۸ سے ۲۰ لاکھ روپے کا خرچہ آتا ہے۔ اس دن سے آج تک ۵۰ سے ۶۰ کے قریب بون میروٹرانسپلانٹ ہو چکے ہیں اور اللہ تعالی کا شکر ہے کہ ٹرانسپلانٹ کی کامیابی کا تناسب بہت اچھا ہے۔

اس کے بعد ہم نے کالج آف فزیشن اینڈ سرجن کے پروفیسر شعیب شفیع صاحب سے درخواست کی کہ ٹرانسپلانٹ سینٹر راولپنڈی اسلام آباد کا اس قدر اچھا اور کامیاب ادارہ بن چکا ہے ہمیں اجازت دی جائے کہ ہم یہاں پوسٹ گریجویشن کلاسز کا اجرا کریں تو انہوں نے دورہ کیا اور اب ماشاءاللہ یہ ادارہ سی پی ایس پی سے رجسٹرڈ ہوگیا ہے اور ایف سی پی ایس اور ایم سی پی ایس کی کلاسز شروع ہو چکی ہیں۔ میں یہ سمجھتا ہوں کہ یہ آخرت میں جانے کے لیے بہترین ذریعہ ہے۔ یہ افضل ترین کام ہے اور ہم اللہ تعالی کے شکر گزار ہیں کہ اس نے ہمیں یہ توفیق دی کہ ہم اس ادارے کے ساتھ وابستہ ہیں جس میں ایک بہترین ٹیم بن گئی ہے جو دن رات کام کر رہی ہے۔

اس سوسائٹی کے عہدیداران نہ صرف تھیلیسیمیا سنٹر کے لئے دن رات کام کرتے ہیں بلکہ خود بھی خون کے عطیات دیتے رہتے ہیں۔ اس وقت مرتضے برہانی جو ایگزیکٹو کونسل کے ممبر بھی ہیں انہوں نے ۱۷۰ مرتبہ اور جنرل کمال اکبر (مرحوم) نے ۱۶۰ مرتبہ خون کا عطیہ دیا ہے جو پاکستان میں ایک ریکارڈ ہے۔ دنیا کا ریکارڈ آسٹریلیا کے ایک ڈونر کا ہے جس نے ۹۱ سال کی عمر میں وفات پائی اور ۲۳۰ مرتبہ خون کا عطیہ دیا۔ امید ہے کہ مرتضے برہانی جن کی عمر ابھی ۵۰ سال ہے وہ انشاءاللہ اس ریکارڈ کو توڑ کر دنیا کے سب سے زیادہ خون کا عطیہ دینے والے شخص بن جائیں گے۔ ۱۹۹۱ء سے آج تک اس سوسائٹی نے تقریباً ۸۵۰۰۰ افراد سے خون کے عطیات وصول کئے ہیں اور تقریباً ۵۵۰۰۰ مریضوں کو بغیر کسی معاوضہ کے خون کے عطیات دیئے۔ یہ خون راولپنڈی اسلام آباد کے مختلف ہسپتالوں کے مریضوں کو بھی عطیات کئے جاتے ہیں۔ ان خون کے عطیات کو حاصل کرنے کیلئے تمام ممبران کی کاوشیں شامل ہیں اور راولپنڈی اور اسلام آباد کے تعلیمی اداروں، دفاتر، میڈیکل کالجز اور سڑکوں کے کنارے کیمپ لگا کر بھی خون کے عطیات حاصل کئے جاتے ہیں۔ تقریباً ۲۰۰۰ سے زائد بچے یا بچیاں سوسائٹی سے رجسٹرڈ ہیں جن کو باقاعدگی سے خون دینے کے علاوہ پمپ، انجکشن اور ادویات بھی فراہم کی جاتی ہیں۔

اللہ تعالی اس ٹیم کے ہر رکن کو اجر عظیم عطا فرمائے اور اس نیک عمل کے صدقے ان سب کی آخرت کو اچھا کر دے اور ہمیں ہمت عطا فرمائے کہ ہم اس طرح کے سوشل کاموں میں بڑھ چڑھ کر حصہ لے سکیں۔ چونکہ تھیلیسیمیا کا تعلق تو انسانی جانوں کے ساتھ ہے اس لیے اس سوسائٹی کے ساتھ تعاون سے انسانی جانیں بچائی جا سکتی ہیں اور اس نیک کام میں ہمیں اپنا حصہ ڈالنے میں دیر نہیں کرنی چاہیے۔ اللہ تعالی ہم سب کو ایسے نیک عمل کی توفیق عطا فرمائے۔

آمین!

پاکستان تھیلیسیمیا ویلفیئر سوسائٹی: متاثرہ بچوں کی آخری امید

تحریر: ڈاکٹر جمال ناصر (نائب صدر پاکستان تھیلیسیمیا ویلفیئر سوسائٹی، سابق صوبائی وزیر صحت و بہبود آبادی پنجاب پاکستان)

پاکستان تھیلیسیمیا ویلفیئر سوسائٹی ایک ایسی تنظیم ہے جو راولپنڈی اسلام آباد میں تھیلاسیمیا کے بیمار بچوں کی بے لوث خدمت کر رہی ہے۔ تھیلیسیمیا موروثی بیماری ہے جو ماں باپ سے بچوں میں منتقل ہوتی ہے۔ اس بیماری میں خون بننا کم ہو جاتا ہے۔ اس کی دو اقسام ہیں: ایک تھیلیسیمیا مائنر ایک تھیلیسیمیا میجر۔ تھیلیسیمیا مائنر میں ہیموگلوبن کی کمی تھوڑی رہتی ہے لیکن انسان نارمل زندگی گزار لیتا ہے اور کوئی مسئلہ نہیں ہوتا۔ تھیلیسیمیا میجر وہ بیماری ہے جس میں خون کی شدید کمی ہوتی ہے اور دونوں جینز (genes) ماں باپ سے آتے ہیں اور اس سے متاثرہ بچے یا بچی کو ہر مہینے خون لگانا پڑتا ہے۔ خون لگانے کا ایک نقصان یہ بھی ہوتا ہے کہ جسم میں فولاد کی زیادتی ہوتی ہے۔ جس کے علاج کے لیے پھر آئرن چیلیشن تھیراپی (Iron chelation therapy) دینی پڑتی ہے کچھ ٹیکے ہوتے ہیں اور کچھ گولیاں بھی ہوتی ہیں۔

پاکستان تھیلیسیمیا ویلفیئر سوسائٹی کے بانی لیفٹیننٹ جنرل (ر) فہیم احمد خان نے اسے ۱۹۹۱ء میں باقاعدہ رجسٹرڈ کروایا اور تقریباً آج سے ۳۰ سال قبل ۱۹۹۴ء میں پاکستان میڈیکل یسوسی ایشن کے چھوٹے سے آفس سے اس کا باقاعدہ آغاز کیا۔ اس وقت ڈاکٹر عبدالقیوم اعوان پی ایم اے راولپنڈی کے صدر تھے۔ ڈاکٹر عبدالقیوم اعوان اور لیفٹیننٹ جنرل فہیم احمد خان کی کوششوں میں جن لوگوں نے ان کا ساتھ دیا ان میں لیفٹیننٹ جنرل سلیم، میجر جنرل افتخار ملک، لیفٹیننٹ جنرل سید اظہر، میجر جنرل سی ایم انور، اور میجر جنرل صہیب جو اس وقت میجر کے عہدے پر فائز تھے شامل ہیں۔ خاص طور پر میجر (ر) بشیر کو اس تھیلیسیمیا سنٹر کے شروع کرانے پر بھولا نہیں جا سکتا۔

پاکستان میڈیکل ایسوسی ایشن کی برانچ میں تھیلیسیمیا سنٹر کے افتتاح کیلئے ڈاکٹر عبدالقدیر، جنرل ریاض احمد چوہان جو اس وقت (KRL) میں ہیلتھ ایڈوائزر تھے کی وساطت سے تشریف لائے اور اسے مکمل تعاون کا یقین دلایا۔ اس وقت، ڈاکٹر عبدالقدیر خان اور چیئرمین سپیشل ہائی وے اتھارٹی، میجر جنرل ہدایت اللہ نیازی نے اپنی طرف سے فریج، فرنیچر اور ۵ بیڈز عطیات میں دیئے۔ جلد ہی اس سنٹر میں تھیلیسیمیا کا علاج کرانے والے بچوں کی تعداد تیزی سے بڑھنے لگی کیونکہ راولپنڈی اسلام آباد میں ایک بھی سنٹر ایسا علاج نہیں کر رہا تھا۔ میں، شیخ سعید اختر اور ایڈووکیٹ مرتضیٰ برہانی بھی پی ایم اے کے اس سنٹر کے افتتاح پر موجود تھے۔ جب اس میں بچوں کی تعداد بڑھتی گئی تو اس سوسائٹی کو راولپنڈی میڈیکل کالج ٹیپو روڈ کے سامنے ۲۰۰۷ء میں شفٹ کر دیا گیا۔ حکومت کی طرف سے لیز پر سوسائٹی کو زمین مل گئی اور وہاں ایک تھیلیسیمیا ہاؤس کی خوبصورت عمارت تعمیر کر دی گئی۔ اس پراجیکٹ میں جنرل فہیم خان کی شبانہ روز کاوشیں لائق تحسین ہیں۔ لیفٹیننٹ جنرل فہیم خان سابق سرجن جنرل آف پاکستان تھے۔ فہیم خان ایسے شخص تھے جو دن رات لوگوں کی خدمت کرنا چاہتے تھے، فرشتہ صفت انسان تھے اور انہوں نے دن رات تھیلیسیمیا کی بڑی خدمت کی اور اپنا ایک نام بنایا۔ انہوں نے مجھے بھی ایک دن کہا کہ آپ اتنے لوگوں کی خدمت کرتے ہیں سوشل ورکر ہیں تو کیوں نہ آپ ہمارے ساتھ اس نیک کام میں شامل ہو جائیں اس طرح جنرل صاحب کے کہنے پر میں ان کے اس نیک کام میں شامل ہو گیا۔ اس وقت انسداد سگریٹ نوشی کے لیے سرگرم ادارہ پناہ کے سربراہ ڈاکٹر عبدالقیوم اعوان، جنرل چوہان، لیفٹیننٹ جنرل کمال اکبر، جنرل کرامت اے کرامت، میجر جنرل مسعود انور، انجینئر عبدالرشید، پروفیسر کرنل لبنیٰ ظفر، پروفیسر طاہرہ ظفر، بریگیڈیئر نادرہ کمال، سعید اختر، مرتضےٰ برہانی، میجر جنرل سی ایم انور، چیف میڈیکل آفیسر ڈاکٹر زہرہ جبین، بریگیڈیئر سرور اور کرنل مجاہد یوسف سوسائٹی کے ساتھ کام کر رہے تھے۔ تھوڑے عرصے کے بعد میجر جنرل صہیب احمد اور میجر جنرل پرویز بھی ایگزیکٹو کمیٹی میں شامل ہو گئے اور دن رات کام کرتے رہے۔

اس سوسائٹی کو کسی سرکاری محکمے یا ادارے کی طرف سے کوئی فنڈ نہیں ملتا جس کی وجہ سے یہ سوسائٹی اپنے اخراجات کا انتظام خود پورے کرتی ہے اور لوگوں سے خون اور مالی عطیات لے کر تھیلیسیمیا کا شکار بچوں کے علاج معالجہ اور انہیں باقاعدگی سے خون فراہم کرنے کی خدمات سرانجام دیتی ہے۔ تھیلسیمیا ہاؤس میں ایک کلینیکل لیبارٹری بھی قائم ہے۔ جن بچوں میں آئرن زیادہ ہو جاتا ہے اس کو ختم کرنے کے لیے گولیاں، پمپ اور انجیکشن بھی دیتے ہیں یہ اچھا خاصا خرچے والا کام ہے لیکن اللہ تعالیٰ ان کا نظام چلا رہا ہے۔ اور میں سمجھتا ہوں کہ جنرل فہیم کی آخرت میں بخشش کے لیے اس سے بڑا کوئی اور کام نہیں ہو سکتا۔ جنرل فہیم اور ہم سب اپنے طور پر اس ادارے کے اخراجات کے لیے فنڈز کا انتظام کرتے تھے۔ لوگوں سے عطیات لے کر اخراجات پورے کرتے تھے۔ میری لیبارٹری مکمل طور پر تھیلیسیمیا کے بچوں کیلئے ہمیشہ ان کے شانہ بشانہ بلا معاوضہ تعاون کرتی رہی ہے۔ جنرل فہیم جب بہت بیمار بھی تھے تب بھی تھیلیسیمیا ہاؤس میں آ کے بیٹھا کرتے تھے اور مریض بچوں کی خدمت کیا کرتے تھے۔ جنرل فہیم کی بیماری کے دوران مجھے کہا گیا کہ آپ سوسائٹی کے صدر بن جائیں لیکن میں نے انکار کر دیا۔ اس کی وجہ یہ تھی کہ میں بہت سارے سوشل اداروں سے منسلک تھا۔ اپنی سیاسی، سماجی مصروفیات اور لیبارٹری کے معاملات میں اس قدر مصروف تھا کہ شائد اس عہدے سے انصاف نہ کر پاتا اور جبکہ مجھ سے بہتر شخصیات سوسائٹی میں موجود تھیں۔ اس وقت پھر جنرل صہیب کو ۲۰۱۶ء کے جنرل الیکشن کے ذریعے جنرل امامی کی زیر نگرانی ہوئے انتخابات میں سوسائٹی کا صدر بنا دیا۔ اس طرح الیکشن کرا کے سوسائٹی کا صدر بنانا ایک جمہوری اقدام تھا اور اس سے ثابت

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