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

PATHWEL times

BIMONTHLY NEWSLETTER
2025 | Nov - Dec | VOL 2.6

CRISPR-Cas9 Gene-Editing therapy exagamglogene autotemcel (exa-cel) result in transfusion independence in patients with transfusion-dependent β-thalassemia *(Page-10)*

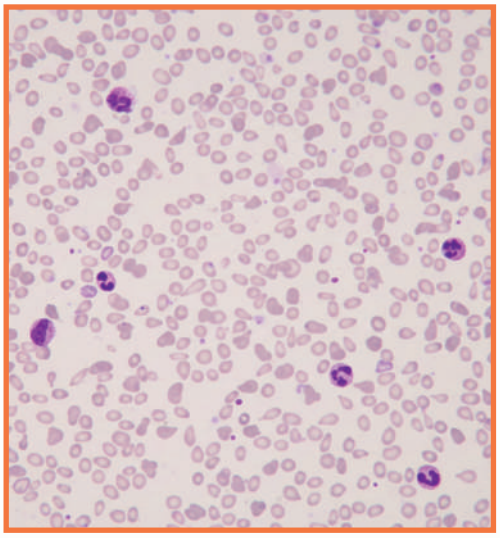
Picture Quiz

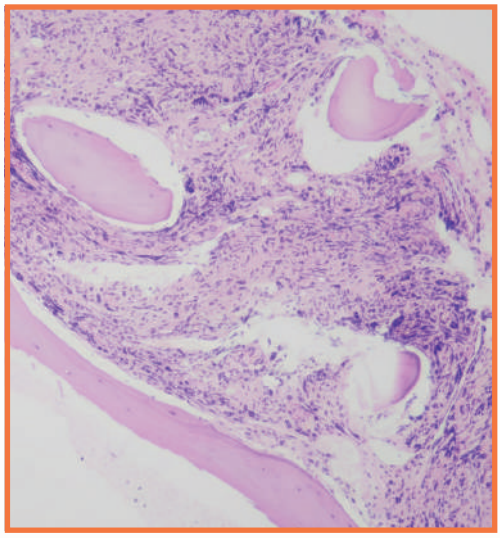
by ***Dr Laila Bahadur***, *Consultant Hematologist, PATHWEL*

Answer on page: 05

A 72-year-old man, known case of polycythemia vera since 2019, previously managed with multiple phlebotomies and oral hydroxyurea, presented with generalized body weakness and weight loss for the last five months. On examination, he was pale, and spleen was palpable 8 cm below the left costal margin. CBC showed WBC 10.7 × 10^9/L (neutrophils 70%, lymphocytes 19%, monocytes 2%, eosinophils 1%, basophils 7%, 1% blasts, 5 NRBCs/100 WBCs). Hb 7.4 g/dL and PLT 46 × 10^9/L . Peripheral blood film revealed anisocytosis, poikilocytosis and tear-drop cells.

What is the most likely diagnosis?





Inside this Issue

Editor
Dr Syed Kamran Mahmood
Publication In-Charge
Mr. Muhammad Waseq Ayaz

"As she fights blood cancer with quiet strength, Zonish's drawing tells us that her spirit continues to dream beyond illness"

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From Editor's Desk

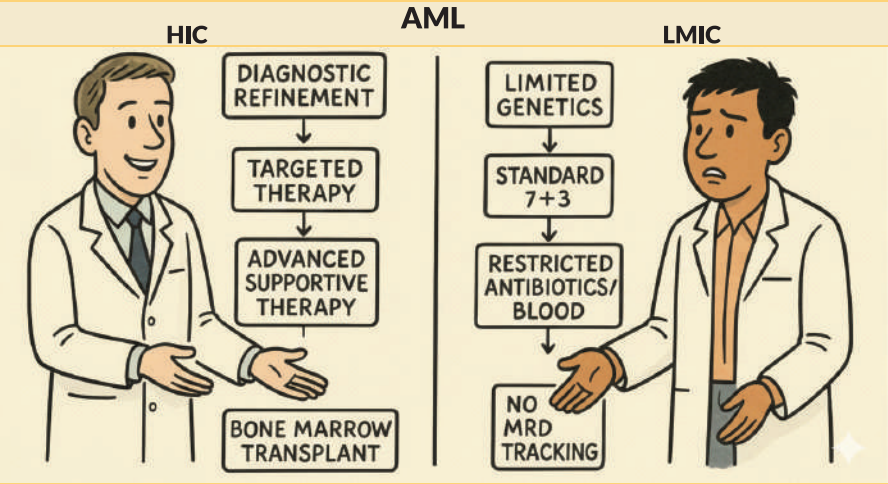
The Pakistan Paradox: Delivering Optimal Care

International recommendations for AML management paint a clear gold-standard pathway—rapid molecular panels, targeted therapies, MRD-guided decisions, and, when indicated, a timely allogeneic transplant. But in Pakistan, the clinical landscape is rarely so straightforward. Imagine an 18-year-old unmarried girl from a poor rural family in South Punjab, newly diagnosed with AML. Her parents had travelled overnight in a hired vehicle; even the cost of baseline cytogenetics felt overwhelming, let alone the full battery of tests and therapies global guidelines expect. Yet she sits before us with the same right to cure as any patient in Boston or Berlin. So, what do we do when the "gold standard" is not within reach? Do silver or even bronze options exist—ethical, evidence-based, and resource-appropriate—that can still offer her a meaningful chance at remission and cure? This tension between ideal recommendations and real-world constraints shapes the daily practice of hematology in our region—and forces us to ask how best to deliver state-of-the-art care within the limits of our system.

Unfortunately, the very bodies that shape global standards—WHO included—remain largely silent on this dilemma. Representation from the global south in formulating hematology guidelines is minimal, and our realities seldom make it into the rooms where recommendations are drafted. As a result, we are handed beautifully structured protocols that work well in high-income settings but offer little guidance for the vast majority of patients in low- and middle-income countries who face life-threatening blood diseases with limited diagnostic capacity and prohibitive treatment costs.

Year after year, we follow the major scientific meetings—ASH, EHA, ASCO—hoping for sessions devoted to resource-constrained settings, for pragmatic pathways that balance evidence with affordability, for trial designs that include patients from environments like ours. Yet very little emerges that can genuinely change the survival curve for our patients in Pakistan. The gap between cutting-edge science and ground reality widens, leaving centers like PATHWEL to improvise ethical, context-sensitive solutions on our own.

And so, we return to our young patient from South Punjab: bright-eyed, frightened, and trusting us with her life. International consensus offers no "tiered" pathways for her, no silver or bronze algorithms calibrated to low-resource circumstances. But our responsibility is to find them anyway—to craft care plans that are realistic yet hopeful, scientifically sound yet financially humane. Her case is not the exception; she is the norm. Until global recommendations begin to reflect the world's true diversity, it falls upon centers like ours to carry the torch for equitable hematology, one patient at a time.



Kindness That Keeps Returning

The Bismillah Charity once again brought warmth & generosity to PATHWEL during their annual visit this year. Like last year, the team donated a handsome amount to support the ongoing care of our patients at PATHWEL & reaffirmed their long-standing commitment to children battling blood diseases. A special highlight of the visit was joyful distribution of gifts among children with thalassemia, filling the day with smiles, laughter, and hope. Their thoughtful gesture not only uplifted the spirits of our young patients but also strengthened our shared mission of compassion and service. We remain deeply grateful for their continued support.

When Institutions Join Hands... Our Patients Get a Better Lifeline

Al-Nafees Medical College & Hospital

Isra University and the Health Services Academy, Islamabad

Al Sadiq Saad Shaheed Hospital

PATHWEL recently signed three key Memoranda of Understanding (MoUs) to enhance safe blood collection and strengthen transfusion services.

The first two partnerships were established with Al-Nafees Medical College & Hospital – Isra University and the Health Services Academy, Islamabad. Through these agreements, the educational institutions will host blood collection camps. In return, PATHWEL will contribute by conducting awareness talks, offering internships, and collaborating on research projects.

The third MoU focuses specifically on ensuring the provision of quality blood bank services by PATHWEL to the Al Sadiq Saad Shaheed Hospital, further expanding access to essential transfusion support. These collaborations underscore PATHWEL's commitment to improving the availability and safety of the national blood supply.

Farewell & Best Wishes to Dr Sidra Barlas

We bid a warm and heartfelt farewell to Dr Sidra Barlas, one of the earliest members of the PATHWEL family. She joined us at a formative time—while preparing for her fellowship—and grew with the institution as she completed her hematology fellowship and later served as Junior Consultant. Dr Sidra played a pivotal role in shaping and expanding the PATHWEL Laboratory, especially the Molecular section. She played an active role in training of postgraduate trainees of PATHWEL.

We are proud of her selection to a government position and congratulate her on her new role in Sialkot. Though she will be greatly missed, her contributions remain deeply woven into the fabric of PATHWEL. We wish Dr Sidra continued success and fulfillment in the next chapter of her career. He leaves with our appreciation, respect, and heartfelt best wishes for success in the journey ahead.

Farewell & Best Wishes to Dr Asad Badshah

We extend our warmest wishes to Dr Asad Ali Badshah as he embarks on a new chapter in the United Kingdom. During his tenure at PATHWEL, Dr Asad served diligently as Medical Officer, providing attentive care in the daycare unit and fulfilling DMO responsibilities with reliability and composure.

Dr. Asad was known for his readiness to step forward whenever extra duty was needed, often volunteering without hesitation. He actively contributed to our blood collection drives and thalassemia awareness campaigns, representing PATHWEL with enthusiasm and professionalism. His courteous manner and kind approach made him well-liked by colleagues and patients alike. We thank Dr Asad for his valuable contributions and the positivity he brought to our team. He leaves with our appreciation, respect, and heartfelt best wishes for success in the journey ahead.

Blood Camps' Diary

By Ms Nigar Shah PRO & Camp Coordinator
Pakistan Thalassemia Welfare Society

Every drop of blood donated today carries hope for someone fighting for life.Our blood camp brought together generosity, purpose, and the quiet courage of everyday heroes. Together, we proved that saving lives can begin with a simple act of kindness.

Sadat Colony, Wah Cantt | 14 September 2025
PATHWEL, in collaboration with the Khan Foundation, successfully organized its inaugural blood donation drive for the Wah Cantt community. The event received an enthusiastic response, with many women stepping forward from their homes to donate blood. The campaign was further amplified by the active participation of social media influencers—including YouTubers, vloggers, and TikTokers—who helped spread awareness and encouraged others to become donors. Their outreach played a vital role in inspiring community members to support this important cause.

Al-Nafees Medical College- Isra University Rawalpindi | 22 September 2025
We organized a highly successful blood donation camp at Al-Nafees Medical College (Campus of Isra University) in close coordination with Dr Tasawar Khawaja (Medical Superintendent). The event saw an impressive turnout, with students demonstrating great enthusiasm for donating blood. Due to the overwhelming number of donors, many students also volunteered to assist the PATHWEL team in managing the blood collection drive. A highlight of the occasion was the signing of a Memorandum of Understanding (MoU) between PATHWEL and Al-Nafees Medical College, further strengthening their collaboration as previously reported.

Fatima Jinnah Women University, Rawalpindi | 7 October 2025
PATHWEL organized a blood donation drive at Fatima Jinnah Women University in coordination with Head Nurse Ms. Nabila (dispensary in-charge). The event attracted a large number of participants; however, the total number of donations was not as high as expected, as several potential donors were found ineligible due to low hemoglobin levels or being underweight.

Foundation University Medical College, (FUMC) Rwp | 9 Oct 2025
A successful blood donation camp was organized at Foundation University Medical College (FUMC) through the coordinated efforts of Col (R) Dr Lubna Zafar, in-charge Blood Donation Society, and Dr Usama, President of the Students' Society. FUMC students showed remarkable enthusiasm, actively participating throughout the drive and donating blood voluntarily for a noble cause, nationwide impact.

Muslim Youth University, Islamabad | 27 October 2025
PATHWEL arranged a donation drive in Muslim Youth University (MY University) Islamabad. Mr Abdul Rauf (Admin Head) from My University coordinated the camp arrangements. Dr Syed Kamran Mahmood, HOD clinical wing of PATHWEL delivered a lecture to the students of My University to spread awareness about thalassemia and other blood disorders. This was our second camp at my university and the response was very good, both the times.

PATHWEL Stars – *Half a Match, Whole-hearted Commitment*

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

As part of the clinical hematology and transplant team at PATHWEL, we first met Mr. Hamza Afzal, a 20-year-old young man who had recently returned from Saudi Arabia after experiencing progressive dizziness, profound fatigue, and generalized weakness. His blood counts revealed marked pancytopenia, and subsequent bone marrow examination confirmed Severe Aplastic Anemia with markedly reduced cellularity (10–15%), along with a 20% PNH clone. His condition required multiple transfusions, and despite a full course of cyclosporine and eltrombopag, he demonstrated no hematologic response.

Given the severity of his disease and the absence of a matched sibling donor, HLA typing was extended, and fortunately, his younger sister Ms. Sadia Afzal, though a haploidentical match, agreed without hesitation to serve as his donor. Her commitment and understanding of the process played an essential role in moving forward with transplant planning.

Mr. Hamza was admitted on 21st February 2024, and underwent a Haploidentical Bone Marrow Transplant on 7th March 2024, using a conditioning regimen of Busulfan, Fludarabine, Thiotepa, and Cyclophosphamide, followed by PTCy-based GVHD prophylaxis. His immediate post-transplant course was complex and required intensive multidisciplinary management. He experienced mucositis, nausea and vomiting, persistent hiccups, azotemia, and delayed platelet recovery. Each complication was monitored closely and managed promptly, allowing him to maintain clinical stability through the engraftment period.

Following discharge he developed hemorrhagic cystitis and episodes of GVHD, both of which were treated according to standard protocols and gradually resolved over time. Throughout these challenges, Mr. Hamza remained compliant, motivated, and remarkably patient—qualities that significantly contributed to his successful recovery.

Today, he is fully engrafted, off all immunosuppression, with stable and normal blood counts, and has resumed a healthy, functional life. His progress stands as an encouraging outcome for patients undergoing haploidentical transplantation for severe bone marrow failure syndromes.

A special acknowledgment is due to his donor, Ms. Sadia Afzal, whose selfless and timely decision to donate stem cells became the cornerstone of his recovery. Her support, trust, and commitment exemplify the profound impact of family involvement in transplantation. Mr. Hamza's story highlights the importance of coordinated multidisciplinary care, donor cooperation, and patient resilience.

Picture Quiz Answer

by **Dr Laila Bahadur**, *Consultant Hematologist PATHWEL*

Answer: Post-PV Myelofibrosis

Diagnostic criteria:

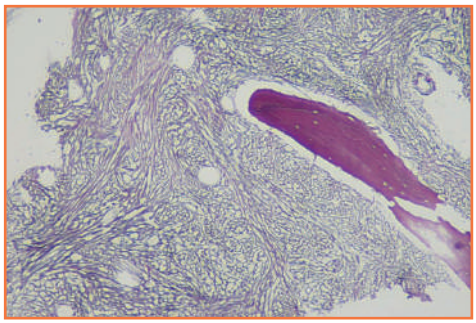
- Documentation of a previous diagnosis of WHO-defined polycythaemia vera
- Bone marrow fibrosis of grade 2–3 on a scale of 0–3

Additional criteria (two are required):

- Anaemia (below the reference range for age, sex, and altitude considerations) or sustained loss of requirement of either phlebotomy (in the absence of cytoreductive therapy) or cytoreductive treatment for erythrocytosis
- Leukoerythroblastosis
- Increasing splenomegaly, defined as either an increase in palpable splenomegaly > 5.0 cm from baseline (distance from the left costal margin) or the development of a newly palpable splenomegaly

Development of any two (or all three) of the following constitutional symptoms:

- 10% weight loss in 6 months
- Night sweats
- Unexplained fever (>37.5°C)



Practice Changing Updates in Hematology 2025

The Pakistan Blood and Marrow Transplant (PBMT) group, in partnership with AFBMTC, PSH & SOHO, convened its annual international hematology and transplant conference: Practice Changing Updates in Hematology 2025 from November 7–9 in Islamabad. The three-day hybrid meeting included treatment sequencing insights from ASH® 2024, ASCO® 2025 and EHA® 2025. The conference brought together leading hematologists, oncologists, nurses, and data specialists from around the world, reaffirming Pakistan's growing footprint in the global transplant community.

The Inaugural Ceremony

Federal Health Minister Syed Mustafa Kamal was the chief guest. President PBMT group Dr Natasha Ali welcomed the guests. Messages from global leaders —including Dr Khurram Bilal Tariq (HOPPE) Dr Phillip Scheinberg (President SOHO), Dr David Porter (President ASTCT), Dr Serdar Bedii Omay (President Türkiye Hematology /BMT), and Dr. Dietger Niederwieser (WBMT)—emphasized international collaboration in advancing transplant medicine. Patron PBMT group Dr Parvez Ahmed highlighted the issues related to stem cell and bone marrow transplant in Pakistan. Prof Yuqian Sun's keynote on "Current Status of HSCT in China" offered an illuminating perspective on regional progress. In the chief guest reaffirmed his support for cause of bone marrow transplantation in Pakistan and emphasized the importance of prevention of blood diseases especially Thalassemia.

Day 1: Nursing, Data, Thrombosis & Coagulation, Lymphoma

The conference opened with a dedicated Nursing Session, underscoring the pivotal role of nursing in transplant success. Topics ranged from comprehensive BMT care and neutropenic fever management to safe handling of cytotoxic drugs & family-centered support in pediatric HSCT. The session reflected the growing professionalism & evidence-based approach of Pakistani nursing teams in high-acuity hematology care. This was followed by the Data Management Session, led by Mr. Shahid Iqbal, highlighting the PBMT's achievements and the central role of data in quality assurance and research development.

A State-of-the-Art lecture by Dr. Alessandro Busca explored challenges in donor selection & GVHD prophylaxis, followed by the first Industry Spotlight on Nilotinib in frontline CML.

The day concluded with sessions on Thrombosis and Coagulation, and High- and Low-Grade Lymphomas, featuring global experts Dr. Stephen Ansell, Dr. Farrukh T. Awan, Dr. Sairah Ahmed, and Dr Jasmine Zain among others.

Day 2: Scientific Exchange and Emerging Therapies

Day two began with the Meet the Expert discussion on optimizing upfront treatment of CML, setting the stage for the Research Abstract Session, where young investigators presented cutting-edge data from local centers—including real-world outcomes of HMA–Venetoclax therapy and stem cell mobilization strategies.

From Left to Right (sitting): Dr Hina Tariq, Dr Sumaira Naseeb, Salma Nigar, Dr Aliah Asif, Dr Khalil Ur Rehman, Dr S Kamran Mahmood, Prof Dr Parvez Ahmed, Dr Husnain Ali, Dr Abdul Salam, Dr Mahnoor, Dr Mehroze Fatima
Standing: Amir Rahim, Abdul Hafiz, Azhar Abbas

From Left to Right: Hon. Syed Mustafa Kamal, Dr Natasha Ali, Dr Khurram B Tariq, Dr Serdar B Omay, Dr D Niederwieser, Dr Parvez Ahmed, Dr Saad Usmani

From Left to Right: Dr Jasmine Zain, Brig (Dr) Tariq Ghafoor, Dr Shahrukh Hashmi, Dr Semra Aydin, Dr Meng Lv, Col (Dr) Raheel Iftikhar, Dr Sebastian Galeano

The morning featured focused sessions on Bone Marrow Failure Syndromes, Acute Lymphoid Leukemia, and Myeloid Malignancies. Talks by Dr. Amy Dezern and Dr. Riad El Fakih provided clarity on sequencing treatment in SAA and IBMF. A highlight was the AML/MDS panel led by Dr. Courtney DiNardo and Dr. Tapan Kadia, offering insight into integration of HMA-Ven and novel triplet therapies.

Later sessions on Myeloproliferative Neoplasms and Plasma Cell Disorders brought deep discussions from Dr. Hagop Kantarjian, Dr. Haris Ali, Dr. Muzaffar Qazilbash, and Dr. Saad Usmani, all emphasizing precision medicine and long-term survivorship.

Industry symposia spotlighted evolving therapies in GVHD, Myelofibrosis, Polycythemia Vera, and CML, demonstrating the productive engagement between academia and pharmaceutical partners.

Day 3: Pediatric Frontiers and Cellular Therapy

The final day opened with the Pediatric Hematology-Oncology and BMT Session, where Dr. Zehra Fadoo and colleagues shared pragmatic approaches to pediatric ALL and AML in resource-limited settings. Dr. Farhan Anjum's talk on gene therapy for thalassemia symbolized the promise of curative genomic medicine for inherited disorders.

Dr. Ayalew Tefferi's "State of the Art II" on CMML 2026 drew considerable attention, bridging current practice with future prognostic tools. Dr. Saad Usmani's leadership address, "Bridging Continents, Building Legacy," provided inspiration to young hematologists about global career pathways.

The concluding Transplant and Cellular Therapy Session—featuring Dr. Shahrukh Hashmi, Dr. Riad El Fakih, and Dr. Meng Lv—summarized modern approaches to GVHD prophylaxis, CAR-T, and cellular therapy integration in lymphomas.

Closing Ceremony

The event ended with distribution of prizes to winners of quiz competition among the postgraduate trainees in hematology and clinical hematology. Prizes were also distributed among the winners of quizzes for the audiences which were held after each session. In the end sponsors were given the shields. The Patron PBMT group thanked the delegates, participants, volunteers and the sponsors for making the conference and huge success.

Grand Round

A Mislabelled Thalassemia: Pyruvate Kinase Deficiency in an Afghan Infant

*By **Dr. Mehroze Fatima**, Resident Clinical Hematology, PATHWEL Center of Hematology & Bone Marrow Transplant*

Case Summary

A 1.5-year-old girl from Afghanistan presented to PATHWEL with a history of jaundice from the first day of life, which resolved spontaneously after 3–4 days. At one month of age, she developed severe anemia with a hemoglobin level of 6.0 g/dL, accompanied by mild unconjugated hyperbilirubinemia. By three months, hemoglobin electrophoresis revealed elevated fetal hemoglobin (HbF 42.4%), leading to a diagnosis of β-thalassemia major, despite both parents having normal hematological indices and hemoglobin fractions.

In the absence of molecular diagnostic facilities, the child was managed as thalassemia major with regular red cell transfusions and had received 17 RCC transfusions by the time of presentation. There was no history of recurrent infections, bleeding episodes, dark urine, or a family history of hemolytic anemia. She was the only child of consanguineous parents. On examination, she was pale but alert, with light brown hair and mild hepatomegaly. There was no splenomegaly or dysmorphic features.

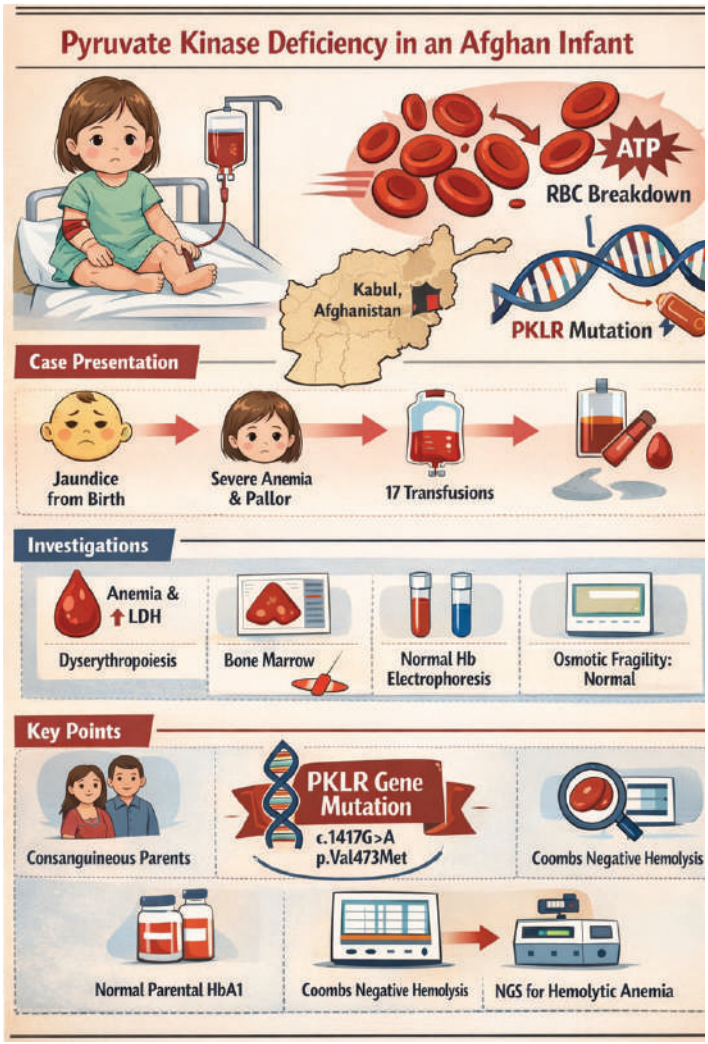
Investigations and Diagnostic Work-up

Laboratory evaluation demonstrated anemia with reticulocytosis (6%), elevated lactate dehydrogenase levels, and indirect hyperbilirubinemia. Both direct and indirect Coombs tests were negative. Molecular testing for common β-thalassemia mutations was negative. Bone marrow examination showed marked erythroid hyperplasia with dyserythropoiesis and significant iron overload, consistent with chronic hemolysis. Osmotic fragility testing was normal, excluding red cell membranopathies. Next-generation sequencing for hereditary hemolytic anemia identified a homozygous PKLR gene mutation (c.1417G>A; p.Val473Met). Although classified as a variant of uncertain significance, the mutation was consistent with the patient's clinical phenotype.

Final Diagnosis: Pyruvate kinase deficiency.

Discussion

Pyruvate kinase deficiency is a rare autosomal recessive enzymopathy causing chronic non-spherocytic hemolytic anemia due to impaired ATP production in red blood cells, resulting in premature erythrocyte destruction. Clinical severity varies from mild anemia to transfusion dependence from infancy. Misdiagnosis as thalassemia is common, particularly in early infancy when HbF is physiologically elevated. This case highlights the limitations of hemoglobin electrophoresis alone and emphasizes the value of molecular diagnostics in unexplained hemolytic anemia.



Learning Points

Not all transfusion-dependent anemias are thalassemia. Normal parental hemoglobin studies should prompt diagnostic reconsideration. Next-generation sequencing is invaluable in resolving complex diagnostic dilemmas.

Conclusion

Revisiting early diagnoses and adopting a structured approach to inherited hemolytic anemias are essential. Early recognition of pyruvate kinase deficiency can prevent unnecessary transfusions, guide appropriate management, and enable accurate genetic counseling.

Morphology Updates

BCR::ABL1-Positive Acute Myeloid Leukemia

Alban Canali* | *Jean-Baptiste Rieu* | *Leopoldine Lapierre* | *Barbara J. Bain
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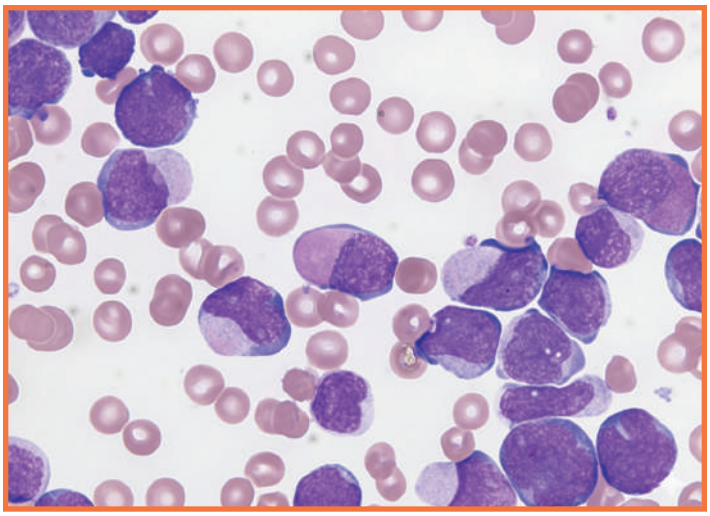
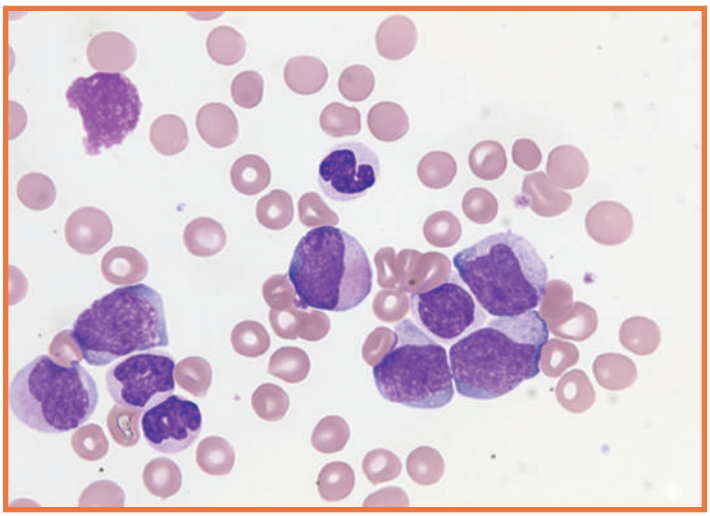
Received: 27 January 2025 | Accepted: 31 January 2025

Morphology Update has recently discussed a patient with chronic myeloid leukemia (CML) presenting in blast crisis [1]. For comparison, we present here a patient with BCR::ABL1 -positive acute myeloid leukemia (AML). The patient was a 48-year-old man with no known history of CML, presenting with hepatomegaly and neurological abnormalities (headaches, agitation, and behavioral disturbance). His blood count showed hemoglobin concentration 64 g/L, white cell count 457.6×10^9/L, & platelet count 31×10^9/L. His blood film (images×100 objective) showed 95% blast cells; these were large, with an intermediate nuclear- cytoplasmic ratio, irregular nuclei, sometimes nucleoli, and cytoplasm containing atypical pink to lilac granules and occasional inclusions. Promyelocytes were present but myelocytes, eosinophils, and basophils were infrequent. Neutrophils were dysplastic with hypogranular cytoplasm and abnormal nuclear forms (right image). A bone marrow aspirate was hypercellular with 84% blast cells, without prominence of eosinophils or basophils. Cytogenetic analysis showed 46,XY,t(9;22)(q34;q11) [21]. A BCR::ABL1 transcript, identified as BCR_E13::ABL1_E2, b2a2, p210, was detected on molecular analysis, together with mutations of SMC3 and WT1. In view of the molecular findings and the lack of prominent basophilia, a diagnosis of BCR::ABL1- positive AML appeared most likely but post-treatment follow-up was needed for confirmation.

The patient was treated with cytarabine, idarubicin, and imatinib as induction treatment (preceded by cytoreduction with hydroxycarbamide), followed by cytarabine & imatinib for consolidation. Additionally, cytarabine, methotrexate, and methylprednisolone were administered intrathecally to treat demonstrated central nervous system infiltration. Complete remission was achieved with the marrow being morphologically normal without neutrophilic, eosinophilic or basophilic hyperplasia. Cytogenetic analysis was normal at 2 months from diagnosis and a deep molecular remission was demonstrated at 4 months.

Diagnosis of BCR::ABL1-positive AML requires the features of AML and demonstration of BCR::ABL1. However, an





Essential diagnostic criterion is that there should be "a lack of features of CML before or at diagnosis and after therapy" [2]. The diagnosis is thus provisional until post-treatment follow-up excludes an alternative diagnosis of blastic presentation of CML. De novo AML cases have less frequent splenomegaly, a higher blast percentage and lower basophil numbers [2]. The precise BCR::ABL1 transcript that is detected is not helpful because p210 is most often observed in both CML and BCR::ABL1-positive AML [2].

Conflicts of Interest
The authors declare no conflicts of interest.

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100, no. 1 (2025): 131–132.
2. S. Hu, T. Haferlach, K. C. Hodge, et al., "Acute Myeloid Leukaemia With BCR::ABL1 Fusion," 2024. In WHO Classification of Tumours Editorial Board, eds. Haematolymphoid Tumours. IARC: 125–126.

Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits

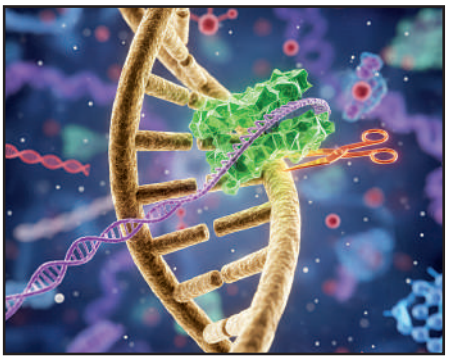
Quality of life and life satisfaction in long-term survivors of acute myeloid leukemia

E Telzerow , D Görlich , C Sauerland et al; Leukemia (2025) 39:2663–2672; https://doi.org/10.1038/s41375-025-02735-y

We performed a questionnaire-based cross-sectional study to analyze Acute Myeloid Leukemia (AML) long-term survivor (LTS) outcomes, including psychosocial well-being and somatic health status. Four-hundred-twenty-seven former AML patients participated (response rate, 63%) ≥5 years[y] and up to 18.6 y past their leukemia diagnosis (median, 11.3 y). Median age at study participation was 61 y (range 28y–93y), 23% had experienced disease relapse, and 63% had received allogeneic hematopoietic stem cell transplantation (alloHSCT). Overall, quality of life (QoL) & general life satisfaction (gLS) summary scores were higher in AML LTS ($p < 0.001$) compared to age-/sex- matched reference cohorts, although differences were small and likely not clinically relevant. However, we identified subgroups of survivors reporting impaired QoL (27%), gLS (13%) and health-related life satisfaction (hrLS; 17%). Using multivariable regression models, we identified predisposing and protective factors for each of these outcomes. Treatment with alloHSCT did not adversely impact QoL, gLS, or hrLS. In summary, global QoL and LS in AML LTS are comparable to the general population, irrespective of treatment modality, although some survivors report clinically significant impairment of global QoL and/or in specific domains. We identified factors associated with impaired outcomes (e.g., comorbidity and fatigue),delineating a subgroup of survivors with unmet needs ≥5 y after their AML diagnosis.

Improvements in health-related quality of life in patients with transfusion-dependent β-thalassemia after exagamglogene autotemcel

Josu de la Fuente, Haydar Frangoul, Peter Lang, et al; https://doi.org/10.1182/bloodadvances.2025016702



Transfusion-dependent β-thalassemia (TDT) can have negative impacts on a patient's health-related quality of life (HRQoL). Exagamglogene autotemcel (exa-cel) is a one-time, ex vivo CRISPR-Cas9 gene–edited cell therapy for TDT shown in a phase 3 clinical trial to result in transfusion independence in most participants. Here, we describe changes in patient-reported outcome (PRO) measures after exa-cel infusion in 54 participants (adults, n = 35; adolescents, n = 19), who had ≥16 months of follow-up. In adults, PRO measures included the EuroQol Quality of Life Scale-5 dimensions-5 levels of severity (EQ-5D-5L) and the Functional Assessment of Cancer Therapy Bone Marrow Transplant (FACT-BMT). In adolescents, the EuroQol Quality of Life Scale-5 dimensions-youth (EQ-5D-Y) and Pediatric Quality of Life Inventory (PedsQL) instruments were used. At baseline, mean EQ-5D-5L visual analog scale (VAS) and US and UK health utility index scores in adults were in line with baseline scores reported for adults with TDT. After exa-cel infusion, all 3 scores improved, exceeding established minimal clinically important differences (MCIDs) at month 48. Mean FACT-General (FACT-G) score and bone marrow transplant subscale score improved through month 48, also exceeding MCIDs, with improvements in all 4 FACT-G subscales (physical, social/family, emotional, and functional well-being). Consistent with HRQoL improvements in adults, adolescents had increases from baseline at month 24 in mean EQ-5D-Y VAS score and PedsQL total score, with sustained improvements in both physical and psychosocial health subcomponents.

These results indicate exa-cel leads to broad, durable, and clinically meaningful improvements in HRQoL in adults and adolescents with TDT.

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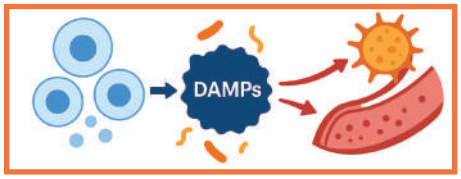
Damage-associated molecular patterns & coagulation

Yong J, Toh C-H. Br J Haematol. 2025;00:1–4. https://doi.org/10.1111/ bjh.70258

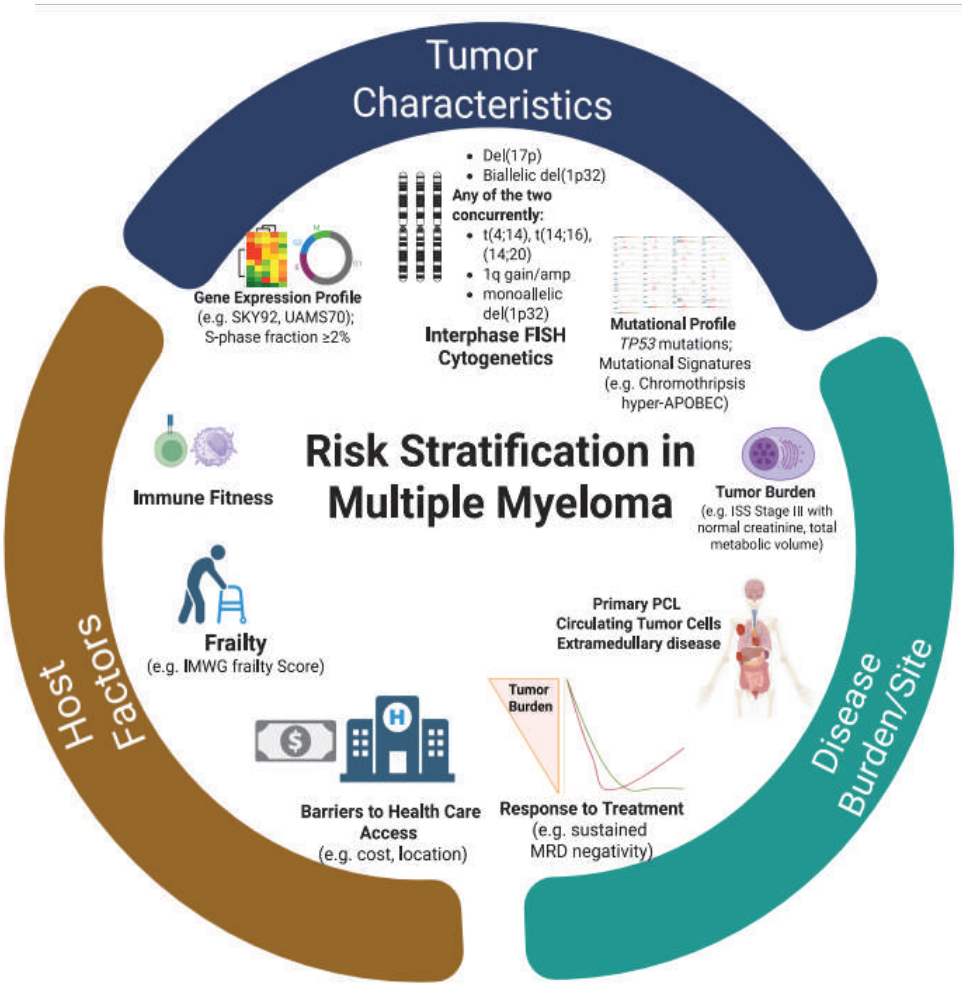


Damage-associated molecular patterns (DAMPs), released into the extracellular space following tissue injury, are increasingly recognised as potent procoagulant molecules integral to haemostasis and the pathogenesis of thrombosis. Their procoagulant influence spans all phases of the cell-based model of coagulation while simultaneously extending beyond traditional haemostatic pathways through direct modulation of inflammatory and innate immune responses. By coupling coagulation and immunity, DAMPs drive the self-perpetuating cycle of immunothrombosis characteristic of many critical illnesses. Targeting this underexplored interface offers the promise of novel diagnostic and therapeutic approaches, particularly in conditions where coagulopathy coexists with hyperinflammatory states.

Guidline Watch

STR techniques currently represent standard of care for chimerism analysis in the United Kingdom as they are rapid, reliable, accurate & reproducible despite limited sensitivity of 1%–5% (n = 61 respondents) (agree/strongly agree: 93%, neutral: 5%, disagree: 2%)

Clark A, Clouston H, Rao K, Folarin N, De la Fuente J, Hamblin A, et al. UK recommendations for chimerism testing & monitoring following allogeneicHSCT: Best practice consensus guidelines from the BSBMTCT, NHS England (GLH) Haematological Malignancies Working Group, UKCGG & the UK NEQAS LI. Br J Haematol. 2025;207(5):1802–1814. https://doi.org/10.1111/bjh.70061



Risk stratification in multiple myeloma.

An evolving paradigm of risk stratification for multiple myeloma involves comprehensive tumor genomics evaluation, consideration for disease burden and location, and various host factors that can determine access and response to existing treatments (Created using Biorender®). ISS international staging system, IMWG International Myeloma Working Group, FISH fluorescence in situ hybridization, MRD measurable residual disease, PCL plasma cell leukemia.

Current risk stratification and staging of multiple myeloma and related clonal plasma cell disorders

Saurabh Zanwar and S. Vincent Rajkumar

Leukemia (2025) 39:2610–2617; https://doi.org/10.1038/s41375-025-02654-y

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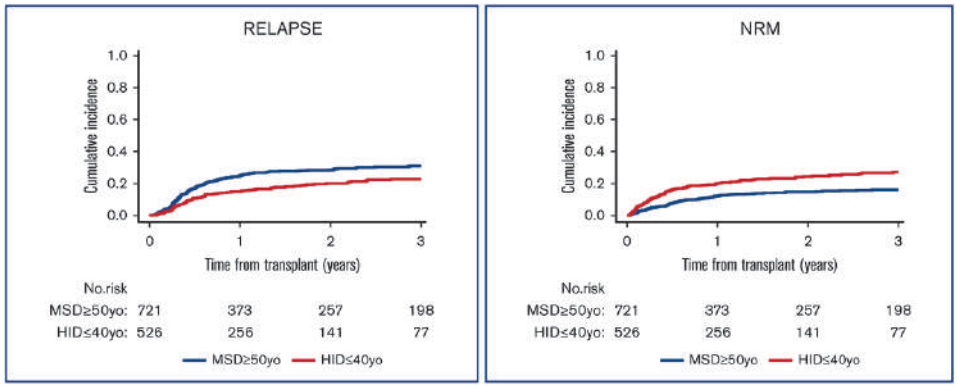
Older matched sibling donor vs young haploidentical donor for older patients with acute myeloid leukemia

X Poiré, M Labopin, E Polge et al; https://doi.org/10.1182/bloodadvances.2024015582

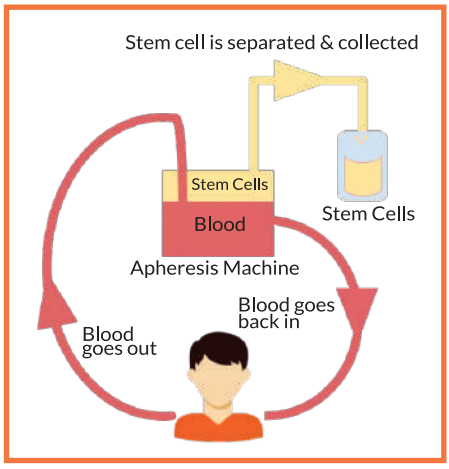
Selection of a suitable donor for allogeneic hematopoietic stem cell transplantation (allo-HCT) has mainly relied on HLA matching and, to date, a matched sibling donor (MSD) remains the first choice. However, patients with acute myeloid leukemia (AML) are older and therefore tend to have older siblings. Haploidentical donors (HIDs) are easily available, and offspring are younger than siblings. As donor age has been associated with worse outcomes, a younger HID might be a better choice than an older MSD for older patients with AML who receive transplantation in first complete remission (CR1).From the EBMT registry database, we selected patients with AML aged ≥60 years who received transplantation in CR1, either from MSD aged ≥50 years or HID ≤40 years. HIDs received posttransplant cyclophosphamide as graftversus-host disease (GVHD) prophylaxis, and MSDs received in vivo T-cell depletion. A total of 1247 patients were identified, including 721 MSDs and 526 HIDs. In univariate analysis, HID was associated with lower relapse incidence (P = .01), higher nonrelapse mortality (NRM; P = .01). The 2-year probability of overall survival (OS), leukemia-free survival (LFS), and GVHD-free and relapse-free survival (GRFS) were 62.5%, 56%, and 47%, respectively for all population. In multivariate analysis, we confirmed that HID was associated with less relapse but more NRM, which translated into similar OS, LFS, and GRFS. Based on this retrospective study, young HIDs led to less relapse but higher NRM than older MSDs after allo-HCT in an older population with AML in CR1.



Long-term benefits of autologous stem cell transplantation versus intensive chemotherapy consolidation for acute myeloid leukemia patients: A propensity score matching analysis from the PETHEMA AML registry

A Alfonso-Pierola et al; Leukemia (2025) 39; doi.org/10.1038/s41375-025-02744-x

While allogeneic stem cell transplantation (allo-SCT) is the preferred consolidation for high and most intermediate-risk acute myeloid leukemia (AML) patients in first remission, the role of autologous SCT (auto-SCT) vs. chemotherapy (CT) when allo-SCT is not feasible or indicated, remains controversial. We conducted a real- world, retrospective cohort study using the PETHEMA AML registry to compare auto-SCT and CT. Multivariate Cox regression and propensity score matching (PS-matching) were used to adjust for confounding factors. A total of 1272 patients in first remission and who received 2 consolidation courses were included (615 receiving additional CT cycles & 657 undergoing auto-SCT). Overall, 78.08% of auto-SCT patients were diagnosed before 2017, compared to 38.11% in the CT cohort (p < 0.001). In the overall cohort, auto-SCT was associated with significantly prolonged overall survival (OS) (HR: 0.73, p < 0.001) and relapse-free survival (RFS) (HR: 0.73, p < 0.001). This benefit was particularly evident in patients ≤65 years, those with normal karyotype, and FLT3-ITD negativity. In the PS-matched cohort, the RFS advantage persisted (HR: 0.80, p = 0.092), but OS differences were not statistically significant (HR: 0.91, p = 0.563). The role of auto-SCT in the genomic and targeted agent era should not be discarded.



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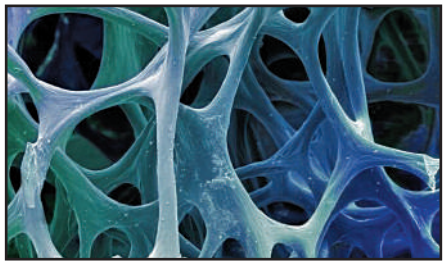
Transplant conditioning intensity (TCI) score predicts allo-HCT outcomes in patients with myelofibrosis: a study of the Chronic Malignancies Working Party of EBMT

Sobieralski, P., Czerw, T., Gras, L. et al. Bone Marrow Transplant (2025). https://doi.org/10.1038/s41409-025-02732-w



Outcomes in myelofibrosis (MF) patients undergoing allogeneic hematopoietic cell transplantation (allo-HCT) appear unaffected by the intensity of the preparative regimen, defined traditionally as myeloablative (MAC) or reduced intensity conditioning (RIC). The Transplant Conditioning Intensity (TCI) index is an objective tool offering a precise measure of conditioning intensity.

We explored the potential association between TCI score and overall survival (OS), progression- free survival (PFS), cumulative incidence of relapse (CIR) and non- relapse mortality (NRM) in 2454 MF patients undergoing allo-HCT between 2012 and 2021, selected from the EBMT registry. Patients receiving TCI-intermediate/high regimens had similar OS (HR 1.12, 95% CI 0.97–1.30) and PFS (HR 1.00, 95%CI 0.88–1.14) compared to TCI-low regimens. However, TCI-intermediate/high regimens were associated with lower risk of relapse (HR 0.74, 95% CI 0.61–0.91, p =0.008) and higher riskof NRM (HR 1.24, 95% CI 1.04–1.48, p = 0.02).

Our findings suggest that the TCI score provides a more clinically relevant stratification of conditioning intensity than the conventional MAC/RIC classification. While higher intensity TCI regimens are associated with lower RI, this benefit is offset by increased NRM, resulting in no survival advantage. However, the TCI index may enable a more personalized approach to conditioning regimen selection by balancing relapse risk with patient frailty

Outcomes following different upfront stem cell transplantation strategies for multiple myeloma: a statistical perspective on behalf of the CMWP of the EBMT

Iacobelli, S., Schönland, S., Koster, L. et al. Bone Marrow Transplant 60, 1361–1368 (2025). https://doi.org/10.1038/s41409-025-02675-2

Multiple myeloma (MM) is a heterogenous malignant disease. Novel agents including bispecific antibodies and chimeric antigen receptor T cells have improved response rates and patient outcome, but the majority of patients ultimately still relapse. High dose chemotherapy followed by autologous hematopoietic stem cell transplantation (auto-HCT) remains standard care of treatment for transplant-eligible patients. While single auto-HCT is commonly used, a planned tandem auto-HCT or auto-allo approach remains controversial, based on conflicting results from clinical trials. Here we compared the outcome of 24,936 MM patients aged between 20 and 65 years who under went first auto-HCT during 2002–2015, reported to the EBMT registry, of whom 3683 and 878 got tandem auto-HCT and auto-allo-HCT respectively. We used non-standard statistical approaches to account for time-dependence of treatments and of their effects, including models with multiple timescales and dynamic prediction. Differences were reported by graphs of hazard functions, hazard ratios and conditional probabilities over time. For both OS and PFS, there was a limited but persistent advantage for the tandem auto-HCT group compared to single auto-HCT, and a clear advantage for the auto-allo-HCT group over both other strategies in the longer term, albeit at the cost of higher early mortality.

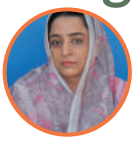
Indications for autologous HSCT in rheumatologic and musculoskeletal diseases (RMDs)

Disease	Indication
Systemic sclerosis	S/I
Systemic lupus erythematosus	CO/II
Idiopathic inflammatory myopathies	CO/II
Inflammatory arthritis	CO/II

EBMT categorisation of type of indication for transplant procedures and strength of evidence.
S = standard, CO = clinical option.

Alexander, T., Roldan, E., Del Papa, N. et al. Autologous haematopoietic stem cell transplantation for rheumatic diseases: best practice recommendations from the EBMT Practice Harmonization & Guidelines Committee. Bone Marrow Transplant 60, 1451–1464 (2025). https://doi.org/10.1038/s41409-025-02695-y

Awareness Seminar: Oral Health and Inherited Bleeding Disorders: Bridging Hematology and Dentistry



By Ms. Hina Fatima; Organized by: Hemophilia Patients Welfare Society (HPWS), Rawalpindi, In Collaboration with PIMS Hospital & School of Dentistry, Shaheed Zulfiqar Ali Bhutto Medical University, SZABMU Islamabad; 6th November 2025.

Introduction
Inherited bleeding disorders (IBDs), including hemophilia and von Willebrand disease, pose unique challenges in dental and oral healthcare. Many patients fear dental procedures due to the risk of excessive bleeding, while dentists often lack practical training on how to safely manage these patients.

The seminar aimed to educate dental professionals, encourage multidisciplinary collaboration and improve patient safety. HPWS, Rawalpindi is committed to improving the lives of individuals with inherited bleeding disorders through awareness campaigns, medical support, community education and collaboration with national healthcare institutions.

The seminar began with the Welcome Note and Tilawat-e-Quran at 10:30 AM. Participants were then introduced to the importance of oral health in individuals with bleeding disorders, setting the stage for a highly informative academic session.

Dr. Tahira Zafar, Director of Hemophilia Treatment Center, Rawalpindi delivered a comprehensive overview of inherited bleeding disorders, including hemophilia, von Willebrand disease and rare clotting factor deficiencies. She explained their clinical presentation and emphasized the importance of early identification of high-risk patients in dental OPDs. Dr Tahira highlighted the dentist's role in recognizing symptoms such as prolonged bleeding after minor cuts, frequent gum bleeding, unexplained bruising and a positive family history, all of which can help prevent severe complications during dental procedures.

Dr. Zahida Ahmad, In-charge Dental Surgeon, Pakistan Sweet Home. Discussed real-case scenarios of hemophilia patients who successfully underwent dental treatments with appropriate planning and hematology support. She described how coordinated care, pre-procedure factor cover and careful postoperative monitoring led to positive outcomes. She covered local measures such as tranexamic acid mouthwash, gelatin sponges, oxidized cellulose, and fibrin glue, along with systemic therapies including factor concentrates and antifibrinolytics. Dr. Zahida further explained preventive dental strategies regular oral hygiene, fluoride application, and routine check-ups to minimize the need for invasive dental work in bleeding disorder patients.

Dr. Lubna Zafar, President of Hemophilia Patient welfare Society & Professor of Hematology at Fauji Foundation University, Rwp, focused on the crucial role of multidisciplinary collaboration between hematologists and dentists. She explained that correct diagnosis begins with a thorough clinical history, including recurrent gum and nose bleeding, family history of bleeding, prolonged bleeding after tooth extraction, any injury, or heavy menstrual bleeding in women and girls. Dr. Lubna highlighted red flags such as delayed clotting, abnormal PT/APTT results, and unexplained bruising, emphasizing that dentists are often the first to suspect an undiagnosed bleeding disorder and

should refer promptly for hematological evaluation if not done.

Dr. Farwa Sajeel, In Charge of Blood bank PIMS, Islamabad, provided detailed guidelines on the use of hemostatic agents and blood components in managing bleeding disorders during dental procedures. Dr. Farwa also discussed postoperative care and emergency management protocols, ensuring that dental clinics are fully prepared to handle unexpected bleeding safely and effectively. She further guided participants on how patients with bleeding disorders can access specialized facilities and support at PIMS, making it easier for them to receive appropriate care

Interactive Question & Answer Session

The Q&A session provided an open forum for dental professionals to address clinical concerns and deepen their understanding of safe practice in patients with bleeding disorders. Key discussion points included the safe management of dental extractions, identifying the right time to refer a patient to a hematologist, and the specific considerations required when treating women and girls with bleeding disorders. Participants also sought guidance on postoperative home-care instructions and the appropriate use of tranexamic acid and other hemostatic options. Overall, the session enhanced communication between dental and hematology teams and reinforced the importance of patient-centered, well-coordinated care.

Impact of the Seminar

- Raised awareness about oral healthcare in hemophilia and other inherited bleeding disorders.
- Trained dentists on safe and appropriate clinical practices for these patients.
- Emphasized the importance of multidisciplinary coordination between dentists and hematologists for safe, complication-free treatment.
- Highlighted the efforts of the Hemophilia Patients Welfare Society, Rawalpindi, in patient support and preventive dental care.
- Reinforced that good dental health is essential for overall disease management and reducing emergencies.

Vote of Thanks and Group Photo

The seminar concluded with a Vote of Thanks, acknowledging HPWS, the speakers, SZABMU administration, and PIMS Hospital for their dedication to patient education and treatment support. A group photograph marked the end of a successful academic event.

Intracranial Bleed in a Child with Severe Hemophilia A: A Success Story By Dr Farah

Hemophilia A is an X-linked inherited bleeding disorder caused by deficiency of clotting factor VIII, leading to impaired secondary hemostasis. Children with severe Hemophilia A (factor VIII activity <1%) are at high risk of spontaneous and trauma-related bleeding, with intracranial hemorrhage (ICH) representing one of the most serious and potentially fatal complications. Even minor head trauma can precipitate significant ICH, making early recognition, urgent neuroimaging, and prompt factor replacement critical to reducing morbidity and mortality.

We report the case of a six-year-old boy from Azad Kashmir, a known patient with severe Hemophilia A, who presented to the Children's Emergency Department at Pakistan Institute of Medical Sciences (PIMS), Islamabad, on 25 June 2025 following a fall at home. He developed intractable vomiting, severe headache, and loss of consciousness. Urgent CT brain revealed a small subacute infratentorial extradural hemorrhage, a hairline fracture of the right parietal bone, and multiple hemorrhagic contusions with surrounding edema. Owing to neurological deterioration, he was transferred to the Pediatric Intensive Care Unit.

Management was conservative and multidisciplinary, including mannitol, antiemetics, intravenous fluids, and blood products. Full factor VIII replacement at 40 IU/kg was provided throughout hospitalization by the Hemophilia Treatment Center, Rawalpindi, followed by prophylactic therapy for three weeks. The child showed gradual neurological recovery over 15 days, with follow-up imaging demonstrating significant resolution of hemorrhages. This case highlights the importance of early intervention, sustained factor replacement, and caregiver education in hemophilia-related ICH.

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