Practice Changing Updates in Hematology (PCUH 2026): Advancing the Future of Hematology Through Knowledge, Collaboration and Innovation

The Practice Changing Updates in Hematology (PCUH 2026) conference was held from 9–11 October 2026 at the Pearl Continental Hotel, Rawalpindi, bringing together hematologists, medical oncologists, bone marrow transplant (BMT) specialists, researchers, nurses and postgraduate trainees from Pakistan and abroad. The well-attended hybrid conference provided an important platform for scientific exchange, professional networking and discussion of the latest developments shaping the future of hematology.

The conference was hosted by the Pakistan Blood and Marrow Transplantation Society (PBMT) and organised by the Armed Forces Bone Marrow Transplant Centre (AFBMTC), Rawalpindi. Its theme, *"Practice Changing Updates in Hematology: Treatment Sequencing Insights from ASH 2025, ASCO 2026 and EHA 2026,"* reflected its emphasis on translating the latest international evidence into clinical practice.

An International Scientific Gathering

A major strength of PCUH 2026 was the participation of distinguished national and international faculty. Experts from leading institutions in the United States, United Kingdom, China, Saudi Arabia, Brazil and other countries joined Pakistani specialists in a comprehensive scientific programme. The hybrid format extended the conference's reach beyond the physical venue, enabling wider participation and facilitating international academic interaction.

The inaugural session featured addresses by prominent leaders in hematology and transplantation, followed by a keynote lecture on the changing landscape of stem cell transplantation. The sessions highlighted how rapidly evolving evidence, new therapeutic options and advances in cellular therapies are reshaping the management of blood disorders and malignancies.

The scientific programme covered a broad spectrum of contemporary hematology. Sessions addressed high-grade lymphomas, chronic myeloid leukaemia (CML), chronic lymphocytic leukaemia (CLL), chronic myelomonocytic leukaemia (CMML), acute myeloid leukaemia (AML), aplastic anaemia, paroxysmal nocturnal haemoglobinuria (PNH), and complications of haematopoietic stem cell transplantation (HSCT).

Particular attention was devoted to CAR-T-cell therapy, haploidentical transplantation in aplastic anaemia, graft-versus-host disease (GVHD), and evolving treatment strategies for acute leukaemia and lymphoma. Discussions on treatment sequencing, transplant indications and evidence-based management in Pakistan were especially relevant, given the challenges of implementing sophisticated therapies in resource-constrained settings.

The research abstract session offered a valuable opportunity for clinicians and researchers to present clinical experience and emerging evidence. Topics included transplantation outcomes, treatment strategies for AML and lymphoma, and therapeutic approaches to transfusion-dependent thalassaemia. These presentations demonstrated the importance of locally generated research in informing clinical decisions and improving patient care.

Learning Beyond the Lecture Hall

PCUH 2026 placed considerable emphasis on interactive learning and multidisciplinary collaboration. Panel discussions following scientific presentations enabled delegates to examine difficult clinical questions, compare institutional practices and explore how international recommendations could be adapted to local circumstances.

Dedicated nursing and data management sessions further broadened the scope of the conference. These sessions reinforced the importance of coordinated teamwork among physicians, nurses, laboratory professionals and data managers in delivering high-quality haematology and transplant services.

One of the highlights was the **HIMMEL fellowship-trainee quiz**, which brought an element of friendly competition to the academic programme. The quiz provided trainees with an opportunity to demonstrate their knowledge, clinical reasoning and ability to respond to challenging questions in a competitive setting.

PATHWEL was represented by Dr Aliah and Dr Mehroze, whose commendable performance secured a prize for their team. Their achievement was a source of pride for PATHWEL and reflected the value of continued academic preparation and participation in professional forums.

Exhibition and Institutional Representation

The conference also featured an exhibition by pharmaceutical companies, providing delegates with opportunities to learn about therapeutic developments, new treatment options and advances relevant to haematology and transplantation. The exhibition complemented the scientific sessions by encouraging interaction between healthcare professionals and industry representatives.

A separate poster exhibition showcased research and clinical work, allowing participants to engage with scientific findings beyond the formal presentations. Such platforms are important for encouraging research, sharing institutional experiences and fostering collaboration among professionals at different stages of their careers.

PATHWEL also established a dedicated stall at the conference. This provided an opportunity to introduce the centre, highlight its work in haematology and bone marrow transplantation, and interact with colleagues from other institutions. The stall helped strengthen PATHWEL's professional visibility and offered a platform to share its experience in providing specialised blood disease services in Pakistan.

Networking, Camaraderie and Lasting Connections

The conference programme extended beyond academic sessions to include two dinner evenings for national and international delegates. These gatherings provided a relaxed setting for colleagues to reconnect, establish new professional relationships and exchange experiences across institutions and countries.

Such informal interactions are an important component of international conferences. They encourage collaboration, facilitate the sharing of expertise and often lay the groundwork for future research partnerships and professional initiatives.

A Step Forward for Hematology in Pakistan

PCUH 2026 was a valuable gathering that combined scientific excellence, interactive learning, research presentations and professional networking. By bringing international advances into conversation with the realities of Pakistani clinical practice, the conference addressed an important need: ensuring that progress in hematology translates into meaningful improvements in patient care.

For PATHWEL, participation in the conference was an opportunity to remain abreast of rapidly evolving developments, strengthen institutional connections and support the academic growth of its team. The success of Dr Aliah and Dr Mehroze in the fellowship quiz added a particularly encouraging note to the centre's participation.

The conference concluded with renewed emphasis on collaboration, evidence-based practice and continued professional development. Its central message was clear: advancing hematology requires not only scientific innovation, but also committed professionals, locally relevant research, multidisciplinary teamwork and sustained efforts to make better treatments accessible to patients who need them most.

“PCUH 2026: Advancing Together, Transforming Lives”

****

ABSTRACTS

Therapeutic Drug Monitoring of Once daily Intravenous Busulfan in Paediatric Patients Undergoing Stem Cell Transplantation in Resource Limited Setting

Hira Tariq

Armed Forces Bone Marrow Transplant Center, Rawalpindi

Background: Busulfan is crucial for myeloablative conditioning in pediatric hematopoietic stem cell transplantation (HSCT), but its use is hindered by variability in pharmacokinetics among children. Traditionally given as four daily intravenous (IV) doses, this method is logistically challenging in resource-limited settings. A once-daily IV Busulfan regimen has been proposed as a more practical solution. Pharmacokinetic-guided dosing with target area under the concentration–time curve (AUC) monitoring is vital to ensure effectiveness and safety.

Objective: To evaluate the efficacy and safety of therapeutic drug monitoring -guided once daily intravenous busulfan in pediatric patients undergoing hematopoietic stem cell transplantation.

Methods: This interventional study involved pediatric patients undergoing hematopoietic stem cell transplantation (HSCT). It utilized a weight-based dosing regimen of intravenous Busulfan from Day −10 to Day −7 before transplantation, with blood samples collected for therapeutic drug monitoring (TDM) at 1, 2, and 3 hours post-infusion. Busulfan plasma concentrations were analyzed using Roche Cobas c501 and MyCare™ Oncology Assay Kit. Pharmacokinetic analysis was performed with PK-Solver, while statistical evaluations utilized SPSS version 25. All participants received a myeloablative conditioning regimen of busulfan, fludarabine, and cyclophosphamide, alongside anti-thymocyte globulin (ATG) prior to stem cell transplantation, with busulfan dosing adjusted to maintain an area under the concentration–time curve (AUC) of 3200–4800 µmol/min.

Results:A total of 19 pediatric patients undergoing stem cell transplantation were included, comprising both malignant (n =4) 21% and non-malignant(n=15) 79% conditions. The majority of patient (n=13) 68.4% were diagnosed with beta-thalassemia major followed by leukemia in (n=4) 21% while osteopetrosis and mucopolysaccharidosis (MPS) accounted for (n=1) 5.3% each. PK-guided dose modifications were required in three patients (15.7%). Doses were increased in two patients (10.5%) and decreased in one patient (5.3%). Acute graft-versus-host disease (GVHD) developed in one patient (5.3%) and one patient (5.3%) died due to posterior reversible encephalopathy syndrome (PRESS).

Conclusion: Once-daily intravenous busulfan, administered using a weight-based dosing strategy, achieved target AUC levels in the majority of pediatric patients. These findings support its use as an effective and practical alternative to conventional four-times-daily dosing, with the added advantage of simplified administration, particularly in resource-limited settings.

Keywords: Busalfan,Therapeutic drug monitoring (TDM),Stem Cell Transplant

Knowledge, Attitude And Practices Towards Pain Management Among Health Care Workers, Working At Military Hospitals Of Rawalpindi

Najia Gul

Armed Forces Post Graduate Medical Institute

Background: Pain is recognized globally as the “fifth vital sign” , Pain management remains a cornerstone of holistic care, yet it is often inadequately addressed due to insufficient knowledge, negative attitudes, and inconsistent practices among health care workers (HCWs). In tertiary care hospitals, where patient acuity is high and expectations of care are rigorous, effective pain control is not only a clinical necessity but also an ethical imperative. Gaps in professional training, misconceptions about opioid use, and limited application of evidence-based tools contribute to suboptimal pain relief and reduced patient satisfaction

Objective: The study aimed to evaluate the knowledge, attitude, and practices (KAP) of health care workers towards pain management in military hospitals of Rawalpindi, thereby identifying existing gaps and providing evidence for targeted interventions.

Methods: It was a cross-sectional study and was conducted at a military tertiary care hospital at Rawalpindi with a non-probability convenient sampling technique. A total of 300 licensed health care workers, including nurses, doctors, and paramedics, were recruited through convenience sampling. Data were collected using a pre-validated KAP questionnaire with established reliability (Cronbach’s alpha = 0.743). Ethical approval was obtained, and informed consent was secured from all participants. Data were analyzed using SPSS (v21).

Results: Out of 300 participants, the male-to-female ratio was 1:2.9, in which most participants 141 (47.0%) were in the 36-40 age group. Most of the professionals in this study held a bachelor's degree, 206 (68.7%); 74 (24.7%) graduated with a diploma, and 12 (4%) had a master's degree. The majority of the participants’ current area of practice was the surgical department, 77 (25.6%). The mean ± st.d of professional work experience was 16.62 ± 10.15 years (min-max: 1-30). The findings revealed that only 20.2% of respondents had received formal training in pain management within the last five years. Overall, participants demonstrated moderate knowledge, with notable deficiencies in pharmacological management, particularly opioid administration. There was a significant strong correlation between the age of the respondents and test scores ($r = 0.74$; $P = 0.01$). Attitudes reflected misconceptions regarding addiction and underestimation of patient-reported pain, while practices indicated inconsistent use of standardized pain assessment tools.

Conclusion: This study highlights significant knowledge gaps, attitudinal barriers, and inconsistent practices among HCWs in military hospitals. Addressing these shortcomings through structured education, continuous professional development, and implementation of evidence-based guidelines is critical to advancing effective pain management. Strengthening the competence of HCWs in this area will not only improve patient outcomes but also uphold the ethical and professional responsibility of ensuring pain relief as a basic human right.

Keywords: Pain management, Knowledge, Attitude, Practices, Health care workers, KAP Model

Outcome of Autologous Stem Cell Transplant in Relapsed/Refractory Classic Hodgkin Lymphoma - A Single Center Study

Nouman Nawaz Ali

Aga Khan University Hospital

Background: In relapsed/refractory (R/R) classic Hodgkin lymphoma (cHL), the preferred treatment is autologous stem cell transplantation (ASCT) after receiving high-dose chemotherapy (HDC).

Objective: Here, we describe and discuss the single-center experience, including outcomes and associated factors.

Methods: To provide insight into our experience, our single-center retrospective cohort study included 33 patients (aged 18 years or older at the time of diagnosis) who received HDC/ASCT at Aga Khan University Hospital, Karachi, Pakistan, from January 2013 to December 2023.

Results: Fourteen (42.4%) patients experienced post-transplant relapse, while 10 (30.3%) patients died. The transplant-related mortality (TRM) was seen in 2 (6.1%) patients. Median overall survival (OS) was 65 months, while the median progression-free survival (PFS) was 31 months. The 2- year PFS and OS were 62.1% (95% CI: 45.8–84.1%) and 77.9% (95% CI: 64.6–93.8%), respectively. On univariate analysis, factors associated with lower survival rates included a relapse within one year of initial chemotherapy and the failure to achieve complete remission (CR), both before and after transplantation.

Conclusion: This study emphasizes that disease status before and after transplant affects outcomes, showing that achieving CR before ASCT yields better outcomes than achieving PR.

Keywords: Autologous stem cell transplant, classic Hodgkin Lymphoma, relapsed/refractory disease

Primary Multifocal Osseous Classic Hodgkin Lymphoma with Spinal Involvement

Nouman Nawaz Ali, . Natasha Ali.
Aga Khan University Hospital

Background: Primary multifocal osseous Hodgkin's lymphoma (PMOHL) is a very rare primary presentation of Hodgkin's lymphoma (HL). Spinal cord compression is a rare presenting feature and is seen in only ~0.2% of cases. Given the vertebral column, the disease can be mistaken for osteomyelitis or Pott's disease.
Objective: This case signifies the need for repeat biopsy to prevent unnecessary delays and polypharmacy. Once a diagnosis is made, ABVD is still a curative and cost-effective regimen in the cost-constrained part of the world.
Methods:ERC was obtained and informed consent was taken.
Results:A 40-year-old male, diagnosed with hypertension, presented to the neurosurgery clinic with back pain, which would intensify in certain postures, such as biking or lying flat. He also had intermittent undocumented fever without chills or rigors. Imaging revealed spinal cord compression, initially suspected to be due to metastatic disease. Biopsy of the lesion confirmed stage IV PMOHL. The patient was administered ABVD (Adriamycin, bleomycin, vinblastine, and dacarbazine) chemotherapy and showed a complete metabolic response after six cycles.
Conclusion: This case highlights the significance of a multidisciplinary approach and repeat biopsy to reach a diagnosis and avoid unnecessary polypharmacy, as this disease can easily be confused with tuberculosis and metastatic disease, hence causing diagnostic delays. Timely diagnosis and initiation of treatment with ABVD chemotherapy led to a favorable outcome.
Keywords: Primary osseous Hodgkin lymphoma, ABVD, Spinal involvement

PREVALENCE OF VARIOUS RED CELL ALLOANTIBODIES IN THE PAKISTANI POPULATION- A TERTIARY CARE CENTRE'S EXPERIENCE

Komal Masroor, Salman Adil Hasan Hayat
Aga Khan University Hospital (AKUH), Karachi Pakistan

Background: Red cell alloimmunization complicates transfusion and pregnancy care; however, its prevalence in Pakistan remains under-studied. This study aimed to determine the prevalence, specificity, and associated risk factors of red cell alloimmunisation in Pakistan.
Objective: This study aimed to determine the prevalence, specificity, and associated risk factors of red cell alloimmunisation in Pakistan.
Methods:A prospective cross-sectional study was conducted at the Section of Hematology and Transfusion Medicine, Aga Khan University, from March to June 2025. Consecutive samples were screened for red cell antibodies using gel cards, and positive samples were further evaluated on an 11-cell identification panel. Patients with autoantibodies were excluded. Data regarding blood group, transfusion, and obstetric history were collected through a structured questionnaire. Statistical analysis was performed using SPSS v26.
Results: Among 5000 screened samples, 253 (5.06%) showed red cell antibodies, while antibody identification was possible in 83 patients (1.66%). Females constituted 90.4% of cases, with a median age of 28 ± 4.4 years. Most patients were Rh-positive (75.9%). Anti-D was the commonest alloantibody (15%), followed by anti-E and anti-M (8% each), and anti-K (5%). Anti-D and anti-C were significantly more frequent among Rh-D negative individuals, whereas anti-M, anti-E, and anti-K predominated in Rh-D positive individuals. Pregnancy was the leading risk factor (79.5%), followed by transfusion (33.7%). Thalassemia was the most frequent indication for repeated transfusions(n=8; 9.64%; $p < 0.001$). Despite anti-D prophylaxis, nine pregnant women developed anti-D antibodies(n=9; 3.64%).
Conclusion: Alloimmunisation in this cohort was low but clinically significant, particularly among pregnant women and multiply transfused thalassemia patients, highlighting the need for routine antibody screening, anti-D prophylaxis, and phenotypically matched transfusions.
Keywords: Alloantibodies, Pregnancy, Anti-D, Thalassemia

Primary Plasma Cell Leukemia with CD138-Negative Circulating Clone and CD138-Positive Bone Marrow Infiltration

Muhammad Shayan Ashfaq, Hareem Alam
Aga Khan University Hospital

.

Background: Primary plasma cell leukemia (PCL) is a rare and highly aggressive plasma cell neoplasm characterized by circulating clonal plasma cells and extensive bone marrow infiltration. Flow cytometric diagnosis of plasma cell neoplasms commonly relies on plasma cell-associated markers including CD38, CD138, and CD45. However, immunophenotypic heterogeneity, particularly aberrant CD138 expression, may create diagnostic challenges and lead to under-recognition of

malignant plasma cell populations. We report a rare case of primary PCL demonstrating CD138-negative circulating plasma cells despite diffuse CD138-positive bone marrow involvement.

Objective: To describe a rare immunophenotypic presentation of primary plasma cell leukemia with CD138-negative circulating plasma cells and CD138-positive bone marrow infiltration. To highlight the diagnostic challenges associated with reliance on single-marker flow cytometric gating strategies in aggressive plasma cell neoplasms. To emphasize the importance of integrating multiparametric flow cytometry with tissue-based immunohistochemistry for accurate diagnosis of plasma cell leukemia.

Methods:A detailed clinicopathological evaluation was performed in a male patient in his 50s presenting with generalized weakness, anemia, and thrombocytopenia at Aga Khan University Hospital. Peripheral blood smear examination, multiparametric flow cytometry, bone marrow aspiration and trephine biopsy, and immunohistochemical studies were conducted. Flow cytometric analysis assessed plasma cell-associated antigen expression, while immunohistochemistry was performed using CD138, CD56, and MUM1 markers to confirm plasma cell lineage.

Results: Peripheral blood smear demonstrated marked plasmacytosis, with plasma cells comprising 60–67% of circulating leukocytes. Flow cytometry identified an aberrant plasma cell population (~79%) characterized by low side scatter, CD45 negativity, CD56 positivity, dim CD117 and CD38 expression, and cytoplasmic kappa light chain restriction. Notably, CD138 expression was absent in the circulating plasma cell population. Bone marrow examination revealed near-complete replacement by plasma cells (~94%) with marked suppression of normal hematopoiesis. In contrast to peripheral blood findings, immunohistochemistry demonstrated diffuse positivity for CD138, CD56, and MUM1 within marrow-infiltrating plasma cells, confirming plasma cell lineage and highlighting discordant CD138 expression between circulating and tissue-based tumor populations.

Conclusion: This case highlights a rare immunophenotypic presentation of primary plasma cell leukemia with CD138-negative circulating plasma cells and preserved CD138 expression in bone marrow tissue. The observed discordance emphasizes the limitations of single-marker gating strategies in diagnostic flow cytometry and underscores the importance of integrating multiparametric flow cytometry with tissue-based immunohistochemical correlation for accurate diagnosis of aggressive plasma cell neoplasms.

Keywords: Plasma cell leukemia; CD138-negative plasma cells; flow cytometry; plasma cell dyscrasia, immunohistochemistry

Beyond Chronic Myeloid Leukemia: BCR::ABL1 p190–Positive Acute Myeloid Leukemia with Co-occurring TET2 Mutations

Muhammad Shayan Ashfaq Muhammad Zeeshan Ansar, Muhammad Usman Shaikh, Muhammad Shariq,SanaS
Aga Khan University Hospital

Background: Philadelphia chromosome–positive acute myeloid leukemia (Ph+ AML) is a rare and diagnostically challenging subtype of AML characterized by the presence of BCR::ABL1 fusion transcripts. Distinguishing de novo Ph+ AML from chronic myeloid leukemia in blast crisis remains difficult because of overlapping clinical and molecular features. Among BCR::ABL1 variants, the p190 transcript is uncommon in AML and has been associated with aggressive disease biology and adverse outcomes. We report two cases of adult Ph+ AML with rare BCR::ABL1 p190 transcripts accompanied by co-occurring TET2 mutations, highlighting their clinicopathologic and molecular characteristics.

Methods: Comprehensive clinicopathologic, cytogenetic, immunophenotypic, and molecular evaluation was performed in two adult patients diagnosed at Aga Khan University Hospital. Diagnostic workup included peripheral blood smear examination, bone marrow aspiration and biopsy, flow cytometric immunophenotyping, conventional cytogenetics, reverse transcriptase polymerase chain reaction (RT-PCR) for BCR::ABL1 transcript analysis, and targeted next-generation sequencing (NGS) for mutation profiling.

Results: Case 1 involved a 49-year-old woman presenting with severe anemia, marked leukocytosis (153 × 10^9/L), thrombocytopenia, elevated erythrocyte sedimentation rate, and 37% circulating blasts. Case 2 involved a 70-year-old man with multiple comorbidities who presented with persistent leukocytosis (37.9 × 10^9/L), thrombocytopenia, and approximately 15% peripheral blasts. In both cases, bone marrow examination and flow cytometry confirmed acute myeloid leukemia. Cytogenetic analysis demonstrated the Philadelphia chromosome, while molecular studies identified BCR::ABL1 p190 transcripts, including e1a3 in case 1 and e1a2 in case 2. Targeted NGS revealed pathogenic TET2 mutations with high variant allele frequencies (45.3% and 49%, respectively). Common AML-associated mutations, including NPM1 and FLT3 alterations, were absent in both patients.

Conclusion: These cases expand the molecular spectrum of Philadelphia chromosome–positive AML by demonstrating the coexistence of rare BCR::ABL1 p190 transcripts and TET2 mutations. The findings support the existence of a distinct molecular subset of AML and emphasize the importance of comprehensive molecular profiling for accurate diagnosis, distinction from chronic myeloid leukemia in blast phase, prognostic stratification, and therapeutic decision-making in rare myeloid neoplasms.

Keywords: Acute myeloid leukemia; Philadelphia chromosome; BCR::ABL1 p190; TET2 mutation; Ph-positive AML; Molecular cytogenetics; Next-generation sequencing; Rare leukemia subtype.

Bone Marrow metastasis in Primary Pulmonary Monophasic Synovial Sarcoma Presenting as Pancytopenia: An Extremely Rare Pediatric Case Report

Muhammad Shayan Ashfaq, Hareem Alam
Aga Khan University Hospital

Background: Primary pulmonary synovial sarcoma is an exceptionally rare malignant mesenchymal tumor accounting for less than 0.5% of all primary pulmonary malignancies. Bone marrow metastasis from synovial sarcoma is exceedingly uncommon, particularly in pediatric patients, and may present with hematological manifestations such as pancytopenia. We report a rare pediatric case of primary pulmonary monophasic synovial sarcoma presenting with pancytopenia secondary to bone marrow metastasis.

Objective: To describe an extremely rare pediatric case of primary pulmonary monophasic synovial sarcoma with bone marrow metastasis presenting as pancytopenia. To highlight the diagnostic significance of bone marrow examination and immunohistochemistry in identifying metastatic marrow infiltration in patients with unexplained cytopenias. To emphasize the importance of clinicopathological correlation in the accurate diagnosis of rare and aggressive soft tissue sarcomas.

Methods:A comprehensive clinicopathological evaluation was performed in a 12-year-old male presenting to Aga Khan University Hospital with fever, generalized weakness, weight loss, and persistent pancytopenia. Diagnostic workup included radiological imaging, complete blood counts, peripheral blood smear examination, bone marrow aspiration and trephine biopsy, histopathological analysis of the pulmonary lesion, and immunohistochemical studies including TLE1, CKAE1/AE3, and SS18.

Results: Radiological evaluation identified a left lung mass. Histopathological examination of the pulmonary lesion confirmed monophasic synovial sarcoma, FNCLCC Grade 2. Laboratory investigations revealed pancytopenia with hemoglobin 7.7 g/dL, leukocyte count 3.31 × 10^9/L, and platelet count 63 × 10^9/L. Peripheral blood smear demonstrated a leukoerythroblastic blood picture with nucleated red blood cells, anisopoikilocytosis, and occasional metamyelocytes. Bone marrow examination revealed infiltration by atypical non-hematopoietic mononuclear cells causing suppression of normal hematopoiesis. Immunohistochemistry demonstrated weak positivity for TLE1, while CKAE1/AE3 was negative and SS18 was non-contributory. Correlation with the previously diagnosed pulmonary tumor supported the diagnosis of bone marrow metastasis from primary pulmonary monophasic synovial sarcoma.

Conclusion: Primary pulmonary monophasic synovial sarcoma with bone marrow metastasis presenting as pancytopenia is an exceptionally rare occurrence, especially in pediatric patients. This case highlights the importance of considering metastatic marrow infiltration in patients with unexplained cytopenias and underlying malignancy. Integrated histopathological, immunohistochemical, and clinicopathological correlation is essential for accurate diagnosis of this rare and aggressive neoplasm.

Keywords: Primary pulmonary synovial sarcoma, monophasic synovial sarcoma, bone marrow metastasis, pancytopenia, soft tissue sarcoma

Primary Cutaneous Gamma-Delta T-Cell Lymphoma: A Rare Entity with Extensive Cutaneous and Systemic Involvement

Muhammad Shayan Ashfaq, Madiha Bilal, Natasha Ali, Zeenat Hadi
Aga Khan University Hospital

.

Background: Primary cutaneous gamma-delta T-cell lymphoma (PCGD-TCL) is a rare and aggressive subtype of cutaneous T-cell lymphoma with poor prognosis and frequent extracutaneous involvement. Diagnosis is often challenging due to its variable clinical presentation and overlap with other dermatological conditions.

Objective: To report a rare case of PCGD-TCL with extensive cutaneous and systemic involvement and highlight its diagnostic and therapeutic challenges.

Methods: An 84-year-old male presenting with disseminated ulcerative skin lesions and systemic symptoms underwent clinical evaluation, skin biopsy with immunohistochemistry, and FDG PET/CT imaging for diagnosis and staging. The patient was treated with dose-adjusted CHOP chemotherapy.

Results: Histopathology and immunophenotyping confirmed PCGD-TCL, showing CD3, granzyme B, CD56, and BCL2 positivity with high Ki-67 index. FDG PET/CT revealed widespread cutaneous, nodal, and visceral involvement consistent with Lugano stage IV disease. Despite chemotherapy and supportive care, the patient developed progressive cardiopulmonary complications and succumbed to the disease.

Conclusion:PCGD-TCL is an aggressive lymphoma with poor clinical outcomes and limited response to conventional therapy. Early diagnosis through integrated clinical, radiological, and histopathological assessment is essential for appropriate disease management.

Keywords: : Primary cutaneous gamma delta T-cell lymphoma; Cutaneous T-cell lymphoma; FDG PET/CT; Immunohistochemistry; Rare lymphoma.

Frequency and outcome of acute GVHD in tertiary care hospital of Pakistan

Isma Akram, Muhammad Ayaz mir

Shifa international hospital

Background:graft-versus-host disease (aGVHD) is one of the toughest problems that can follow an allogeneic hematopoietic stem cell transplant (allo-HSCT). It accounts for a large part of the illness and death seen after transplant, and the problem hits hardest where money and resources are tight, since the newer drugs used to prevent or rescue these patients are often out of reach. In Pakistan, very little has been published on how common this complication actually is.

Objective: We wanted to find out, in our own patients, how often aGVHD shows up after allo-HSCT, which organs it tends to hit, how bad it gets, and what happens to these patients in the first few months — all within a single tertiary care hospital in Pakistan.

Methods: This was a descriptive, observational study run in the Department of Clinical Hematology at Shifa International Hospital, Islamabad. We followed 100 patients who had an allo-HSCT between July 2025 and January 2026; both fully HLA-matched and haploidentical donor transplants were included. Each patient was given the standard GVHD prophylaxis our unit uses. We looked for aGVHD within the first 100 days and graded it with the modified Glucksberg criteria. The numbers were crunched in SPSS version 26, using chi-square tests together with Kaplan–Meier survival analysis.

Results: On average, patients were 32.4 ± 14.6 years old. A malignant blood disorder was the reason for transplant in 56 patients (56%), while the other 44 (44%) had a benign condition. Seventy-two transplants (72%) came from fully HLA-matched donors and 28 (28%) were haploidentical. In all, 27 patients (27%) went on to develop aGVHD. The gut was hit most often — 15 patients (15%) — followed by the skin in 8 (8%), the mouth in 3 (3%), and the lungs in just 1 (1%). By day 100, 91% of patients were still alive; the 9 who died had all developed Grade IV gastrointestinal aGVHD, and 7 of those 9 deaths (77.8%) were in haploidentical recipients. Survival was clearly worse for haploidentical patients than for those with a full match on Kaplan–Meier analysis (log-rank p = 0.03).

Conclusion:aGVHD is still a serious, and at times deadly, complication of allogeneic stem cell transplantation, and the risk of dying from the transplant itself falls most heavily on haploidentical recipients. Our results point to a real need for better prophylaxis, picking out high-risk patients early, and building transplant guidelines that fit the day-to-day realities of a resource-limited setting like Pakistan.

Keywords: Graft Versus Host Disease,*GVHD*

EXPRESSION OF CD73 AND CD123 IN PATIENTS WITH ACUTE LEUKEMIA FOR ASSESSMENT OF MINIMAL RESIDUAL DISEASE (MRD): EXPERIENCE FROM A TERTIARY CARE HOSPITAL IN KARACHI.

Suman Ahuja, Muhammad Zulqurnain Imran, Anjly Ahuja

Department of Haematology

Indus Hospital Health and Network karachi

Background: Developments in diagnostic hematopathology have made multiparameter flow cytometry (MFC) an essential component of both an initial diagnosis and response-to-treatment evaluation in patients with acute leukemia. MRD positive patients after induction or consolidation in AML and ALL are reported to be associated with high threat of decline and poor over-all existence). One of the major challenges of MRD detection in B-ALL is the interference from hematogones, which are normal B-cell precursors that significantly increase in number following marrow regeneration after chemotherapy and have overlapping immunophenotypic characteristics with leukemic blasts expressing CD19, CD10, CD34, CD38, TdT, and CD45 . To circumvent this issue, newer LAIP markers, notably, CD73 and CD123 are increasingly favored. CD73 is an ecto-5'-nucleotidase involved in adenosine-mediated immunosuppression . CD123 is the alpha chain of the interleukin-3 receptor. This differential expression renders CD123 a highly useful marker for MRD application, as well as a promising target for therapy . However, it has been shown that CD73 and CD123 are also expressed in subsets of T-ALL and therefore could also be considered for T-ALL MRD panels

Objective: To analyze the expression of CD73 and CD123 in patients with acute leukemia and assess their significance in minimal residual disease detection using flow cytometry.

Methods:A descriptive cross-sectional investigation was carried out in the Hematology Laboratory of Indus Hospital and Health Network Karachi. 260 newly diagnosed acute leukemia patients were recruited through consecutive sampling.

Results: Of the 260 patients, 71.9% had CD123 and 17.3% had CD73. The mean age of the CD73-positive and CD73-negative groups did not differ significantly (123.1 ± 72.2 vs. 138.0 ± 63.8 years, p = 0.204) or between CD123-negative and CD123-positive groups (130.6 ± 74.6 vs. 122.5 ± 69.8 years, p = 0.408). Frequency distributions and stacked bar analyses were used to display the distribution of minimal residual disease (MRD) across CD73 and CD123 expression levels.

Conclusion: Because of its greater prevalence and prognostic value, CD123 should be given priority in routine MRD monitoring, with CD73 perhaps acting as an additional marker. To improve the sensitivity and specificity of detection, multiparametric flow cytometry panels are advised.

Keywords: Acute leukemia; Minimal residual disease (MRD); CD73 expression; CD123 expression; Flow cytometry

SPECTRUM AND CLINICAL IMPACT OF HOTSPOT MUTATIONS IN ACUTE MYELOID LEUKAEMIA (AML) DETECTED BY TARGETED NEXT-GENERATION SEQUENCING (NGS): EXPERIENCE FROM A RESOURCE-LIMITED SETTING

Wajeeha Iftikhar, Bushra Moiz, Usman Shaikh: MBBS, Zeeshan Ansar
Aga Khan University Hospital

Background: The WHO 5th edition and International Consensus Classification emphasize comprehensive molecular profiling in acute myeloid leukemia (AML), with next-generation sequencing (NGS) increasingly important for prognostication, therapeutic decisions, and assessment of co-mutational effects. However, data from Pakistan remain limited.

Objective: The objective of this study is to evaluate the NGS-defined mutational spectrum of adult AML in Pakistan and its association with cytogenetics, ELN 2022 risk categories, and mortality.

Methods:A retrospective cross-sectional study was conducted at the Section of Hematology and Transfusion Medicine, Aga Khan University Hospital from June 2022 to December 2025. Adult AML patients (≥18 years) analyzed using a 29-gene NGS panel were included. AML diagnosis was established according to WHO criteria using bone marrow examination, flow cytometry, and/or AML-defining genetic abnormalities. ELN 2022 criteria guided risk stratification. Demographic, laboratory, cytogenetic, molecular, and outcome data were analyzed.

Results: Ninety-seven patients were included with mean age 43.3 ± 15.6 years and male predominance (1.6:1). Anemia was present in all patients, thrombocytopenia in 79 (81.4%), and hyperleukocytosis in 12 (12%). Conventional karyotyping was available in 89 patients, revealing normal karyotype in 47 (52.8%) and abnormal cytogenetics in 42 (47.2%), including 9 complex karyotypes. NGS identified at least one mutation in 32/47 (68%) patients with normal karyotype and 26/42 (62%) with abnormal cytogenetics. ELN stratification classified 24 patients as adverse-risk, 23 favourable-risk, and 48 intermediate-risk. TP53 and RUNX1 predominated in adverse-risk AML, while NPM1 and DNMT3A were common in favorable-risk AML. Overall mortality was 47% (46/97), occurring most frequently in intermediate-risk patients harboring FLT3 ± NPM1 mutations.

Conclusion:ELN 2022 criteria may not fully predict outcomes in Pakistani AML patients, as co-mutational profiles appear to modify prognosis. Population-specific refinement of risk stratification is warranted.

Keywords: Acute Myeloid Leukemia, Next Generation Sequencing, ELN stratification

THERAPEUTIC DRUG MONITORING OF ONCE DAILY INTRAVENOUS BUSULFAN IN PAEDIATRIC PATIENTS UNDERGOING STEM CELL TRANSPLANTATION IN RESOURCE LIMITED SETTING

Hira Tariq, Tariq Ghafoor ,Saima Humayun Toor, Tariq Azam Khattak, Mehwish Gillani, Ayesha Bibi, Amir Aslam Awan

Armed Forces Bone Marrow Trasnplant Center ,Rawalpindi

Background: Busulfan is crucial for myeloablative conditioning in pediatric hematopoietic stem cell transplantation (HSCT), but its use is hindered by variability in pharmacokinetics among children. Traditionally given as four daily intravenous (IV) doses, this method is logistically challenging in resource-limited settings. A once-daily IV Busulfan regimen has been proposed as a more practical solution. Pharmacokinetic-guided dosing with target area under the concentration–time curve (AUC) monitoring is vital to ensure effectiveness and safety.

Objective: To evaluate the efficacy and safety of therapeutic drug monitoring -guided once daily intravenous busalfan in pediatric patients undergoing hematopoietic stem cell transplantation.

Methods: This interventional study involved pediatric patients undergoing hematopoietic stem cell transplantation (HSCT). It utilized a weight-based dosing regimen of intravenous Busulfan from Day −10 to Day −7 before transplantation, with blood samples collected for therapeutic drug monitoring (TDM) at 1, 2, and 3 hours post-infusion. Busulfan plasma concentrations were analyzed using Roche Cobas c501 and MyCare™ Oncology Assay Kit. Pharmacokinetic analysis was performed with PK-Solver, while statistical evaluations utilized SPSS version 25. All participants received a myeloablative conditioning regimen of busulfan, fludarabine, and cyclophosphamide, alongside anti-thymocyte globulin (ATG) prior to stem cell transplantation, with busulfan dosing adjusted to maintain an area under the concentration–time curve (AUC) of 3200–4800 µmol/min.

Results:A total of 19 pediatric patients undergoing stem cell transplantation were included, comprising both malignant (n =4) 21% and non-malignant(n=15) 79% conditions. The majority of patient (n=13) 68.4% were diagnosed with beta-thalassemia major followed by leukemia in (n=4) 21% while osteopetrosis and mucopolysaccharidosis (MPS) accounted for (n=1) 5.3% each. PK-guided dose modifications were required in three patients (15.7%). Doses were increased in two patients (10.5%) and decreased in one patient (5.3%). Acute graft-versus-host disease (GVHD) developed in one patient (5.3%) and one patient (5.3%) died due to posterior reversible encephalopathy syndrome (PRESS). A total of 19 pediatric patients undergoing stem cell transplantation were included, comprising both malignant (n =4) 21% and non-malignant(n=15) 79% conditions. The majority of patient (n=13) 68.4% were diagnosed with beta-thalassemia major followed by leukemia in (n=4) 21% while osteopetrosis and mucopolysaccharidosis (MPS) accounted for (n=1) 5.3% each. PK-guided dose modifications were required in three patients (15.7%). Doses were increased in two patients (10.5%) and decreased

in one patient (5.3%). Acute graft-versus-host disease (GVHD) developed in one patient (5.3%) and one patient (5.3%) died due to posterior reversible encephalopathy syndrome (PRESS).
Conclusion: Once-daily intravenous busulfan, administered using a weight-based dosing strategy, achieved target AUC levels in the majority of pediatric patients. These findings support its use as an effective and practical alternative to conventional four-times-daily dosing, with the added advantage of simplified administration, particularly in resource-limited settings.
Keywords: Busalfan,Therapeutic drug monitoring (TDM) ,Area under the curve (AUC)

DIAGNOSTIC THRESHOLD OF IMMATURE GRANULOCYTES IN PEDIATRIC INFECTIONS

Fatima Farhan, . Shariq Sheikh , Arshalooz Rahman, Bushra Moiz
Aga Khan University Hospital Karachi

Background: Fever is a significant cause of pediatric emergency visits, and distinguishing viral illnesses from severe bacterial infections or early sepsis remains challenging due to limitations of current biomarkers such as white blood cell (WBC), absolute neutrophil count (ANC), C-reactive protein (CRP), and procalcitonin. Immature granulocytes (IG) can be measured promptly and cost-effectively by automated hematology analysers, rise early in systemic infections, and may outperform established traditional biomarkers in diagnosing bacterial disease.

Objective: Despite evidence in adults and specific pediatric diseases, IG thresholds for detecting general infections in children are yet unknown. This study aimed to assess the optimal cutoff and the diagnostic utility of IG in common pediatric infections.

Methods: This cross-sectional study was conducted at Aga Khan University Hospital from December 2024 to July 2025 and included children aged 1–17 years with infection and sepsis. Clinical features, vital signs, laboratory markers (IG%, IG absolute, WBC, ANC), and culture results were recorded within 24 hours of presentation and compared with age-matched controls. IG% was measured using the Sysmex XN-1000 (Singapore). Receiver Operating Characteristic (ROC) curve analysis was performed to evaluate diagnostic performance and calculate the area under the curve (AUC).

Results: In 150 pediatric patients with suspected infection (56% male, mean age 5.74 ± 4.59 years), gastrointestinal (50%) and respiratory (31%) infections predominated. Patients showed significantly higher IG% (0.91 ± 1.31 vs 0.22 ± 0.09, p=0.001) and absolute IG count (0.13 ± 0.26 vs 0.02 ± 0.01, p<0.001) compared with 150 age-matched healthy controls. Absolute IG count outperformed WBC and ANC among hematological parameters, demonstrating the best diagnostic performance (sensitivity 84.6%, specificity 78.7%, AUC 0.867) at cut-off of 0.25 x 10E9/L. Multivariable analysis confirmed IG% as an independent predictor of infection (p < 0.001).

Conclusion: Immature Granulocytes are an effective and a reliable early hematological biomarker for early detection of pediatric infections, offering superior diagnostic accuracy compared with conventional leukocyte indices and facilitating timely clinical decision-making.

Keywords: Immature granulocytes, C-reactive protein, biomarker, pediatric infection

PREVALENCE OF CLOTTING FACTOR INHIBITORS UTILIZING MIXING STUDIES IN A TERTIARY CARE SETTING

Fatima Farhan, Rimsha Imran , Bushra Moiz
Aga Khan University Hospital Karachi

Background: Acquired clotting factor inhibitors arise as a serious complication in the management of bleeding disorders, particularly in hemophilia A and B. Most of these clotting factor inhibitors develop following replacement therapy, or are often associated with post-partum state, malignancy, autoimmune conditions, antiphospholipid antibody syndrome or advanced age. True prevalence of clotting factor inhibitors is still unknown due to limited diagnostic facilities.

Objective: This study aimed to assess the prevalence of clotting factor inhibitors in patients with prolonged PT and APTT.

Methods: This descriptive study was conducted at Aga Khan University Hospital Karachi from December 2022 to December 2024 and included plasma samples with initially prolonged PT and APTT. Mixing studies with normal pooled plasma (NPP) in a 1:1 ratio was utilised for differentiating clotting factor deficiency from inhibitors. Clotting times of the PT/aPTT mix that fell below the upper reference interval (URI) were reported as corrected, indicating clotting factor deficiency. Non-correction within the URI and non-parallelism was used to identify clotting factor inhibitors.

Results:A total of 243 patients, including 158 males and 85 females, with a mean (± SD) age of 14.9 years (± 18.9), were studied. Most frequent single factor deficiencies (80.7%) were those of clotting factors FVII (21.0%), FX (18.9%), and FVIII (17.7%) followed by deficiency of multiple clotting factors (19.3%). A total of 376 mixing studies were conducted on samples with prolonged PT (n = 54), aPTT (n = 56), and combined PT/aPTT (n=133). Inhibitors were suspected in 10 of 194 samples (5.1%) with single clotting factor deficiency and in 10 of 49 samples with multiple clotting factor deficiencies (20.4%) using ICSH recommendations. Prevalence of aPTT inhibitors was greater in patients with multiple clotting factor deficiencies (7/45, 15.5%) compared to those with a single deficiency (7/142, 4.9%).

Conclusion: This study identified a clotting factor deficiency in 94.4% of 376 samples and a possible PT/aPTT inhibitor in 5.6% of the samples.

Keywords: Mixing studies, clotting factor deficiency, clotting factor inhibitor

MOLECULAR PITFALLS IN ACUTE PROMYELOCYTIC LEUKAEMIA (APL): A CASE OF CRYPTIC t (15;17) TRANSLOCATION MASKED BY MONOSOMY 17 AND A MARKER CHROMOSOME

Fatima Farhan, Shariq Shaikh, Salman Arain Zeeshan Ansar
Aga Khan University Hospital Karachi

Background: Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML), defined by the presence of abnormal promyelocytes in the bone marrow and translocation between chromosomes 15 and 17, known as t(15;17) which results in the PML-RARA fusion gene. However, a small number of APL cases involve variant translocations where RARA fuses with other genes, or cryptic rearrangements that may not be visible on standard cytogenetic testing. Additional chromosomal abnormalities are also found in over a third of APL patients, and these can influence both the course of the disease and its response to treatment.

Objective: The objective of this study was to combine cytogenetic, molecular, and morphological analyses to achieve accurate diagnosis and risk assessment in APL, particularly in patients with uncommon or complex chromosomal findings.

Methods: A 58-year-old woman with a history of hepatitis C-related chronic liver disease, presented with pancytopenia. Her bone marrow showed abnormal promyelocytes, with immunohistochemistry positive for myeloperoxidase (MPO) and CD117.

Results: Cytogenetic testing revealed two unusual findings: monosomy 17 (loss of one copy of chromosome 17) and a marker chromosome; however, there was no visible t (15;17). Molecular testing using reverse transcriptase- polymerase chain reaction (RT-PCR) confirmed the presence of the PML-RARA fusion, establishing the diagnosis of APL. TP53 deletion was detected by FISH.

Conclusion: This case emphasizes the value of combining cytogenetic, molecular, and morphological studies for accurate diagnosis and risk assessment in APL, particularly in patients with uncommon or complex chromosomal findings. Monosomy 17 is rarely seen in APL and carries important clinical implications. The loss of chromosome 17 suggests deletion of the tumor proetein p53 (TP53) tumor suppressor gene, which may be linked to a more aggressive disease and poorer outcomes. These patients may not respond as well to standard treatment and often require more careful follow-up. While fluorescence in situ hybridization (FISH) testing can detect PML-RARA in many cases, complex or hidden rearrangements can be missed, highlighting the importance of using sensitive molecular methods like RT-PCR, which can confirm diagnosis and help monitor minimal residual disease.

Keywords: AML, APL, translocation, monosomy, cytogenetics.

REAL WORLD OUTCOMES OF AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA: A LOW MIDDLE INCOME COUNTRY EXPERIENCE

Kashaf ad Duja Awais, Kashaf ad Duja Awais, Maryam Khan, Nighat Shahbaz, Mehreen Ali Khan,Jahanzeb ur Rehman, Saima Humayun, Hammad Javed, Yasir Abbass, Ammad Akram, Tariq Ghafoor, Raheel Iftikhar,
Armed Forces Bone Marrow Transplant Centre, Rawalpindi

Background: High dose chemotherapy followed by autologous stem cell transplantation (ASCT) remains the standard consolidation strategy for transplant eligible newly diagnosed multiple myeloma (TE-NDMM). Data from low-and middle-income countries (LMICs) is limited, especially where anti-CD38 based induction and maintenance is inaccessible.

Objective: To report real world outcomes of MM patients receiving ASCT in Pakistan.

Methods: We retrospectively analyzed 127 patients undergoing ASCT at the Armed Forces Bone Marrow Transplant Centre (AFBMTC) from 2005-2025. The primary outcomes were overall survival (OS) and progression-free survival (PFS). Secondary outcomes were engraftment kinetics, response depth (as per IMWG criteria), cumulative incidence of relapse (CIR) and transplant related mortality (TRM) at day 100. Kaplan-Meier, Aalen Johansen and Fine and Gray methods were used where appropriate.

Results: The median age of the study cohort was 51 (IQR: 41-58) years. The male to female ratio was 2.17:1. ISS staging was available for 84 (66.14%) patients; ISS-I (45.2%), ISS-II (23.8%) and ISS-III (31%). R-ISS staging was available for 38 (29.9%) patients; R-ISS I (23.7%), R-ISS II (39.5%), R-ISS III (36.8%). The most commonly used regimen was IMiD based triplet (VRd) used in 76 (61.8%) patients, followed by alkylator-based triplet (CyBorD) in 30 (24.4%), thalidomide-based triplet (MPT/VTd/CTD) in 6 (4.9%), doublet regimens (TD/Vd) in 5 (4.1%), and other regimens in 4 (3.2%) patients. Daratumumab based quadruplet induction was used in 2 (1.6%) patients. Among those with documented responses post-induction, VGPR or better was seen in 66.9% patients (sCR in 25.9%, CR in 64.7% and VGPR in 9.4% patients). At transplant], 33.3% patients were in sCR, 55.8% in CR, 1.7% in VGPR and 9.1% in PR or less. Mobilization was performed with G-SCF alone in 0.8%, G-CSF plus plerixafor in 62.3%, cyclophosphamide plus G-CSF in 36.1% and cyclophosphamide, G-CSF and plerixafor in 0.8% patients. High dose melphalan 200mg/m2 was used in 78.5% of patients, melphalan 140mg/m2 in 19.8% and alternative melphalan dosage in 1.7% of patients. The median CD34 dose was 4.8x106/kg (IQR 3.38-7.37). Median time to neutrophil and platelet engraftment was 11 and 12 days respectively. Of the 99 (77.95%) patients with documented post ASCT responses 49.5% were in sCR, 34.3% were in CR, 14.1% were in VGPR and 2% had stable or progressive disease. Bortezomib plus IMid maintenance was used in 28 (25.2%) of patients, carfilzomib maintenance in 20 (18%), lenalidomide monotherapy in 47 (42.3%), and others in 16 (14.4%) patients. At a median follow-up of 30.7 months, the 2-year PFS and OS were 79.9% and 84.6%, respectively. The cumulative incidence of day 100 TRM was 2.52% (95% CI 0.00–5.33%). The cumulative incidence of relapse post-ASCT was 18.3% (95% CI: 11.2–29.1%). Cox regression after adjusting for covariates demonstrated age < 60 years (OS: p=0.039, PFS: 0.002) and < CR at transplant (OS: p=0.025; PFS: p= 0.004) as independent predictors of OS and PFS. Response at transplant (p= 0.014) and post-ASCT response were significant predictors of CIR (p=0.027).

Conclusion:ASCT is a feasible consolidation strategy for MM in LMICs with survival and engraftment kinetics comparable to international data. Deeper pre-ASCT response is associated with better survival. In the absence of advanced diagnostics for risk stratification, bispecifics and CAR-T cell therapy; ASCT remains the standard consolidation therapy for all TE-MM patients in low middle income countries.

Keywords: Multiple myeloma; IMWG response; induction; R-ISS

When Fibrosis Masks Dysplasia: Pediatric Myelodysplastic Neoplasm with Low Blasts and Severe Marrow Fibrosis in a 2-Year-Old

Zainab Shah, Ayesha Junaid, Yasir Iqbal
Shifa International Hospital

Background: Pediatric myelodysplastic neoplasm is a rare clonal hematopoietic disorder. Presentation with significant marrow fibrosis and low blast count is uncommon and may pose diagnostic challenges.

Objective: Take-Home Points 1. Trephine biopsy is essential when aspirate is inconclusive 2. Marrow fibrosis can redirect diagnosis in pediatric Myelodysplastic neoplasm 3. Differentiation from MDS/MPN overlap syndromes is critical 4. Early transplant planning is important in progressive disease 5. Role of cytogenetics/genetic studies in diagnosis

Methods: We present the clinical, hematological, morphological, immunohistochemical, cytogenetic, and molecular findings of a 2-year-old child diagnosed with myelodysplastic neoplasm with low blasts and severe bone marrow fibrosis. Clinical data, complete blood count, peripheral blood smear, bone marrow aspirate and biopsy findings, and relevant ancillary investigations were reviewed.

Results:A two-year-old boy presented with persistent cytopenias and mild hepatosplenomegaly. There was no lymphadenopathy or dysmorphic features. Peripheral blood film shows bicytopenia with hemoglobin 7.3 g/dL, RBC count 3.01 $\times 10^6$/µL, and platelet count 132 $\times 10^3$/µL. Red cell indices indicate microcytic hypochromic anemia (MCV 74.8 fL, MCH 24.3 pg) with marked anisopoikilocytosis, including tear-drop cells, spherocytes, polychromasia, and occasional nucleated red cells. Total leukocyte count was 7.85 $\times 10^3$/µL with differential showing absolute neutropenia, few reactive lymphocytes, and occasional atypical cells. Platelets are reduced with giant forms noted. Bone marrow aspirate was hemodiluted (dry tap) due to fibrosis with background showing dyserythropoietic features including megaloblastoid changes. Trephine biopsy from the posterior iliac crest demonstrated an adequate core with thickened bony trabeculae and markedly increased cellularity (approximately 100%). There was prominent megakaryocytic proliferation (14–16 per high-power field), with clustering and marked dysplastic features, including hypolobated and variably sized forms. Granulopoiesis showed evidence of maturation with increased paratrabecular, while erythropoiesis demonstrated mild megaloblastoid changes. Blasts were infrequent, comprising less than 5% of total marrow cellularity. Immunohistochemical stains (CD34, TdT, MPO, CD117, CD30, E-cadherin, CD41) supported a low blast population and increased erythroid component. Mild histiocytic activity was present (CD68, CD163). Reticulin staining revealed diffuse grade 3 fibrosis (scale 0–3). Lymphoid markers (PAX5, CD20, CD3, CD4) showed a normal distribution of B- and T-lymphocytes. Overall, the findings were consistent with a hypercellular marrow showing multilineage dysplasia and diffuse grade 3 fibrosis.

Conclusion: Based on the combined morphological and immunophenotypic findings, a diagnosis of pediatric myelodysplastic neoplasm with low blasts and significant marrow fibrosis was made, most consistent with a refractory cytopenia of childhood-like phenotype. MDS/MPN overlap syndromes, including juvenile myelomonocytic leukemia, were considered less likely due to the absence of monocytosis, leukocytosis, or other proliferative features.

Keywords: Pediatric Myelodysplastic Neoplasm, marrow fibrosis, low blasts, refractory cytopenia of childhood, pediatric hematology

THE ASSOCIATION BETWEEN FACTOR V LEIDEN MUTATION AND THE PRESENCE AND SEVERITY OF CORONARY HEART DISEASE

Irfan Ahmed, Faheem Ahmed
Centre of Postgraduate Studies,

Background: Coronary heart disease (CHD) is a leading global cause of morbidity and mortality. While traditional risk factors are well-established, thrombosis plays a critical terminal role in the clinical manifestation of acute coronary syndromes. Factor V Leiden (FVL) mutation is the most prevalent inherited thrombophilia, known to cause resistance to activated protein C and a hypercoagulable state. However, its specific contribution to arterial thrombosis and the angiographic severity of CHD has remained controversial and under-investigated.

Objective: The primary objective was to investigate the association between the FVL mutation and the presence and severity of CHD. Secondary objectives included assessing this correlation using standardized coronary angiographic scoring systems and evaluating if the FVL mutation acts as an independent risk factor when controlling for traditional cardiovascular variables.

Methods:A descriptive cross-sectional observational case-control study was conducted. The study included adult participants aged 30 to 70 years. The "Cases" group consisted of patients with angiographically confirmed CHD, while "Controls" were age- and sex-matched individuals with no clinical or angiographic evidence of CHD. Venous blood samples were analyzed to detect the FVL mutation using PCR-based methods. Angiographic disease severity in the case group was quantified objectively via the SYNTAX and Gensini scoring systems. Multivariate logistic regression was utilized for data analysis.

Results:A total of 130 participants were enrolled (65 cases and 65 controls). The FVL mutation was detected in 15.3% (n=10) of the CHD cases compared to only 4.6% (n=3) of the healthy controls, demonstrating a statistically significant association with the presence of CHD ($p < 0.05$). Furthermore, among the CHD cases, individuals carrying the FVL mutation

exhibited significantly higher mean SYNTAX scores (28.4 ± 6.2 vs. 19.1 ± 5.4, p = 0.01) and Gensini scores compared to non-carriers. After adjusting for traditional cardiovascular risk factors (hypertension, diabetes mellitus, dyslipidaemia, and smoking), multivariate logistic regression confirmed that the FVL mutation remained an independent predictor for both the occurrence and the multi-vessel severity of coronary heart disease (OR: 2.8, 95% CI: 1.2-6.5).

Conclusion: The Factor V Leiden mutation is significantly associated with both the presence and the angiographic severity of coronary heart disease, independent of traditional cardiovascular risk factors. These findings suggest that inherited thrombophilia plays a distinct role in exacerbating coronary atherosclerosis and multi-vessel involvement. Integrating genetic screening for FVL could enhance risk stratification and guide personalized therapeutic interventions in patients presenting with severe or premature coronary events.

Keywords: Factor V Leiden mutation; Coronary heart disease; Inherited thrombophilia; Angiographic severity; SYNTAX score; Gensini score.

Adherence to Institutional Transfusion Thresholds for Red Cells and Platelets in Adult Acute Leukemia: A Clinical Audit at a Tertiary Care University Hospital

Maria Owais, Hasan Hayat, Zeenat Haadi, Salman Naseem Adil
Aga Khan University and Hospital

Background: Adults with acute leukaemia (AL) require frequent red cell and platelet transfusion, and inappropriate use carries clinical, economic and donor-supply costs. Audits addressing both components concurrently in AL are few, and none have been reported from South Asia. We audited adherence to institutional pre-transfusion thresholds for red cells and platelets in adult AL and characterised the documented reasons for above-threshold transfusion.

Objective: To assess adherence to institutional pre-transfusion haemoglobin and platelet count thresholds in adult acute leukaemia

Methods:A retrospective, cross-sectional audit of consecutive adult AL patients transfused between March and May 2025 at a 700-bed tertiary care university hospital. Each event was adjudicated against institutional thresholds (pre-transfusion haemoglobin ≤ 8 g/dL for packed red cells; platelet count ≤ 20 × 10^9/L for prophylactic platelets). Above-threshold events were classified by documented clinical reason. Adherence is reported with 95% Wilson confidence intervals; analyses were performed in Python 3.11 with cross-verification in SPSS v27.

Results: Eighteen patients (median age 40 years; 72.2% male) contributed 300 events (132 red cell, 168 platelet). Overall adherence was 85.3% (95% CI 80.9–88.9), comprising 86.4% for red cells and 84.5% for platelets. Mean pre-transfusion haemoglobin was 7.4 ± 0.8 g/dL and mean pre-transfusion platelet count 15.1 ± 11.2 × 10^9/L. Single-unit transfusion was the dominant red cell practice (78% of episodes). Of 44 above-threshold events, the largest category was absence of any documented justification (47.7%), followed by active bleeding (25.0%). Over-transfusion (post-transfusion haemoglobin > 10 g/dL) occurred in 6.8% of red cell events.

Conclusion: Adherence to institutional thresholds was high with low over-transfusion. Undocumented justification, not threshold violation, is the principal target for stewardship intervention. Structured justification fields within the electronic transfusion request system, and a staged revision of the institutional platelet threshold toward the 2025 AABB standard, follow directly from these findings.

Keywords: Acute leukaemia; blood transfusion; guideline adherence; clinical audit; patient blood management

Efficacy and Safety of combination of Thalidomide and Hydroxyurea in Transfusion Dependent Thalassemia: Phase II Trial

Khawaja Asad Imtiaz, Aamir Aslam Awan
Armed Forces Bone Marrow Transplant Center, Rawalpindi

Background: Transfusion-dependent thalassemia is the most prevalent disorder in Pakistan. The survival rate is lower than that in the developed world, mainly due to poor transfusion services and inconsistent chelation. The Thal-H trial explored the role of a combination of thalidomide and hydroxyurea in reducing transfusion requirements and documented its safety profile

Objective: Primary objectives: To establish the effectiveness of using thalidomide and hydroxyurea as a combination to decrease the number of transfusions in patients with β-thalassemia major.

Secondary objectives: To determine the frequency of adverse drug reactions and mean changes in the spleen size as well as serum ferritin levels

Methods: Study Design: A single-arm non-randomized prospective clinical trial. Setting: Armed Forces Bone Marrow Transplant Centre (AFBMTC) and Pediatric Department, Combined Military Hospital (CMH), Rawalpindi. Duration of Study: 6 months after CPSP approval. Sampling Technique: Non-probability consecutive sampling. Sample size: This prospective study had a sample size of 100, which was calculated using the WHO calculator. The minimum sample size is 87 participants with a confidence level of 95% (p = 0.6593), an estimated response prevalence of (p = 0.6593)4, and a precision of 10% (d

= 0.10). The sample size will be 100 participants in order to reflect a 15% rate of dropout. Sample Size Calculation (WHO Formula):

Results: Among 109 patients, 61 (56%) were male and 48 (44%) were female. The mean Age at diagnosis was 8 months (3-36) and mean age at the time of enrolment was 7.6 years (2-20). After 3 months of treatment with thalidomide and hydrae, 69 (63.3%) patients continued to require transfusion and 40(36.7%) patients became transfusion-free. Response was assessed at 3 months which showed excellent response 25 (22.9%), good response 22 (20.2%), partial response 42(38.5%) and no response 20 (18.3%). Response was reassessed at 6 months, which showed improved in response with excellent response 51(49%), good response 3 (2.9%), partial response 32(30.9%) and no response 18 (17.3%). At 1 year, 54(50.4%) no longer required transfusion, while 35(32.7%) still required transfusion support. Data showed excellent response 52(60.5%), good response 3(3.5%), partial response 19(22.1%) and No response in 12(14%). Treatment was discontinued in 26 cases (25%) due to no response. There was a treatment interruption in 36(34.6%) due to side effects and no interruption in 68 (65.4%). Neutropenia (27.5%), jaundice (3%), and seizures (1.03%) were the most common side effects. At Univariate analysis, there was a significant association of Hb and ferritin with responses at 3 months (Median=8.90 g/dl, P=0.001 and Median=1463ng/ml, P=0.005), 6 months (Median=8.90g/dl, P=0.001 and Median=1083ngml, P=0.07) and 1 year (Median=9.20g/dl, P=<0.001 and Median= 992ng/ml, P=0.004) with the combination of thalidomide and hydroxyurea.

Conclusion: Thalidomide and Hydroxyurea reduce transfusion requirements in transfusion-dependent thalassemia. This combination is relatively safe, with no life-threatening adverse events. Long-term outcomes need to be studied to validate the safety of this regimen.

Keywords: Beta Thalassaemia Major,ydrae, Thalidomide,

Comparative Analysis of Calcineurin Inhibitors in the Prevention of Acute GVHD: Tacrolimus versus Cyclosporine — A Single-Centre Experience from Gambat Institute of Medical Sciences

Faiza kanwal, Asghar Ali kerio

Gambat Institute of Medical Sciences

Background: Calcineurin inhibitors (CNIs) are the backbone of acute graft-versus-host disease (GVHD) prophylaxis following allogeneic hematopoietic stem cell transplantation (HSCT). Tacrolimus and cyclosporine are most widely used, yet comparative data from resource-limited centres remain scarce. This study compared the efficacy, safety, and survival outcomes associated with both CNIs in a single-center cohort.

Objective: To compare Tacrolimus and Cyclosporine for the prevention of acute GVHD after allogeneic HSCT by evaluating GVHD incidence, transplant-related complications, graft outcomes, overall survival, and disease-free survival.

Methods:A retrospective single-center study was conducted at the Bone Marrow Transplant Department, Gambat Institute of Medical Sciences, Pakistan. Patients who underwent allogeneic hematopoietic stem cell transplantation (HSCT) and survived for ≥100 days post-transplant were included. Patients were divided according to the calcineurin inhibitor used for GVHD prophylaxis: Tacrolimus (n=36) and Cyclosporine (n=54). The primary outcome was grade II–IV acute GVHD. Secondary outcomes included chronic GVHD, graft failure, transplant-related complications, overall survival (OS), and disease-free survival (DFS). Continuous variables were analyzed using the Mann–Whitney U test, categorical variables using Fisher's Exact test, and survival outcomes were assessed by Kaplan–Meier analysis with the log-rank test. A p-value <0.05 was considered statistically significant.

Results: In this retrospective cohort, 90 patients were analyzed (Tacrolimus n=36, Cyclosporine n=54). Baseline characteristics were comparable between the two groups. The incidence of grade II–IV acute GVHD, chronic GVHD, graft failure, and transplant-related complications showed no statistically significant differences between Tacrolimus and Cyclosporine cohorts. Overall survival and disease-free survival were also similar between groups on Kaplan–Meier analysis, with no significant difference observed (log-rank p>0.05).

Conclusion: In this single-centre cohort, Tacrolimus and Cyclosporine were equally effective in preventing grade II–IV acute GVHD. However, Cyclosporine was associated with higher rates of azotemia and graft failure but paradoxically showed superior OS and DFS, likely reflecting follow-up differences. Tacrolimus demonstrated a more favorable toxicity and graft outcome profile but inferior survival. These findings highlight the need for prospective studies with standardized follow-up and multivariable adjustment to determine the optimal CNI for GVHD prophylaxis in resource-limited settings.

Keywords: Allogeneic Hematopoietic Stem Cell Transplantation, Calcineurin Inhibitors, Tacrolimus, Cyclosporine, Acute Graft-versus-Host Disease

Outcome of Allogenic Bone Marrow Transplantation in Aplastic Anemia:A Comprehensive Analysis of 100 Days Post-Transplant at a Single-Center in a Remote Area

Faiza kanwal, Asghar Ali Kerio
Gambat Institute of Medical Sciences

Background: Allogeneic bone marrow transplantation is a potentially curative treatment for patients with aplastic anemia. This study aims to evaluate the clinical outcomes of the procedure in a single tertiary care transplant center by assessing engraftment, transplant-related complications, graft-versus-host disease (GVHD), graft failure, overall survival (OS), and disease-free survival (DFS).

Objective: To evaluate the clinical outcomes of allogeneic bone marrow transplantation in patients with aplastic anemia by assessing engraftment, transplant-related complications, graft-versus-host disease (GVHD), graft failure, overall survival (OS), and disease-free survival (DFS) at a single tertiary care transplant center

Methods: This study was conducted as a retrospective analysis at a single tertiary care transplant center. Patients diagnosed with aplastic anemia who underwent allogeneic bone marrow transplantation were included. Clinical data were reviewed to assess transplant outcomes, including time to engraftment, incidence of transplant-related complications, development and severity of graft-versus-host disease (GVHD), graft failure rates, overall survival (OS), and disease-free survival (DFS). Standard institutional protocols were followed for conditioning regimens, stem cell infusion, and post-transplant care. Survival outcomes and complications were evaluated through regular follow-up and review of medical records.

Results: With a median age of 19, the 37 individuals obtained 73% overall and disease-free survival. Most stem cells (64.9%) were from bone marrow, with a mean dosage of 6.78x10^6/kg for total nucleated cells (TNCs) and 6.1x10^8/kg for CD34. Engraftment of neutrophils and platelets took Place on average after 12 and 17 days, respectively. Fungal infections accounted for 45.9% of immediate post-transplant problems, whereas cyclosporine-induced hypertension accounted for 21.6%. In 18.9% of patients, acute GVHD was present, with cutaneous symptoms accounting for 75.1% of cases. 32.4% of patients had CMV reactivation, which was treated with valganciclovir.

Conclusion: Findings from our research indicate that allogeneic bone marrow transplantation also shows promising results in patients with aplastic anemia in a region of limited resource. With a central survival rate of 73%, we affirm nonetheless always its rightness as medical treatment an infinite number of times, despite such barriers as fungal infection and guru failure. The results of our study highlight the importance of implementing infection control measures and following transplant care standards rigorously. In order to improve the results achieved by patients who require bone marrow transplants

Keywords: Aplastic anemia,allogeneic bone marrow transplantation, graft-versus-host disease (GVHD), overall survival (OS), disease-free survival (DFS)

Drug or disease? A diagnostic dilemma in an on treatment PCNSL patient presented with generalised motor weakness

Muhammad Irtiza Irshad, Muneer Ahmad Khan, Kainat Shift, Nawaz Khan Niazi, Munira Moosa Jee
Aga Khan University Hospital

Background: Generalised motor weakness during vincristine-containing chemotherapy for primary CNS lymphoma (PCNSL) poses a major diagnostic dilemma. Vincristine-induced peripheral neuropathy (VIPN), a vincristine-triggered Guillain–Barré-like immune polyradiculoneuropathy, and paraneoplastic neurological syndrome (PNS) can produce clinically indistinguishable motor debility, yet their management diverges: VIPN requires vincristine withdrawal, whereas immune-mediated mechanisms demand immunomodulation alongside tumour-directed therapy.

Objective:A 42-year-old man with biopsy-confirmed PCNSL (high-grade DLBCL; CD20+, BCL2+, Ki-67 80%) developed subacute generalised motor weakness (power 3/5 in all four limbs) after two cycles of R-MVP (rituximab, methotrexate, vincristine, procarbazine). Investigations ruled out our main differential diagnoses of cord compression, leptomeningeal or spinal disease progression, spinal abscess, and metabolic derangement, leaving VIPN versus an immune-mediated process. Electrodiagnostic studies showed chronic multilevel radiculopathy (bilateral L5–S1, left C6–C8), severe left femoral mononeuropathy, and mild lower-limb sensorimotor polyneuropathy without acute denervation these findings that did not fully account for the clinical severity. Absence of neurological symptoms at presentation and imaging confirming treatment-responsive disease argued against PNS, while the temporal association favoured VIPN. Nonetheless, the disproportionate weakness with atypical proximal and upper-limb involvement, with neurology endorsement, prompted a dual strategy: switching from R-MVP to MTR (methotrexate, thiotepa, rituximab) to eliminate vincristine exposure, and commencing prednisolone for a possible immune-mediated or paraneoplastic mechanism. The patient achieved complete motor recovery. Onconeural antibody testing was unavailable institutionally.

Results: Pure VIPN results from microtubule disruption and impaired axonal transport, producing a length-dependent, dying-back axonopathy that is typically distal and symmetric hence, making the proximal, upper-limb, motor-predominant picture atypical. Two immune mechanisms therefore warranted consideration. First, vincristine can trigger, unmask, or potentiate a Guillain–Barré-like polyradiculoneuropathy that mimics severe VIPN but, unlike toxic axonopathy, responds to

immunomodulation; coexisting Charcot–Marie–Tooth disease similarly exaggerates vincristine toxicity. Second, a rare paraneoplastic subacute motor neuropathy, characterised by proximal leg-predominant weakness, is described almost exclusively in lymphoma, and demyelinating polyradiculopathies predominate in non-Hodgkin lymphoma. Onconeural antibodies support, but sero-negativity does not exclude, PNS; current criteria caution that a Guillain–Barré- or CIDP-like picture should not be labelled paraneoplastic without a high-risk antibody. With antibody testing unavailable, which is case for most of the LMIC, these entities could not be definitively separated, justifying empirical coverage of every plausible mechanism rather than diagnostic delay.

Conclusion: This case highlights the challenge of distinguishing VIPN from immune-mediated and paraneoplastic neuropathy in PCNSL when classical features and confirmatory testing are absent. Management grounded in temporal reasoning, electrodiagnostic data, neurology input, and simultaneous coverage of all plausible mechanisms achieved complete neurological recovery.

Keywords: primary CNS lymphoma,vincristine-induced peripheral neuropathy,paraneoplastic syndrome, onconeural antibodies

Real-World Outcomes of Acute Myeloid Leukemia, Myelodysplasia-Related: A Single Centre Study from Pakistan

Kashaf ad Duja Awais, Maryam Khan, Sidra Zafar, Mehreen Ali Khan,Nighat Shahbaz, Tariq Ghafoor, Raheel Iftikhar
Armed Forces Bone Marrow Transplant, Rawalpindi

Background: Acute myeloid leukemia with myelodysplasia related changes (AML-MR) is characterised by adverse-risk biology, low response to intensive chemotherapy and inferior survival. We aim to report real world outcomes from resource constrained settings where access to molecular diagnostics, novel therapeutics such as CPX-351 and allogeneic hematopoietic stem cell transplantation is limited.

Objective: To report real-world outcomes of AML-MR from a tertiary care transplant center in Pakistan.

Methods: We retrospectively analysed 59 patients with AML-MR at Armed Forces Bone Marrow Transplant Centre from 2015-2024. Primary outcome was overall survival (OS). CR, CRi, and CRh were determined based on the 2022 ELN guidelines. Kaplan Meier method was used for survival analysis where appropriate.

Results: The median age of the study cohort was 45 (IQR 30-61) years. The male to female ratio was 1.68:1. Of the 49 (96.1%) were classified as adverse-risk and 2 (3.9%) were classified as favourable-risk. Of the total cohort 6 (10.2%) patients were newly diagnosed while 53 (89.8%) were relapsed at presentation. Of 50 evaluable patients 16 (32%) patients received intensive induction chemotherapy, 29 (58%) received hypomethylating agent-based induction while 5 (10%) received palliative chemotherapy. Post-induction remission responses were: CR in 16 (40%), CRi in 4 (10%), CRh in 3 (7.5%), PR 2 (5%) and refractory 15 (37.5%) cases. Of the 10 patients who received consolidation, 7 (70%) received HiDAC whereas 3 (30%) received IDAC. Post-consolidation 7/10 patients were in CR and 3/10 patients were in CRi. The most common salvage therapy was intensive chemotherapy in 3/8 patients, followed by HMA-Ven in 3/8 patients. Maintenance therapy included Venetoclax in 3/4 and HMA-based in in 1/4 patients. Allogeneic hematopoietic stem cell transplant was performed in 8 (13.6%) AML-MR patients, comprising matched allogeneic transplant in 7 (87.5%) and haploidentical transplant in 1 (12.5%). The 2-year OS and DFS were 39.3% and 37.1%, respectively. Median OS was 16.5 months (95% CI: 11.5–21.6 months) and median DFS was 16.5 months (95% CI: 9.4–23.7 months).

Conclusion: In resource constrained setting, access to molecular diagnostic and HSCT consolidation is required to improve outcomes.

Keywords: Acute myeloid leukemia, myelodysplasia related, hypomethylating agent, hematopoietic stem cell transplantation

High Fluorescence Lymphocyte Count and Immature Platelet Fraction; Distinguishing Parameters between Dengue and Immune thrombocytopenic Purpura.

Mahnoor Mumtaz, Ayesha Imran
Chughtai Lab,Lahore

Background: Dengue is one of the most prevalent mosquito borne viral infection, with thrombocytopenia as a salient feature. Immune thrombocytopenic purpura is an autoimmune disorder characterized by persistent thrombocytopenia. Excluding febrile illness, thrombocytopenia and clinical presentation in both these conditions is similar. Reactive lymphocytes are increased in the blood of patients infected with dengue, enumerating these lymphocytes as HFLC and comparing it with IPF which is raised in patients with ITP can help in distinguishing the two disorders as soon as the sample is run on XN-1000 hematology analyzer

Objective: To distinguish between Dengue and ITP using new parameters on automated hematology analyzer XN1000.

Methods:A Cross-sectional study conducted at Chughtai Institute of Pathology during August 2025 to November 2025. A total of 100 patients belonging from different age groups were included in the study. CBC, IPF and HFLC analysis was done within 3-4 hours of sample collection on Hematology analyzer XN-1000. Patients with the suspicion of dengue fever were

tested for NS1 antigen. IPF and HFLC were reported in percentages, Normal range of IPF was considered 1-7% and of HFLC was 0-1.4%

Results: Mean IPF was significantly higher in patients with Immune thrombocytopenia (25 ± 10%) when compared with Mean IPF in dengue patients (6 ± 2%). On the other hand, Mean HFLC was high in Dengue patients (6.4 ± 2 %) as compared to ITP patients (0.5 ± 0.2 %). Using Pearson's correlation, a significant correlation (p: 0.02) between raised IPF and decreased platelet count was found in ITP subgroup. Likewise, correlation was significant (p-value < 0.05) between HFLC and platelet count in dengue subgroup. Independent t-test (P=<0.05) showed a statistically significant difference between IPF and HFLC in both subgroups.

Conclusion: Dengue fever can be differentiated from ITP on the basis of raised HFLC as soon as CBC is run on XN1000 hematology analyzer. Similarly high IPF and low HFLC in ITP can help to differentiate it from Dengue fever.

Keywords: Thrombocytopenia, High fluorescence lymphocyte count, Immune thrombocytopenia, immature platelet fraction

Losing CD20, keeping the label: oscillating NLPHL and THRLBCL histology across four biopsies

Muneer Ahmed, Muhammad Irtiza Irshad, Munira Shabbir Moosajee
Aga Khan University Hospital, Karachi

Background:NLPHL and THRLBCL sit on one biological spectrum, separated by growth pattern and by sampling; over half of NLPHL biopsies show more than one pattern. The diagnostic label is therefore unstable across serial biopsies. CD20 expression is not. Rituximab-associated CD20 loss leaves anti-CD20 agents without a target.

Objective: Case report

Methods:A 48-year-old hepatitis B carrier on tenofovir presented in 2023 with three years of right axillary swelling. Excision biopsy showed NLPHL; PET-CT stage IV. Five R-CHOP cycles gave complete metabolic response; he declined to the sixth. He relapsed in 2024. The nodal biopsy showed a THRLBCL pattern, and CD20 was now negative. ICE restored remission; he declined autologous transplant. In January 2026 disease returned above and below the diaphragm with hepatic and splenic deposits. That biopsy was read as NLPHL; CD20 remained negative. Rituximab–bendamustine gave a partial response; by June 2026 splenic disease was progressing. A fourth biopsy, a small splenic core, showed a histiocyte-rich infiltrate with scattered large B-cells, PAX-5 and CD79a positive, CD20, CD3 and CD30 negative. It was reported as recurrent NLPHL.

Results: Across four biopsies the diagnosis alternated while CD20, lost in 2024, never returned. The shifting morphology was acted on; the fixed antigen loss was not. Two years later rituximab was given again; the partial response is attributable to bendamustine. Retained PAX-5 and CD79a confirm B-cell lineage. CD20 negativity on three consecutive biopsies rules out rituximab and, since CD20×CD3 bispecifics need a minimum antigen density, that class too. Lenalidomide and PD-1 blockade, each described in single case reports of transformed NLPHL, do not require CD20. Clonality was not tested, though shared CD20 negativity argues for one clone.

Conclusion: The label will move. Antigen expression is the stable variable. CD20 should be retained at every relapse and should decide anti-CD20 and CD20-bispecific use, whatever the report says.

Keywords: nodular lymphocyte-predominant Hodgkin lymphoma; nodular lymphocyte-predominant B-cell lymphoma; T-cell/histiocyte-rich large B-cell lymphoma; CD20 loss; antigen escape; rituximab resistance; relapsed/refractory lymphoma

Thrombosis-related deaths among cancer patients in the United States, 1999–2024: A 25-year CDC WONDER database analysis

Muhammad Nawaz Khan, Abdul Rehman, Angela Sajid, Abrar Ahmed Khan, Saad Nasir
Aga Khan University Hospital, Karachi

Background: Cancer-associated thrombosis is a major contributor to morbidity and mortality, complicating cancer treatment, increasing healthcare utilization, and contributing to potentially preventable deaths. Despite advances in oncology care and thrombosis management, the national burden of thrombosis-related mortality among cancer patients remains insufficiently characterized. This study evaluated temporal trends and geographic variation in thrombosis-related mortality among U.S. adults with cancer from 1999 to 2024.

Objective: To evaluate temporal trends, demographic patterns, geographic variation, and place-of-death distribution of thrombosis-related mortality among U.S. adults with cancer from 1999 to 2024 using the CDC WONDER database.

Methods: Mortality data were obtained from the CDC WONDER database. Cancer-related deaths were identified using the International Classification of Diseases (ICD-10) codes for malignant neoplasms, while thrombosis-related deaths were identified using corresponding codes for pulmonary embolism and venous thromboembolic events. Adults aged ≥25 years were included. Age-adjusted mortality rates (AAMRs) per 100,000 population were evaluated by sex, thrombotic subtype, census region, and place of death. Joinpoint regression was used to calculate annual percent change (APC) and detect significant changes in mortality trends.

Results: Between 1999 and 2024, 253,217 deaths were recorded among adults with cancer. Pulmonary embolism accounted for represented 93.7% of all thrombosis-related deaths. Among females, AAMR increased from 3.1 in 1999 to 4.3 in 2016 (APC: 1.06%; p<0.05), followed by a sharper rise to 6.7 in 2024 (APC: 5.75%; p<0.05). Among males, AAMR

remained largely stable until 2014, followed by a nonsignificant increase from 2014 to 2018. The steepest rise occurred from 2018 to 2021, with AAMR increasing from 5.5 to 7.0 (APC: 8.35%; p<0.05), followed by a more gradual increase to 7.3 in 2024. Males consistently had higher AAMRs than females throughout the study period. Geographic analysis showed persistent regional variation, with the Midwest demonstrating the highest AAMR during both 1999–2020 and 2018–2024. Most deaths occurred in inpatient medical facilities (52.9%), followed by decedents' homes (23.1%), nursing homes or long-term care facilities (8.2%), hospice facilities (6.4%), and outpatient or emergency room settings (5.9%).

Conclusion: Thrombosis-related mortality among U.S. adults with cancer increased substantially from 1999 to 2024, with pulmonary embolism accounting for most deaths. The recent acceleration in mortality, higher rates among males, regional variation, and predominance of inpatient deaths highlight the need for improved thrombosis risk assessment, early recognition, timely management, appropriate thromboprophylaxis, and better integration of supportive and palliative care pathways.

Keywords: Cancer-associated thrombosis; Pulmonary embolism; Venous thromboembolism; Cancer mortality

Extranodal Rosai-Dorfman Disease Masquerading as Spinal Mass and Chronic Osteomyelitis: A Two-Case Series

Muhammad Nawaz Khan, Saad Nasir, Kabir Jitendir, Saad Naviwala, Munira Moosajee

Aga Khan University Hospital, Karachi

Background: Rosai-Dorfman disease (RDD) is a rare non-Langerhans cell histiocytic disorder classically presenting with painless cervical lymphadenopathy. Extranodal disease is well recognized but diagnostically challenging, particularly when involving the spine or bone, where nonspecific imaging may mimic infection, inflammatory disease, or malignancy.

ObjectiveCase Presentation

Methods;Cases Presentation: We report two cases of atypical extranodal RDD. The first was a 32-year-old man with HLA-B27 positivity and presumed ankylosing spondylitis who developed progressive back pain, lower limb weakness, sensory loss, and sphincter dysfunction. MRI showed a long-segment posterior extradural spinal mass from D4 to L2 with significant cord and conus compression. He underwent staged decompressive laminectomy and tumor debulking. Histopathology showed fibrocollagenous tissue with mixed inflammatory infiltrates and prominent histiocytes, positive for S100 and CD68 and negative for CD1a and BRAF V600E, supporting extranodal RDD. Given progressive spinal and systemic disease, methotrexate and 6-mercaptopurine were initiated, with next-generation sequencing advised. The second was a 54-year-old hypertensive woman with chronic left leg pain initially treated as suspected osteomyelitis due to an enhancing distal tibial diaphyseal lesion with possible sinus tract formation. Persistent symptoms led to saucerization, debridement, and washout. Cultures were negative, while histopathology showed emperipolesis with S100B/CD68 positivity and CD1a negativity, confirming osseous RDD. After symptom resolution, she was placed on active surveillance.

Results;Discussion: RDD has a broad clinical spectrum and may remain unrecognized outside the classical nodal pattern. Management depends on disease extent, symptoms, lesion site, and risk of organ compromise. Observation is appropriate for asymptomatic or stable disease, whereas localized symptomatic lesions may require excision or debulking. Cladribine has shown activity in systemic disease, while MEK inhibition, particularly cobimetinib, has shown promising responses in patients with MAPK pathway alterations such as KRAS or MEK mutations. Molecular profiling should therefore be considered in refractory, progressive, or disseminated RDD to identify candidates for targeted therapy.

Conclusion;Extranodal RDD may present with misleading spinal or osseous lesions that mimic infection or malignancy, making histopathologic confirmation essential. Management should be individualized according to disease extent, symptoms, organ compromise, and molecular findings where available.

Keywords: Rosai-Dorfman disease; extranodal disease; non-Langerhans cell histiocytosis; emperipolesis

Primary Splenic Follicular Lymphoma Presenting with Massive Splenomegaly and Cytopenia: A Rare Case Report

Sadia Anwar, Sajjad Ahmad, Danaish Kumar, Salman Adil
Aga Khan University Hospital

Background: Primary splenic lymphoma (PSL) is a rare extranodal lymphoma, accounting for less than 1% of all lymphomas. Primary splenic follicular lymphoma is exceptionally uncommon and often presents a diagnostic challenge because of its nonspecific constitutional symptoms, cytopenias, and isolated splenomegaly in the absence of significant lymphadenopathy.

Objective: Primary splenic lymphoma accounts for less than 1% of all lymphomas. Primary splenic follicular lymphoma is exceptionally uncommon and presents a diagnostic challenge because of nonspecific constitutional symptoms, cytopenias, and isolated splenomegaly in the absence of significant lymphadenopathy. We describe the diagnostic pathway and outcome of such a case.

Methods: Case report, Department of Clinical Hematology, Aga Khan University Hospital, Karachi. A 59-year-old woman with hypertension presented with a five-month history of abdominal fullness and a two-month history of low-grade fever,

weight loss, and poor appetite. Evaluation included blood counts, bone marrow aspiration and trephine biopsy, FDG PET/CT, and histopathology with immunohistochemistry of the splenectomy specimen.

Results: Examination revealed massive splenomegaly without palpable peripheral lymphadenopathy. Investigations demonstrated microcytic anemia and thrombocytopenia with preserved leukocyte counts. Bone marrow showed trilineage hematopoiesis without lymphomatous involvement. FDG PET/CT demonstrated isolated intensely hypermetabolic massive splenomegaly measuring 29.7 cm (SUVmax 11), with a single mildly FDG-avid preaortic node and no extranodal disease. Following multidisciplinary discussion, the patient underwent splenectomy. Histopathology revealed follicular lymphoma, Grade 1-2, composed predominantly of centrocytes. Immunohistochemistry was positive for CD20, CD10, and BCL2 and negative for CD5 and CD43, confirming primary splenic follicular lymphoma. Hematologic parameters improved significantly, with resolution of cytopenias.

Conclusion: This case highlights the importance of considering lymphoma in patients with unexplained massive splenomegaly despite negative bone marrow examination. PET/CT followed by splenectomy was essential for establishing the diagnosis and guiding management. In selected patients with localized low-grade disease, active surveillance following splenectomy may be appropriate while preserving excellent clinical outcome.

Keywords: Primary splenic lymphoma; Follicular lymphoma; Splenomegaly; Splenectomy; FDG PET/CT; Cytopenias

Feasibility of Outpatient Follow-Up after High-dose Cytarabine Consolidation in Patients with Acute Myeloid Leukemia (AML)

Md Foys Ullah
Contenental Hospital Dhaka

Background: High-dose cytarabine (HiDAC) consolidation is an essential component of post-remission therapy for acute myeloid leukemia and is usually delivered in inpatient settings due to anticipated cytopenias, infection risks, and transfusion needs. However, rising healthcare burdens have prompted interest in outpatient administration. However, evidence remains limited, particularly in resource-constrained environments. This study aimed to evaluate the feasibility, safety, and clinical outcomes of outpatient follow-up after HiDAC consolidation compared with those of inpatient management

Objective: To find out the feasibility of outpatient follow-up of post-high-dose cytarabine (HiDAC) consolidation chemotherapy in patients with Acute Myeloid Leukemia (AML)

Methods: This prospective observational study included 50 AML patients aged 12–60 years who achieved complete remission following induction therapy and subsequently received HiDAC consolidation at Dhaka Medical College Hospital from 1st March 2023 to 29th February 2024. Participants were assigned to outpatient (n=25) or inpatient (n=25) follow-up groups on the basis of planned monitoring pathways. Demographic characteristics, comorbidities, hematologic parameters, adverse events, infection patterns, and healthcare utilization, particularly the duration of hospitalization, were compared between the groups. Statistical analyses included t tests and chi-square tests, with significance set at $p \leq 0.05$

Results: Baseline characteristics were comparable across groups. All patients experienced expected cytopenias, with no significant differences in nonhematologic toxicities. Severe neutropenia (ANC $<0.5\times10^9$/L) was less common in the outpatient group (28% vs 68%, p=0.005), and the nadir ANC was significantly greater. The infection rates were low overall, with no infection-related mortality. Outpatient follow-up markedly reduced the duration of hospital stay (10.76 ± 0.78 vs 17.2 ± 1.68 days, $p<0.001$) without increasing complications, readmissions, or documented infections. The patterns of culture-positive infections and hematologic recovery were comparable across settings

Conclusion: Outpatient follow-up after HiDAC consolidation appears safe and feasible for carefully selected AML patients, offering substantial reductions in hospitalization without compromising safety. With structured monitoring, early warning education, and standardized supportive care, outpatient management can effectively reduce the healthcare burden. Larger multicenter studies with longer follow-up periods are warranted to refine patient selection and validate long-term outcomes

Keywords: Acute myeloid leukemia, High-dose cytarabine, Outpatient chemotherapy, Neutropenia, Consolidation therapy

Dissociation between direct antiglobulin test positivity and clinically significant haemolytic disease of the fetus and newborn in Rhesus D-incompatible pregnancies: a single-centre analysis from an academic hospital in Pakistan

Maria Owais, Bushra Moiz, Muhammad Hasan, Salman Naseem Adil, Sumaira Naz
Aga Khan University and Hospital

Background: Haemolytic disease of the fetus and newborn (HDFN) from Rhesus D (RhD) incompatibility is a preventable cause of neonatal morbidity. Pakistan has approximately 270,000 RhD-incompatible pregnancies annually, with an estimated 87% of eligible women receiving no anti-D prophylaxis. A positive direct antiglobulin test (DAT) does not equate to clinical disease, and local data are scarce. We determined the frequency of DAT positivity and clinically significant HDFN

Objective: We determined the frequency of DAT positivity and clinically significant HDFN

Methods: In this cross-sectional study at Aga Khan University Hospital (AKUH), Karachi, from January to December 2024, DAT was performed routinely on RhD-positive neonates of RhD-negative mothers. Clinically significant HDFN required a positive DAT with evidence of immune-mediated haemolysis. Diagnostic performance and prophylaxis associations were assessed.

Results: Of 4,840 births, 191 neonates were born to 188 RhD-negative mothers, 140 RhD-positive. DAT was positive in 23 of 139 RhD-positive neonates (16.5%), yet only 4 (2.9%) had clinically significant HDFN. Of 138 at-risk mothers, 136 (98.6%) received at least one anti-D dose. Among 19 DAT-positive neonates whose mothers received antenatal and postnatal doses, 1 (5.3%) developed HDFN, a multigravida with prior packed-cell transfusion, versus 3 of 4 (75.0%) without antenatal coverage. All four cases were multigravida; the most severe (pericardial effusion; maternal anti-D titre 1:256) occurred in an unbooked mother without prophylaxis. DAT showed 100% sensitivity, 85.9% specificity, and 17.4% positive predictive value.
Conclusion: Institutional prophylaxis yielded low HDFN frequency despite limited national coverage. Antenatal anti-D drove the dissociation between DAT positivity and clinical disease, supporting prioritisation of the antenatal dose and risk-stratified neonatal surveillance over serology-based intervention.
Keywords: Haemolytic disease of the fetus and newborn (HDFN), Direct antiglobulin test (DAT), Rhesus D incompatibility Anti-D prophylaxis, Neonatal haemolysis, Maternal alloimmunization

Modified versus Standard DHAP Regimen in Relapsed/Refractory Diffuse Large B-Cell Lymphoma: Preliminary Analysis of an Open-Label Randomized Controlled Trial

Inbsat iqbal, Muhammad Abbas Khokhar, Hafiz Muhammad Ehsan Arshad, Zain Raza, Maaz Muqsood, Ahmad Raza
Department of Oncology
King Edward Medical University / Mayo Hospital Lahore

Background: Standard DHAP (cisplatin, cytarabine, dexamethasone) is an effective salvage regimen for relapsed/refractory diffuse large B-cell lymphoma (DLBCL), but its use is limited by severe toxicities, particularly nephrotoxicity and myelosuppression. A modified DHAP regimen fractionating cisplatin and cytarabine over two days may reduce toxicity while maintaining efficacy.
Objective: Comparing Efficacy and Toxicities of modified DHAP with Standard DHAP in Relapsed/Refractory DLBCL
Methods: In this onoing open-label, randomized trial (NCT07739654), adult patients with relapsed/refractory DLBCL were assigned 1:1 to modified DHAP (dexamethasone 40mg; days 1–4, cisplatin 50mg/m² over 6h; days 1–2, cytarabine 2g/m² over 3h; days 1–2) or standard DHAP (dexamethasone 40mg days 1–4, cisplatin 100mg/m² continuous 24h day 1, cytarabine 2 g/m² over 3h twice on day 2). The primary endpoint is overall response-rate (ORR) per RECIL 2017. Secondary endpoints include complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD), toxicity (CTCAEv5.0), progression-free survival (PFS), and quality of life (EORTC QLQ-C30). This interim analysis includes the first 46 of planned 74 patients (23 per arm). PFS and QoL data remain immature.
Results: Baseline characteristics were balanced between arms. ORR was 73.9% (17/23) with modified DHAP versus 65.2% (15/23) with standard DHAP (P=0.749). CR was seen in 26.1% (6/23) vs 34.7% (8/23); PR in 47.8% (11/23) vs 30.4% (7/23); SD in 17.4% (4/23) vs 21.7% (5/23) in standard DHAP (P=1.00); and PD in 8.7% (2/23) vs 13.0% (3/23). Both groups had similar incidences of grade ≥3 neutropenia (P=0.059), and thrombocytopenia (P=0.749). Grade≥3 anaemia was 73.9% vs 30.4% (P=0.07). The distribution of CTCAE grades differed significantly for several toxicities: median nephrotoxicity grade was 0 (IQR:0-1) with modified DHAP versus 2 (IQR:2-3) with standard (P<0.001), with grade≥3 nephrotoxicity in 0% vs. 39.1% (P<0.01); and median mucositis grade was 0 (IQR:0-0) vs. 0 (IQR:0-1) (P=0.008). Conversely, median anaemia grade was worse in the modified arm (3, IQR:1-4 vs. 1, IQR:1-3; P=0.006), with grade≥3 anaemia in 73.9% vs. 30.4% (P=0.07). The distribution of neutropenia (P=0.515), thrombocytopenia (P=0.499), hepatotoxicity (P=0.077), nausea/vomiting (P=1.00), and peripheral neuropathy (P=0.149) grades were similar. No treatment-related deaths were observed.
Conclusion: In this interim analysis, modified DHAP demonstrated comparable ORR and a trend toward less hematologic and renal toxicity compared with standard DHAP. These preliminary results support the feasibility of outpatient administration and warrant completion of full and mature PFS/QoL analyses
Keywords: DHAP, relapsed/refractory diffuse large b cell lymphoma, Toxicities

Effect of Adding Umbilical Cord Blood Derived Stem Cells to Haploidentical Stem Cell Transplant (Haplo-Cord) on Post-Transplant Survival and Graft-versus-Host Disease in Patients with Hematological Malignancies: A Systematic Review and Meta-analysis

Inbsat iqbal, Zain Raza, Hafiz Muhammad Ehsan, Maaz Muqsood, Abbas Khokhar, Ahmad Raza
Department of Oncology
King Edward Medical University / Mayo Hospital Lahore

Background: Haploidentical stem cell transplantation (haplo-SCT) carries a substantial risk of graft-versus-host disease (GvHD), whereas umbilical cord blood (UCB) transplantation offers lower GvHD risk but slower engraftment. The haplo-cord

approach combines both graft sources, aiming to mitigate GvHD while ensuring timely engraftment. This meta-analysis compares haplo-cord transplantation with haplo-SCT alone for the treatment of hematological malignancies.

Objective: This meta-analysis compares haplo-cord transplantation with haplo-SCT alone for the treatment of hematological malignancies.

Methods: Four electronic databases and two clinical trial registries were systematically searched. Effect sizes from eligible studies were pooled using odds ratios (ORs) for dichotomous outcomes and hazard ratios (HRs) for time-to-event outcomes.

Results: Twelve studies met the inclusion criteria. Haplo-cord was associated with a statistically significant reduction in chronic GvHD (OR=0.62, 95%-CI: 0.42–0.93), while no significant difference was observed for grade II–IV acute GvHD (OR=0.75, 95%-CI: 0.52–1.09). Survival outcomes favored haplo-cord, with lower HRs for overall survival (HR=0.68, 95%-CI: 0.53–0.86) and event-free survival (HR=0.61, 95%-CI: 0.52–0.72), while non-relapse mortality was not significant. Relapse at 3 years was significantly lower with haplo-cord (OR=0.54, 95%-CI: 0.35–0.82). Haplo-cord also demonstrated higher day-30 engraftment, along with lower relapse-related and GvHD-related mortality, while CMV and EBV viremia showed no difference between groups. CD34 selection in the haplo graft significantly influenced effect sizes and heterogeneity in both subgroup analyses and meta-regression for acute GvHD.

Conclusion: Haplo-cord transplantation improves GvHD outcomes, survival, and relapse risk compared with haplo-SCT alone. However, whether protocol optimization, possibly via CD34 selection, confers additional benefit remains uncertain and requires confirmation in future studies

Keywords: Haploidentical stem cell transplant; Umbilical cord blood; Haplo-cord, Graft-versus-host disease; CD34 positive stem cells

Spectrum and clinical impact of hotspot mutations in acute myeloid leukaemia (AML) detected by targeted next-generation sequencing (NGS): experience from a resource-limited setting

Wajeeha Iftikhar, Bushra Moiz, Usman Shaikh, Zeeshan Ansar

Department of Haematology,Aga Khan University Hospital,Karachi

Background: The WHO 5th edition and International Consensus Classification emphasize comprehensive molecular profiling in acute myeloid leukemia (AML), with next-generation sequencing (NGS) increasingly important for prognostication, therapeutic decisions, and assessment of co-mutational effects. However, data from Pakistan remain limited.

Objective: To evaluate the NGS-defined mutational spectrum of adult AML in Pakistan and its association with cytogenetics, ELN 2022 risk categories, and mortality.

Methods:A retrospective cross-sectional study was conducted at the Section of Hematology and Transfusion Medicine, Aga Khan University Hospital from June 2022 to December 2025. Adult AML patients (≥18 years) analyzed using a 29-gene NGS panel were included. AML diagnosis was established according to WHO criteria using bone marrow examination, flow cytometry, and/or AML-defining genetic abnormalities. ELN 2022 criteria guided risk stratification. Demographic, laboratory, cytogenetic, molecular, and outcome data were analyzed.

Results: Ninety-seven patients were included with mean age 43.3 ± 15.6 years and male predominance (1.6:1). Anemia was present in all patients, thrombocytopenia in 79 (81.4%), and hyperleukocytosis in 12 (12%). Conventional karyotyping was available in 89 patients, revealing normal karyotype in 47 (52.8%) and abnormal cytogenetics in 42 (47.2%), including 9 complex karyotypes. NGS identified at least one mutation in 32/47 (68%) patients with normal karyotype and 26/42 (62%) with abnormal cytogenetics. ELN stratification classified 24 patients as adverse-risk, 23 favourable-risk, and 48 intermediate-risk. TP53 and RUNX1 predominated in adverse-risk AML, while NPM1 and DNMT3A were common in favorable-risk AML. Overall mortality was 47% (46/97), occurring most frequently in intermediate-risk patients harboring FLT3 ± NPM1 mutations.

Conclusion:ELN 2022 criteria may not fully predict outcomes in Pakistani AML patients, as co-mutational profiles appear to modify prognosis. Population-specific refinement of risk stratification is warranted.

Keywords: Acute Myeloid Leukemia, Next Generation Sequencing, ELN stratification

Clinico-pathological Characteristics of Calreticulin Type 1 versus Calreticulin Type 2 Mutated Myeloproliferative Neoplasms: A Cross-Sectional Analysis

Fariha Ali Khan, Rafia mahmood

Department of Haematology, Armed Forces institute Of Pathology,Rawalpindi

Background: Myeloproliferative neoplasms (MPNs) are clonal hematopoietic stem cell disorders characterized by excessive proliferation of myeloid cells. Calreticulin (CALR) mutations are commonly found in JAK2-negative essential thrombocythemia (ET) and primary myelofibrosis (PMF), with Type 1 and Type 2 being the most frequent variants. These subtypes are associated with distinct clinical and hematological features; however, local data from Pakistan remain limited.

Objective: To compare the clinicopathological characteristics of CALR Type 1 and CALR Type 2 mutated myeloproliferative neoplasms (MPNs).

Methods:A total of 113 adult patients diagnosed with MPNs and positive for CALR mutations were included using non-probability consecutive sampling. Patients harboring BCR-ABL1, JAK2, or MPL mutations were excluded. Peripheral blood

samples (3 ml EDTA) were collected for genomic DNA extraction. CALR mutation subtypes (Type 1 and Type 2) were detected using polymerase chain reaction (PCR) followed by gel electrophoresis. Demographic data, clinical features, hematological parameters (hemoglobin, platelet count, white blood cell count), and disease subtypes (ET and PMF) were recorded. Data was analyzed using R Studio with appropriate statistical tests, and a p-value ≤ 0.05 was considered statistically significant.

Results: Out of 113 CALR-mutated MPN cases, 86 were analyzed (37 ET, 49 PMF). Type 1 mutations were most common (57%), followed by type 2 (33%) and others (10%). No JAK or MPL mutations were detected. Type 1 mutations were slightly more frequent in PMF, while type 2 mutations were more common in PMF than ET. ET patients with type 2 mutations showed lower marrow cellularity and atypical megakaryocytic features compared to type 1. No major differences were observed in age, gender, or blood counts between ET subgroups, although type 2 mutations in PMF showed a trend toward higher platelet counts. Cytogenetic abnormalities were more frequent in PMF, especially in type 2 and other mutations.

Conclusion: Type 2 CALR mutations in ET are associated with lower marrow cellularity and morphological features suggestive of progression toward myelofibrosis. These mutations may also be linked to higher platelet counts and increased cytogenetic abnormalities in PMF. Overall, CALR type 1 and type 2 mutations likely represent distinct disease subgroups with different biological behavior and prognostic significance.

Keywords: Myeloproliferative neoplasms, CALR mutation, Type 1, Type 2, Essential thrombocythemia, Primary myelofibrosis, Pakistan

Clinical Presentation and Outcomes of patients with Acute Promyelocytic Leukemia; a Real World Experience

Farzeen Gull Khan, Maryam Khan, Raheel Iftikhar

Armed Forces Bone Marrow Transplant Center,Rawalpinidi

Background: Acute Pro myelocytic Leukemia (APL) is a discrete subtype of Acute Myeloid Leukemia resulting from a specific translocation t(15;17), between chromosomes 15 And 17 resulting to formation of PML/RARA fusion gene. There is characteristic block in myeloid progenitor cell differentiation and resulting in promyelocytes accumulation in the bone marrow. Typical clinical presentations include haemorrhagic manifestations and thrombotic events.

Objective: To analyze treatment outcomes of patients with APL presenting to a Tertiary Care Hospital

Methods: This retrospective observational study was conducted at Armed Forces Bone Marrow Transplant Centre Rawalpindi. Institutional ethical approval was obtained. We Analyzed the data of all patients diagnosed with APL at our center between January 2014 and December 2025. Patient records included age, sex, presenting complaints, laboratory parameters (including blood counts, molecular studies, bone marrow examination, DIC profile), chemotherapy regimens and their complications, treatment response and survival outcomes.

Results: Data of 56 patients diagnosed with APL was available for final analysis, among whom 6 were children. The median age at diagnosis was 30 years. 54% (n=30) were male and 46% (n=26) were female. Low risk and high-risk disease were present in 70% (n=39) and 30% (n=17) patients respectively. Main presenting feature was bleeding i.e. 61% (n=34) followed by thrombotic complications 7% (n=4). 60% (n=34) received ATRA+ATO regimen, 40% (n=22) patients with ATRA + chemotherapy (Dauno +ATRA, Ida +ATRA). Early death, recognized as death occurring within 30 days of hospitalization, was observed in 2 patients (4%). Cause of death was haemorrhagic complications. 89% (n=50) patients experienced complete remission (CR). Post Consolidation Minimal Residual Disease (MRD) was evaluated in all patients. 11% (n=6) experienced relapse, and were given salvage chemotherapy. Among them 3 were consolidated with Hematopoietic Stem Cell Transplant (HSCT). At a median follow-up of 41 months, the 2-year overall survival (OS) was 93% (95% CI: 87%–99%), and the 2-year disease-free survival (DFS) was 83.5% (95% CI: 72%–95%).

Conclusion: This study highlights various challenges in the management of patients with APL. Despite resource limited settings, the outcomes of patients with APL in LMICs are comparable to those in high-income countries. Early diagnosis, improved risk stratification, MRD assessment, rigorous and tailored supportive care strategies are a backbone of improved outcomes in patients with APL.

Keywords: Acute Prolmyelocytic Leukaemia

Real world insights into Demographic Profile and Barriers to Hematopoietic Stem Cell Transplantation in Pakistan: a single center experience

Maleeha Akbar, Anam Shafiq, Sadaf Zulfiqar , Raheel Iftikhar, Kashaf ad Duja Awais , Hira Tariq, Jahanzeb ur Rehman , Ammad Akram Chaudhary , Tariq Ghafoor

Armed Forces Bone Marrow Transplant Center

Background: Pakistan, the fifth most populous country globally, allocates only 2.8% of its gross domestic product to healthcare, posing significant challenges in the delivery of high-cost, life-saving therapies. Hematopoietic Stem Cell Transplant (HSCT) remains the definitive curative therapy for several malignant and non-malignant hematological disorders. Data exploring patient demographics and barriers to HSCT access in low-resource settings remain limited. This study

presents a single-center analysis of HSCT evaluation and key factors limiting HSCT utilization at a major transplant center in Pakistan.

Objective: The main objective of our study is to assess the demographic profile of patients evaluated for HSCT and to identify the barriers preventing eligible patients from undergoing transplantation at a major center in Pakistan.

Methods: This retrospective, descriptive, single-center study was conducted at the Armed Forces Bone Marrow Transplant Centre (AFBMTC), Rawalpindi, Pakistan. Using non-probability convenience sampling, data was collected for patients evaluated for HSCT between January, 2024 to December 2024 with 1-year follow-up time. Patients with hemoglobinopathies were excluded due to the absence of formal transplant evaluation and discussion. Analysis was performed using SPSS V.25. Patients deemed eligible by the pre-transplant evaluation committee but not proceeding to HSCT were systematically reviewed to identify access-limiting factors.

Results:A total of 311 patients were evaluated for HSCT, with a median age of 31.34 years (range: 0.5 months-72 years); 212 (68.2%) were male and 99 (31.8%) were female. Malignant disorders constituted the majority of indications 173 (55.6%), followed by aplastic anemia 80 (25.7%) and immunodeficiency disorders 58(18.6%). Despite eligibility, only 97 patients 31.2% ultimately underwent HSCT. Of the 214 patients (68.8%) who did not proceed to transplant, the principal barriers included disease progression or failure to achieve remission 43 (13.8%), financial constraints 42 (13.5%), pre-transplant mortality 40 (12.9%), donor unavailability 20 (6.4%), poor functional status or comorbidities 18 (5.8%), psychosocial refusal 13(4.2%), and loss to follow-up 27(8.7%). . Among patients who underwent transplant, the survival rate was 76.3% with a mean survival of 514 days (Figure 3). A total of 311 patients were evaluated for HSCT, with a median age of 31.34 years (range: 0.5 months-72 years); 212 (68.2%) were male and 99 (31.8%) were female. Malignant disorders constituted the majority of indications 173 (55.6%), followed by aplastic anemia 80 (25.7%) and immunodeficiency disorders 58(18.6%). Despite eligibility, only 97 patients 31.2% ultimately underwent HSCT. Of the 214 patients (68.8%) who did not proceed to transplant, the principal barriers included disease progression or failure to achieve remission 43 (13.8%), financial constraints 42 (13.5%), pre-transplant mortality 40 (12.9%), donor unavailability 20 (6.4%), poor functional status or comorbidities 18 (5.8%), psychosocial refusal 13(4.2%), and loss to follow-up 27(8.7%). The primary factors impeding access to HSCT were categorized in Table 1. Among patients who underwent transplant, the survival rate was 76.3% with a mean survival of 514 days . A total of 311 patients were evaluated for HSCT, with a median age of 31.34 years (range: 0.5 months-72 years); 212 (68.2%) were male and 99 (31.8%) were female. Malignant disorders constituted the majority of indications 173 (55.6%), followed by aplastic anemia 80 (25.7%) and immunodeficiency disorders 58(18.6%). Despite eligibility, only 97 patients 31.2% ultimately underwent HSCT. Of the 214 patients (68.8%) who did not proceed to transplant, the principal barriers included disease progression or failure to achieve remission 43 (13.8%), financial constraints 42 (13.5%), pre-transplant mortality 40 (12.9%), donor unavailability 20 (6.4%), poor functional status or comorbidities 18 (5.8%), psychosocial refusal 13(4.2%), and loss to follow-up 27(8.7%). The primary factors impeding access to HSCT were categorized in Table 1. Among patients who underwent transplant, the survival rate was 76.3% with a mean survival of 514 days. A total of 311 patients were evaluated for HSCT, with a median age of 31.34 years (range: 0.5 months-72 years); 212 (68.2%) were male and 99 (31.8%) were female. Malignant disorders constituted the majority of indications 173 (55.6%), followed by aplastic anemia 80 (25.7%) and immunodeficiency disorders 58(18.6%). Despite eligibility, only 97 patients 31.2% ultimately underwent HSCT. Of the 214 patients (68.8%) who did not proceed to transplant, the principal barriers included disease progression or failure to achieve remission 43 (13.8%), financial constraints 42 (13.5%), pre-transplant mortality 40 (12.9%), donor unavailability 20 (6.4%), poor functional status or comorbidities 18 (5.8%), psychosocial refusal 13(4.2%), and loss to follow-up 27(8.7%). The primary factors impeding access to HSCT were categorized in Table 1. Among patients who underwent transplant, the survival rate was 76.3% with a mean survival of 514 days .

Conclusion: This real-world analysis reveals a substantial gap between HSCT eligibility and actual transplant delivery in Pakistan, with nearly two-thirds of evaluated patients unable to access transplantation. Financial constraints, delayed disease control, and limited supportive infrastructure remain the predominant obstacles. These findings complement national transplant activity surveys by highlighting an urgent need for healthcare policy reforms and underscore the need for integrated national funding models, early referral pathways, establishing donor registries, and psychosocial interventions to improve equitable access to HSCT in Pakistan.

Keywords: Barriers to transplant, HCST, Low-resource settings, Financial constraints, Transplant eligibility, Demographic profile

Clinicopathological Features and Treatment Outcomes of Chronic Lymphocytic Leukemia in a Lower-Middle-Income Country - Real World Data from Pakistan

Ayesha Nasrullah, Mahnoor , Muhammad Fahim, Hira Tariq , Maryam Khan, Mehreen Ali Khan , Raheel Iftikhar
Armed Forces Bone Marrow Transplant Centre

Background: Data on the demographic profile, clinical features and the outcomes of Chronic Lymphocytic Leukemia (CLL) remain limited in low-and middle-income countries. This study aims to analyze the clinical, cytogenetic, and molecular

characteristics of CLL patients in a tertiary care center of Pakistan and analyze their association with treatment response and survival.

Objective: To assess the association of clinicopathological features and treatment outcomes of CLL patients with overall survival (OS) and progression free survival (PFS) in a lower-middle-income country.

Methods:A retrospective single-center analysis of CLL patients treated between 2012 and 2026 at the Armed Forces Bone Marrow Transplant Centre was conducted. Data on the demographics, clinical features, molecular mutations, cytogenetics, treatment modalities, and survival were retrieved. Overall survival (OS) and progression-free survival (PFS) was estimated using Kaplan-Meier analysis. Univariate and multivariate Cox regression models were applied to assess prognostic variables such as age, ECOG status, cytogenetics and treatment type.

Results: The study cohort included 317 patients diagnosed with CLL. Median age at diagnosis was 64 years (IQR 54.5-70.8) and 72% were male. One or more Comorbid was present in 47.9%, with 10.2% having an ECOG ≥2. Common presenting symptoms included lethargy (20.8%) and weight loss (15.8%). Majority (59.2%) presented in Binet Stage A. Of the current study sample, 46.1% had insurance, 47% paid out of pocket, while 6.9% received treatment on charity and donations. 66.5% of the patients had their cytogenetics reported and the abnormalities included del(13q) in 37.6%, del(17p) in 12.8%, trisomy 12 in 12.2% and del(11q) in 7.9%. Only 30 (9.5%) patients were tested for IgHV mutation and out of these 23 (76.7%) had unmutated IgHV. For patients requiring treatment, the median time from diagnosis to treatment was 69 (IQR 22-421) days. Most common first-line therapies included Chlorambucil ± Prednisolone (61.7%) and BR (14.2%). Most common second-line therapies included Ibrutinib (25%) and BR (17.3). Novel therapies (BTKi/BCL2i) were used in 26.45%. The overall response rate (ORR) to first-line therapy was 63%, with complete remission seen in 11%. The overall response rate (ORR) to second-line therapy was 56%, with complete remission seen in 33%. Median OS and PFS were not reached at a median follow up of 27.6 months (Figure 1 and 2). Richter's transformation occurred in 1.26%. On univariate and multivariate analysis, none of the assessed variables showed any significant association with Overall Survival nor with Progression Free Survival.

Conclusion: This data shows that the median age of diagnosis of CLL is relatively younger as compared to the west, with overwhelming majority being male. While international standard for CLL has evolved to utilize BTK inhibitors and BCL2 inhibitors in first line, our patients continue to receive conventional chemotherapy as the first line treatment due to cost constraints and limited access.

Keywords: Chronic Lymphocytic Leukemia, Cytogenetics, Molecular Mutations, Health Outcomes Non-Biological Therapies, Real-World Evidence, Chemotherapy

Etiologies, Clinical presentation and Outcomes of venous thromboembolism in tertiary care hospital

Attiya Shah, Raheel Iftikhar Nabeela khan
Armed Forces Bone Marrow Transplant Center,Rawalpindi

Background: Venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) and pulmonary embolism (PE), is a cause of morbidity. Identification of thrombophilic risk factors is important for preventing recurrence. This study evaluated the profile, risk factors, treatment patterns, and outcomes of patients with VTE in a tertiary care hospital.

Objective: To Evaluate Etiologies, Clinical presentation and Outcomes of venous thromboembolism in tertiary care hospital

Methods: This prospective observational study included 50 patients with confirmed VTE presenting to AFBMTC and followed for one year. Demographic characteristics, thrombosis site, symptoms, risk factors, treatment, and outcomes were recorded. Thrombophilia evaluation included Factor V Leiden, Protein S deficiency, prothrombin gene mutation, antiphospholipid antibodies, lupus anticoagulant, and Hyperhomocysteinemia

Results: Mean age was 34.10 ± 11.44 years (range 13–67 years); 29 (58%) patients were male and 21 (42%) females. Most cases were unprovoked (42, 86%), while 8 (16%) were provoked, predominantly due to postpartum status. DVT was the commonest site (27, 54%), followed by abdominal thrombosis (11, 22%) and CNS thrombosis (6, 12%). Among patients with DVT, leg pain (50%) and swelling (42%) were the commonest symptoms. Hyperhomocysteinemia was the frequent risk factor (15, 30%). Inherited thrombophilia included Factor V Leiden mutation in 9 (18%), Protein S deficiency in 5 (10%), prothrombin gene mutation in 2 (4%), and MTHFR mutation in 1 (2%). Antiphospholipid-related abnormalities were present in 15 patients, including β2-glycoprotein antibodies in 6 (12%), lupus anticoagulant in 5 (10%), and anticardiolipin antibodies in 4 (8%). Paroxysmal nocturnal hemoglobinuria was detected in 2 (4%). Direct oral anticoagulants were used in 39 (78%), warfarin alone in 7 (14%), and warfarin followed by a DOAC in 4 (8%). During follow-up, partial recanalization occurred in 10 (20%), recurrent DVT in 7 (14%), recurrent PE in 3 (6%), and chronic DVT in 8 (16%). Complete resolution occurred in 10 patients. Two developed chronic venous ulcers. No pulmonary arterial hypertension or deaths occurred.

Conclusion:VTE in this cohort predominantly affected young adults and was largely unprovoked. Hyperhomocysteinemia and inherited thrombophilia were important contributors. Despite predominantly DOAC-based treatment, recurrent thrombosis and chronic DVT remained significant complications, emphasizing the importance of thrombophilia evaluation, individualized anticoagulation and follow-up.

Keywords: Venous thromboembolism, Anticoagulants, Outcomes

****

One Year of Clinical Haematology Practice in Khyber Pakhtunkhwa, Pakistan: Patient Burden, Diagnostic Gaps and Barriers to Transplant Referral

Uzma Rahim

Kuwait Teaching Hospital,Peshawar

Background: Timely diagnosis and access to specialised testing, treatment, and supportive care are central to good haematology practice. In Khyber Pakhtunkhwa (KPK), Pakistan, gaps in these services can delay clinical decisions and limit access to appropriate care, including transplant referral. However, these challenges remain poorly documented.

Objective: To describe the patient case-mix and examine the key diagnostic, treatment, transfusion, financial, and referral barriers encountered in clinical haematology practice in KPK.

Methods: We retrospectively reviewed the clinic registry and hospital electronic database records of 1,876 consecutive patients managed at a teaching hospital in Peshawar and a once weekly peripheral haematology clinic from 1 May 2025 to 30 April 2026. All patients who presented to either site during the study period were included. Data were summarised for disease category, completeness of the diagnostic evaluation at presentation, and documented barriers affecting diagnostic assessment and care. Barriers were classified as diagnostic and infrastructure limitations, treatment-related constraints, blood-product availability and safety concerns, and referral and affordability barriers.

Results: Among 1,876 patients, 35% had a haematological malignancy, 50% had other benign haematological disorders, 10% had platelet or coagulation disorders, and 5% remained undiagnosed. Less than 5% presented with a complete diagnostic evaluation. Common gaps included bone-marrow assessment without immunohistochemistry and failure to obtain samples for indicated flow-cytometric or molecular/genetic testing. Flow cytometric and molecular/genetic testing were unavailable at the participating sites and required referral to external laboratories, resulting in turnaround times exceeding one week and delays in treatment initiation. Specialised platelet or coagulation testing also required referral outside the local service network. Additional documented constraints included inconsistent access to standard registered medicines, limitations in supportive care, concerns regarding the availability and safety of blood products, out-of-pocket expenditure, and delays in referral pathways. Collectively, these barriers adversely affected the entire haematology care pathway, including timely diagnosis, treatment initiation, supportive and transfusion care, advanced diagnostic assessment, and referral for transplantation when indicated.

Conclusion: This one-year review highlights how limited diagnostic capacity, delayed access to specialised testing, inconsistent availability of registered medicines and safe blood products, and financial and referral barriers disrupts the entire haematology care pathway—from diagnosis and treatment initiation to supportive care and transplant evaluation. Strengthening regional diagnostic services, essential medicine and blood-product supply, and affordable, coordinated referral pathways is crucial for delivering timely and equitable haematology care in KPK

Keywords: Clinical haematology, diagnostic barriers, referral pathways, blood and marrow transplantation

****

Knowledge and awareness of Hematopoietic Stem Cell Transplantation (HSCT) among doctors in Khyber Pakhtunkhwa, Pakistan: A Cross-Sectional online Survey

Uzma Rahim

Kuwait teaching hospital,Peshawar

Background: Hematopoietic stem cell transplantation (HSCT) is a potentially curative treatment for selected malignant and non-malignant hematological disorders. Timely referral depends on physicians' awareness of indications, donor selection, referral pathways, and service availability. This study aimed to assess HSCT-related awareness, knowledge, referral practices, attitudes, and perceived barriers among physicians practicing in Khyber Pakhtunkhwa (KPK), Pakistan.

Objective: To assess awareness, knowledge, attitudes, referral practices, and perceived barriers regarding HSCT among physicians practicing in Khyber Pakhtunkhwa, Pakistan.

Methods: This cross-sectional descriptive survey was conducted from March to May 2026 among registered doctors practicing in KPK, including house officers and above. Participants were recruited through WhatsApp-based medical professional groups after electronic informed consent. Data were collected using a structured Google Forms questionnaire developed after literature review and hematology consultant review. Data were analyzed using IBM SPSS version 25, and knowledge and awareness scores were categorized as poor (<50%), moderate (50–75%), and good (>75%).

Results:A total of 199 physicians participated. Most respondents had heard of HSCT, 187 (94.0%), but self-rated knowledge remained limited, with 158 (79.4%) reporting average or below knowledge and only 44 (22.1%) attending an HSCT-related educational activity. Awareness of HSCT indications was reported by 138 (69.3%), while 129 (64.8%) knew HSCT services are available in Pakistan. Only 83 (41.7%) knew where to refer patients requiring HSCT. Cost was the most reported barrier, identified by 158 (79.4%).

Conclusion:HSCT awareness was high, but practical knowledge, referral preparedness, and cost awareness were limited. Structured education and clearer referral pathways may improve timely HSCT access in KPK.

Keywords: Hematopoietic stem cell transplantation; physician awareness; donor selection

Comparative Real-World Efficacy and Safety of 4-1BB-based (Liso-cel/Tisa-cel) versus CD28-construct Containing (Axi-cel) CAR T-Cell Therapy for Relapsed/Refractory Large B-cell Lymphomas: A Meta-analysis

Ahmad Raza, Inbsaat Iqbal, Hafiz Muhammad Ehsan Arshad, Maryam Maqsood, Muhammad Zain Raza, Musab Maqsood, Anas Babar, Ahmad Raza and Omar Abdullah Gill

King Edward Medical University, Lahore

Background: Despite the availability of three commercial CD19-directed chimeric antigen receptor (CAR) T-cell therapies for relapsed/refractory (R/R) large B-cell lymphoma (LBCL), their comparative efficacy is not well established. This meta?analysis seeks to address this evidence gap by comparing clinical outcomes associated with 4?1BB?based constructs (lisocabtagene maraleucel [liso-cel] and tisagenlecleucel [tisa-cel]) against a CD28-based construct (axicabtagene ciloleucel [axi-cel]) using real?world evidence.

Objective: To evaluate the influence of costimulatory domain selection on treatment response, i.e., Overall-response rate (ORR), overall-survival (OS), and progression-free survival (PFS), and toxicity profiles in routine clinical practice.

Methods: PubMed, Embase, Cochrane, and two trial registers were systematically searched. Using a random-effects model, pooled hazard ratios (HRs) were used for PFS and OS, while pooled odds ratios (ORs) were used for dichotomous outcomes.

Results: Fourteen cohorts comprising 4,288 participants were included. Compared to CD28-containing construct, axi-cel, liso-cel demonstrated comparable ORR (OR:1.14; 95%-CI:0.56–2.29; I2=73%), whereas tisa-cel had significantly lower ORR (OR:0.66; 95%-CI:0.48–0.90; I2=14%). A significant difference was observed between the two 4-1BB-based constructs (P=0.04). Similarly, OS and PFS were significantly inferior with tisa-cel (HR:1.45; 95%-CI:1.43–1.80; and HR:1.39; 95%-CI:1.15–1.69, respectively) while liso-cel had comparable HRs for both (HR:1.19; 95%-CI:0.66–2.14; and HR:1.03; 95%-CI:0.55–1.91, respectively). Duration of response did not differ significantly across groups. Regarding safety, liso-cel had a significantly lower incidence of moderate-to-severe cytokine release syndrome (CRS) (OR:0.33; 95%CI:0.23–0.47), while tisa-cel remained comparable (OR:0.88; 95%CI:0.67–1.11). Immune effector cell-associated neurotoxicity syndrome (ICANS) incidence was significantly lower in both Tiso-cel (OR:0.23; 95%CI:0.17–0.30) and liso-cel (OR:0.27; 95%CI:0.18–0.40) groups.

Conclusion: Based on real-world evidence, liso-cel and axi-cel demonstrate superior clinical efficacy compared to tisa-cel in the treatment of R/R LBCL. Notably, liso-cel represents a favourable therapeutic middle ground, offering a toxicity profile significantly more manageable than axi-cel while maintaining comparable survival and response outcomes. Conversely, tisa-cel was associated with inferior response rates and survival, despite its low neurotoxicity. Given the nonrandomized nature of the included studies and potential selection and confounding biases, these findings should be considered hypothesis-generating rather than definitive.

Keywords: Relapsed/refractory large B-cell lymphoma; CAR T-cell therapy; axicabtagene ciloleucel; lisocabtagene maraleucel; tisagenlecleucel; costimulatory domain; real-world evidence; meta-analysis.

The impact of spleen size and splenectomy on the outcome of allogenic hematopoietic stem cell transplantation in beta thalassemia major patients

Nabeela Bahadar, Jehanzeb Ur Rehman, Ayesha Bibi, Ayesha Nasrullah

Armed Forces of Bone Marrow Transplant center (AFBMTC)

Background: The role of splenectomy before hematopoietic stem cell transplantation (HSCT) is controversial. Only a few studies have compared the outcomes of splenectomized and non-splenectomized children with transfusion-dependent thalassemia (TDT) undergoing allogeneic HSCTs.

Objective: To evaluate the impact of splenomegaly and splenectomy on neutrophilic engraftment following allogeneic hematopoietic stem cell transplantation (allo HSCT) and to analyze the correlation between spleen size and engraftment of both neutrophils and platelets.

Methods: We retrospectively collected data on thalassemia major with allo HSCT in our institute from Jan 2002 to Jun 2025. In univariate analysis, we performed a Spearman correlation test to check the correlation between spleen size and engraftment (neutrophils and platelets), and the Kaplan-Meier test for OS and DFS. In multivariate analysis, the Cox regression test was applied.

Results: Data from 385 patients with beta thalassemia major were analyzed. Median age at diagnosis was 7 (IQR 4.4- 11.6) years, and the majority diagnosed were Male (63.6%). Median days of neutrophil engraftment were 14 (IQR 13-14), while median days of platelet engraftment were 26 (IQR 20-39). Out of 363 patients, 351 (96.7%) had early engraftment, and 48 out of 322 (14.9%) faced graft rejection. Median spleen size among patients was 0 cm (IQR: 0-2). Abnormal spleen size was seen in 134 (34.8%) patients, and 11 (2.9%) underwent splenectomy. There was a significant but weak, direct correlation between spleen size (cm) and neutrophil engraftment days (r=0.17, p=0.001) (Figure 1), and with platelet engraftment days (r=0.18, p=0.001) (Figure 2), but there was no significant relationship of engraftment and splenectomy. The OS was 80.3% with mean Survival 6201.86 days (CI 95%: 5838.70 - 6565.01), and the DFS was 69.6% with a mean DFS of 4916.301 days (CI 95%: 4442.30 - 5390.29) (Figures 3 and 4). Median OS and DFS days were not reached. In univariate analysis, there was a significant association of graft rejection with OS (OR: 1.78, 95% CI: 1-3.17, p=0.05) and DFS (OR: 5.9, 95% CI: 1-3.17,

p=<0.001). Early engraftment showed improved DFS (OR: 2.8, 95% CI: 1.44-5.73, p=0.003) compared with late engraftment. In multivariate analysis, only graft rejection showed a significant association with DFS (p = <0.001).

Conclusion: There was a direct correlation between spleen size and stem cell engraftment of neutrophils and platelets. However, no association was found between splenectomy and engraftment; a plausible reason was the small number of splenectomized patients. Further studies are needed to evaluate engraftment outcomes in splenectomized individuals

Keywords: Allo HSCT, Beta Thalssemia, spleen size, splenectomy

Outcomes of stem cell boost for poor graft function after allogeneic stem cell transplant in patients with aplastic anemia

Anees Ur Rahman, Nighat Shahbaz
Armed forces bone marrow transplant

Background: Poor graft function and graft failure is one of the major complication in patient with aplastic anemia following AlloHSCT. It is characterized by persistently low blood counts which frequently required blood transfusion support. Poor graft function is characterized by low blood count while having complete donor chimerism. Stem cell boost without condition could be a good salvage option for patient who developed poor graft function following AlloHSCT. But the patient who received stem cell boost are in significant risk of developing graft verse host disease.

Objective: To evaluate the outcomes of stem cell boost in patient of aplastic anemia who developed poor graft function following HSCT

Methods: This retrospective longitudinal study which included the patient of aplastic anemia who underwent HSCT and then developed poor graft function which was diagnosed with bone marrow examination and chimerism analysis. Institutional ethical approval was taken and those patient who fulfilled the criteria were enrolled in study. Overall survival (OS) was defined as the time from time of transplant till last follow up or death. Friedman test was applied to check the relationship of blood counts with time (pre boost ,day14, 28 and 60). Kaplain meir test was applied for OS. The data was analyzed utilizing SPSS 25.

Results: Out of 16 patient, male were 13(81.3%) while female were 3(18.8%) and most common donor relationship was brother 10(62.5%). Fully matched HSCT with conditioning Flu Cy ATG was performed in 10 patients (62.5%), while haplo HSCT with Bu Flu ATG Cy with ptCy was performed in 6 patients (37.5%). BMH was stem cell source for 11(68.8%) and BMH+PBSC for 5(31.3%). Median CD34 dose 4.5(IQR: 3.5-7.1) x106 per kg and median TNC dose was 5.4(IQR: 4.8- 9.8) X108 per kg. Neutrophil engraftment was achieved on day +15(IQR 13-16) while platelets engraftment was achieved on day + 21(IQR 17-35). On day +30 marrow 8(50%) patient had adequate graft function, 4(25%) patient had poor graft function while 4(25%) patient had primary graft failure. Complete donor chimerism was observed in 7 patients (43.8%) and mixed donor chimerism in 6 patients (37.5%), while chimerism was not assessed in 3 patients (18.8%). All 16 patient received stem cell boost without conditioning due to drops in blood count on day + 87(IQR 30-144).Out of 16 patients 11(68.8%) had poor graft function while 5(31.3%) had graft failure. A total CD34 dose of 6.17x106 per kg was given with out conditioning and ANC,Hb and Platelets was assessed on day +14,Day+28 and Day+60. The relationship of Hb with respect to time was statistically significant(p=0.01) (Table 1).Out of 16 patient 6(37.7%) developed GVHD in 2(12.5%) required topical steroid while 3(18.8%) and 1(6.3%) required oral and IV steroid respectively. Out of 16, The OS was 50%with median 630 survival day(95%CI:0-1878) (Figure 1).The OS of patient who had pre boost poor graft function was 63.6% while those who had primary graft failure was 20.0%(p=0.02)(Figure 2).The patient with preboost complete donor chimerism had 66.7%OS and Mixed chimerism had 50% OS(p=0.001)

Conclusion:A stem cell boost with out condition is potential salvage option for patient with poor graft function and graft failure following HSCT. Preboost marrow and pre boost chimerism are the strong predictor of outcomes and overall survival, with poor graft function and complete donor chimerism is associated with better outcome and better over all survival

Keywords: Stem cell boost, Poor graft function, Allogeneic stem cell transplantation, Aplastic anemia

PRIMARY CUTANEOUS GAMMA DELTA T-CELL LYMPHOMA: A RARE ENTITY WITH EXTENSIVE CUTANEOUS AND SYSTEMIC INVOLVEMENT

Bushra Ali, Muhammad Shayan Ashfaq,Zenat, Bushra, Madiha, Natasha Ali
Aga khan university hospital

Background: Primary cutaneous gamma delta T-cell lymphoma (PCGD-TCL) is an exceedingly rare and aggressive subtype of cutaneous T-cell lymphoma, characterized by proliferation of mature cytotoxic gamma delta T-cells in the skin.(1) It accounts for less than 1% of all cutaneous T-cell lymphomas and typically presents with rapidly progressive, often ulcerated or necrotic skin lesions, frequently associated with systemic symptoms such as fever and malaise.(2) PCGD-TCL has a high propensity for extracutaneous spread, involving lymph nodes, viscera, and occasionally other extranodal sites. Its clinical presentation can mimic more common cutaneous lymphomas or inflammatory dermatoses, making early diagnosis challenging.(3) Histopathology and immunophenotyping are essential for definitive diagnosis, with gamma delta T-cell receptor expression serving as a key diagnostic criterion. (4) Prognosis is generally poor, particularly in elderly patients or those with advanced disease at presentation, due to the lymphoma's aggressive course and limited response to conventional

chemotherapy.(5) Radiological imaging, such as FDG PET/CT, is increasingly utilized for accurate staging and assessment of systemic involvement, which is critical for treatment planning.(6) We present a rare case of primary cutaneous gamma delta T-cell lymphoma in an elderly male, highlighting its clinical, radiological, and histopathological features, as well as the challenges in management of this aggressive malignancy.

Objective: To describe the clinical, histopathological, immunohistochemical, radiological, and treatment-related features of primary cutaneous gamma-delta T-cell lymphoma (PCGD-TCL) with extensive cutaneous and systemic involvement, highlighting the diagnostic challenges and aggressive clinical course of this rare entity

Result &Conclusion: Primary cutaneous gamma-delta T-cell lymphoma is a rare and highly aggressive malignancy that requires a high index of suspicion for early diagnosis. In this case, the diagnosis was established through the integration of clinical presentation, histopathological findings, immunohistochemistry, and FDG PET/CT, which demonstrated extensive cutaneous and systemic involvement. Despite treatment with dose-adjusted CHOP chemotherapy, the patient experienced rapid clinical deterioration and ultimately died from cardiorespiratory failure. This case highlights the aggressive nature and poor prognosis of PCGD-TCL, particularly in elderly patients with advanced-stage disease and significant comorbidities. Early recognition and comprehensive clinicopathological and radiological evaluation are essential for accurate diagnosis, staging, and timely management.

Keywords: Primary cutaneous gamma delta T-cell lymphoma; Cutaneous T-cell lymphoma; FDG PET/CT; Immunohistochemistry; Rare lymphoma

Pyoderma Gangrenosum Associated with Myelodysplastic Syndrome: A Rare Case Report

Sajjad Ahmad, Muammad Usman Shaikh

Background: Myelodysplastic syndrome (MDS) is a clonal hematologic disorder characterized by ineffective hematopoiesis, dysplasia, and risk of progression to acute myeloid leukemia. It may also be associated with autoimmune and inflammatory manifestations due to immune dysregulation. Pyoderma Pyiderma gangrenosum (PG) is a rare sterile neutrophilic dermatosis that is frequently linked to hematologic malignancies, and its bullous variant is particularly associated with myeloid disorders.

Case :This case highlights the diagnostic challenge of PG, which may closely mimic necrotizing soft tissue infection. In patients with MDS, PG should be considered early, especially when lesions are sterile, recurrent, and worsened by trauma or procedures.

Keywords: Myelodysplastic syndrome, pyoderma gangrenosum, bullous pyoderma gangrenosum, azacitidine, neutrophilic dermatosis.

PREVALENCE AND CLINICAL HETEROGENEITY OF RARE BLEEDING DISORDERS: A SINGLE CENTER STUDY

Nimra Mazhar, Ghazala Qamar, Ayisha Imran, N. A. Malik

Chughtai Institute of Pathology,Lahore

Background: Rare bleeding disorders are recessively inherited genetic disorders which are characterized by a deficiency in coagulation factors. These disorders encompass patients with deficiencies of factor I, II, V, VII, combined factor V and VIII, XI, XII and XIII deficiency. Patients with rare bleeding disorders present with a wide spectrum of clinical presentations with some patients being asymptomatic or mildly symptomatic to another group requiring replacement therapies and blood transfusions to maintain haemostasis.

Objective: To identify the frequency and wide spectrum of clinical manifestation with which patients with rare bleeding disorders presented in our center. This will aid clinicians to diagnose these patients early and will help in their timely management.

Methods: This was a cross-sectional study in which we analysed data of patients from the Hemophilia treatment center of Chughtai Institute of Pathology. Data was taken from files and a detailed history was also obtained directly from patients. Patients who were known cases of Hemophilia A, Hemophilia B, Von Willebrands disease and platelet function disorder were excluded from the study. International Society on Thrombosis and Haemostasis Bleeding Assessment Tool (ISTH-BAT Score) was calculated and its correlation with relevant factor deficiencies were seen.

Results: In our study we came across a total of 91 patients. The most common encountered deficiency was found to be factor VII (29%) while least common factor deficiency seen was combined factor V and VIII which was seen in only one patient (1.09%). Most of the patients had clinical features of cutaneous bruising (57%) and oral bleeds (54%). Significant correlation of ISTH BAT Score was found with factor V deficiency ($p = 0.032$) and factor X deficiency ($p = 0.034$) respectively.

Conclusion: Although, majority of the patients in this study had clinical features of bruising and oral cavity bleeding. A significant proportion of patients also presented with other symptoms like menorrhagia, epistaxis, prolonged bleeding from minor wounds, intracranial bleeds, haematomas and haemarthrosis as well. Hence, it is important for us to investigate patients presenting with any bleed so as to reach to the root cause which will help in future management of these patients.

Keywords: Rare bleeding disorder, factor levels, BAT score

APPLICATION OF THE TRIPLE-A (AAA) PROGNOSTIC MODEL IN PATIENTS WITH POLYCYTHEMIA VERA: A SINGLE-CENTRE STUDY FROM PAKISTAN

Muhammad Fahim, Mehreen Ali Khan,Anees ur Rehman, Abdur Rehman
Armed Forces Bone Marrow Trasnplant Center,Rawalpindi

Background: Polycythemia vera (PV) is a chronic myeloproliferative neoplasm associated with an increased risk of thrombosis, disease progression and mortality. Conventional risk stratification is mainly based on age and previous thrombosis and may not fully reflect the biological heterogeneity of PV. The Triple-A (AAA) prognostic model, incorporating age, absolute neutrophil count (ANC), and absolute lymphocyte count (ALC), offers an additional approach to prognostic risk assessment. However, its applicability in Pakistani patients with PV remains poorly studied.

Objective: To evaluate the distribution and prognostic significance of the Triple-A model in patients with PV at a tertiary-care centre in Pakistan, and to assess its association with overall survival (OS) and progression-free survival (PFS).

Methods: A single-centre observational study was conducted among 36 patients diagnosed with PV. Demographic, clinical and haematological data were collected from clinical records. Patients were stratified according to the Triple-A score into low (0–1), intermediate-1 (2–3), intermediate-2 (4), and high-risk (5–6) groups. Overall survival and progression-free survival were evaluated using Kaplan–Meier survival analysis, with differences between Triple-A groups assessed using the log-rank test.

Results: The cohort had a median age of 51 years, with 72.2% males. JAK2 V617F mutation was present in 94.4% of patients, and 30.6% had a previous history of thrombosis. According to the Triple-A model, 15 (41.7%) patients were classified as low risk, 14 (38.9%) as intermediate-1, 6 (16.7%) as intermediate-2, and 1 (2.8%) as high risk. Overall survival differed significantly across Triple-A categories (log-rank χ^2=22.394, $p<0.001$), suggesting increasing mortality with higher prognostic risk. In contrast, no significant difference in progression-free survival was observed between the Triple-A groups (log-rank χ^2=0.790, p=0.852).

Conclusion: In this single-centre Pakistani cohort, the Triple-A model demonstrated significant prognostic discrimination for overall survival. The model may therefore provide useful additional prognostic information beyond conventional risk stratification in PV. However, the small sample size and limited number of events warrant cautious interpretation, and larger multicentre studies are needed to validate these findings in the Pakistani population.

Keywords: Polycythemia Vera, thrombosis, Absolute Neutrophil Count, Absolute Lymphocyte Count, JAK2 V617F mutation

ROLE OF CEPXX/YY FLUORESCENT IN SITU HYBRIDIZATION IN DONOR CHIMERISM IN SEX MISMATCHED ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANT

Zunera Maryam, Shawana Shahid, Aima Naseer Bukhari
Shifa International Hospital, Islamabad

Background: Donor chimerism is used as a primary metric to measure donor stem cell engraftment and possibility of graft failure after allogeneic hematopoietic stem cell transplantation (allo- HSCT) for malignant and non- malignant hematological diseases. Fluorescent in situ hybridization (FISH) targets the X and Y chromosomes using dual colour Centromeric Enumeration Probes (CEP X/Y) which provides direct visualization to quantify XX and XY cells and monitor engraftment.

Objective:1. To measure donor chimerism in sex-mismatched allo-HSCT using FISH CEP X/Y 2. To monitor stem cell engraftment and its clinical correlation in sex-mismatched allo- HSCT

Methods: Study design: Retrospective cohort Study setting: Tertiary care hospital Study duration: 2020-2026 Sampling method: Peripheral blood or bone marrow aspirate Sample size: 100 patients Follow-up period: 3 months, 6 months and 1 year Inclusion criteria: All patients undergoing sex mismatched aloo-HSCT Exclusion criteria: Sex matched and allogenic HSCT

Results: Of the100 patients who received sex mismatched allogenic HSCT, 60% were male and 40% were female. They were diagnosed with various hematological disorders (AML, aplastic anemia, ALL, MDS, MPN and Thalassemia). Donor chimerism that remained high at 3 months, 6 months and 1 year, and was comparable with their CBCs (TLC, Hb, ANC and Platelets), showed remission in 57% of the patients, relapse in 4% and death in 14% of patients while 25% of the patient were lost to follow-up. Full/increasing donor chimerism is not typically associated with relapse.

Conclusion: With the advent of specialized molecular investigations, like short tandem repeat (STR) analysis and lineage specific chimerism status, FISH Centromeric Enumeration Probes (CEP X/Y) is a simple yet reliable and convenient tool to monitor the stem cell engraftment in sex mismatched allo-HSCT.

Keywords: Donor chimerism, sex mismatched allo-HSCT, Fluorescent In Situ Hybridization, Stem cell engraftment

ASSESSMENT OF FUTURE BLEEDING RISK IN WOMEN AND GIRLS WITH INHERITED BLEEDING DISORDERS USING ISTH BLEEDING ASSESSMENT TOOL (BAT) SCORE

Syeda Aliah Asif, Khalil Ur Rahman, Laila Bahadur , Husnain Ali , Hina Fatima , Mehroze Fatima , Mahnoo,Hina Tariq , Muhammad Kalim Raza, Abdul Salam Khan , Kiran Jamil , Zohra Jabeen Wazir, Syed Kamran Mahmood , Tahira Zafar , Parvez Ahmed

PATHWEL Center of Hematology and Bone Marrow Transplant, RWP

Background: Inherited bleeding disorders cause recurrent morbidity in women and girls, but evidence is limited on whether ISTH-BAT scores predict subsequent bleeding. Risk stratification remains difficult in low-resource clinical settings.

Objective: To determine whether baseline ISTH-BAT scores predict bleeding frequency and severity during 12-month follow-up in women and girls with inherited bleeding disorders.

Methods: This descriptive longitudinal study used non-probability consecutive sampling at PATHWEL Center of Hematology and Bone Marrow Transplant, Rawalpindi, Pakistan, from November 2024 to July 2026. Forty-four newly diagnosed females aged 1 to 40 years were enrolled. Baseline analyses included all participants; nine without follow-up were excluded only from follow-up outcomes, leaving 35 who completed 12 months. Spearman correlation and negative binomial regression assessed the relationship between ISTH-BAT and bleeding count.

Results: Median age was 11 years (IQR 6-14), and mean ISTH-BAT score was 8.9±4.3 (n=43). Glanzmann thrombasthenia (40.9%) and von Willebrand disease (31.8%) predominated. Among 35 followed participants, 33 (94.3%) bled; median bleeding count was 7 (IQR 2-11). Bleeding was minor in 21 (60%), major in 12 (34.3%), and clinically not applicable in two zero-bleed participants (5.7%). Epistaxis (54.3%) and oral bleeding (45.7%) were common. ISTH-BAT score was unrelated to bleeding count (Spearman r=0.004; p=0.981) and remained non-significant after adjustment for age, age at first bleed, and diagnosis group, (IRR 1.00, 95% CI 0.91-1.11; p=0.924).

Conclusion: Baseline ISTH-BAT did not predict 12-month bleeding burden in this cohort. Larger studies with prospective event-level recording are required before using it for individual risk stratification.

Keywords: ISTH-BAT score; Inherited Bleeding Disorders; Bleeding Risk

Impact of Renal Impairment on Outcomes of Allogeneic Hematopoietic Stem Cell Transplantation: A Single-Centre Retrospective Analysis

Zara Tul Ain, Syed Waqas Imam Bokhari, Mahwish Sajjid,Usman Ahmad, Bushra Ahsan, Misbah Manzoor, Ayesha Masood, Sabina Rasheed, Areeba Mujeeb, Waseem Anwar, Bilal Shehzad Azam Khan

Shaukat khanum Memorial Cancer and Research Centre

Background: Allogeneic hematopoietic stem cell transplantation (allo-HCT) is a potentially curative treatment for many hematologic malignancies. However, it is associated with various serious complications, including graft-versus-host disease (GVHD), which is an immune-mediated disorder that can impact several organs, including the kidneys. Acute kidney injury (AKI) of a different stages is frequently encountered complication following allo-HCT and may be associated with increased morbidity and mortality. Despite improvement in transplant care, the impact of different stages of post-transplant AKI on survival outcomes, particularly in current cohorts of predominantly young adult allo-HCT recipients, remains incompletely understood

Objective: The objective of this study was to evaluate the incidence, stages, and clinical associations of post-transplant acute kidney injury (AKI) in allogeneic hematopoietic cell transplantation (allo-HCT) recipients, and to determine its impact on overall survival (OS) and progression-free survival (PFS).

Methods: We conducted a retrospective cohort study of 69 consecutive patients who underwent allogeneic hematopoietic stem cell transplantation (allo-HCT) at Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, between January 2019 and June 2026. The primary objective was to assess impact on transplant outcomes of post-transplant acute kidney injury (AKI), defined according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria (any stage). Overall survival (OS) and progression-free survival (PFS) were calculated from the date of transplantation (day 0). Survival outcomes were estimated using the Kaplan–Meier method and compared with the log-rank test. Cox proportional hazards regression was used to estimate hazard ratios (HRs)

Results: The median age was 21 years (range 17 – 51) with male: female ratio of 51:18.

Stem cell source was peripheral blood in all patients with median CD34 dose of 5.3 million CD34+ cells / kg (range 2.08 – 8.3). HCT-CI score was 0-2 in 54 and 3 or more in 15 patients. Indication for transplantation was Acute myeloid leukemia (AML), Acute lymphoblastic leukemia (ALL), Classic Hodgkin lymphoma and CML / transformed / therapy-related in 33 (47.8%), 22 (31.9%), 7 (10.1%) and 7 (10.1%) patients respectively. Donors were Matched siblings and Haploidentical related in 48 (69.6%) and 21 (30.4%) transplants respectively. Myeloablative (MAC) and Reduced-intensity / Non-myeloablative conditioning was used in 39 (56.5%) and 30 (43.5%) recipients.

Median days to Neutrophil and platelets engraftment were 16 (range 11-30) and 16 (range 10-35) respectively and CMV reactivation occurred in 43 / 69 (62.3%) patients. Post-transplant AKI developed in 44 patients (63.8%), including stage 1 (n=30), stage 2 (n=6), and stage 3 (n=8). With median follow up of 14.9 months (range 0.3 – 71.4), the median OS for the entire cohort was 50.6 months, while patients who developed AKI had a median OS of 22.9 months. In contrast, the median

OS was not reached among patients without AKI, as more than half remained alive at the last follow-up. AKI was associated with significantly inferior OS (p=0.024, HR 2.86, 95% CI 1.15–7.12). A similar trend toward poorer PFS was observed in patients with AKI (p=0.062, HR 2.16, 95% CI 0.96–4.86), although this did not reach statistical significance. Acute graft-versus-host disease (GVHD) and documented infections were the clinical factors most strongly associated with the development of AKI, whereas other factors including underlying diagnosis, donor type, conditioning intensity or HCT-CI did not have significant impact on survival.

Conclusion: Post-transplant AKI is a frequent complication following allo-HCT and is independently associated with inferior overall survival. Early recognition of patients at risk and implementation of renal-protective strategies may improve post-transplant outcomes.

Keywords: Renal failure, acute kidney injury; allogeneic hematopoietic cell transplantation; overall survival; progression-free survival; risk factors

Pancytopenia stories; revelations from bone marrow examinations at a tertiary care center.

Amara Urooj, Kiran Aamir

Liaquat University of Medical and Health Sciences

Background: The spectrum of pancytopenia etiologies ranges from benign to malignant. Previous studies have proven megaloblastic anemia to be the most prevalent cause. Since pancytopenia is a frequently encountered clinicohematological condition with a multitude of symptoms owing to the reduction of all three lineages of blood cells, regular assessment of its underlying derangements is imperative.

Objective: This study was conducted to ascertain the frequency and etiology of pancytopenia in patients presenting for the bone marrow examination at a tertiary care center.

Methods:A descriptive cross-sectional study was conducted at the Diagnostic and Research lab, Liaquat University of Medical and health sciences, Jamshoro from July 2024 to June 2026. 140 cases presented with pancytopenia and were included in this study. Study variables included careful history, examination, CBC indices and bone marrow examination findings. Data was analysed using simple statistics and frequencies were calculated.

Results:A total of 434 patients presented for bone marrow biopsy in the 2 years, among these 140 presented with pancytopenia. In the first year 75 out of 237 had pancytopenia and in the second 65 out of 197. 36/140 (25.7%) were diagnosed with megaloblastic anemia, and same number of cases had aplastic anemia 36/140 (25.7%), Acute leukemia was 2nd 22/140 (15.7%) and Hypocellular bone marrow were 16/140 (11.4%) cases. 9 (6.4%) cases had normal trilineage hematopoiesis and 9(6.4%) cases were inconclusive requiring further investigations. There were 5 cases of lymphoproliferative disorder, 2 cases of mixed deficiency, 2 MDS, 1 lysosomal storage disease, 1 myelofibrosis and 1 multiple myeloma The most common clinical presentations were Fever, Generalized weakness and Weight loss.

Conclusion: Bone marrow aspirate and trephine biopsy are useful tools in the search for the cause of pancytopenia and also for detecting any changes in previous patterns. While the majority of cases had a benign and treatable cause (megaloblastic anemia), similar number of cases of aplastic anemia is a cause for concern for the health care system.

Keywords: Pancytopenia, bone marrow examination, megaloblastic anemia, aplastic anemia.

Clinical Outcomes of AML1-ETO-Positive Acute Myeloid Leukemia in Adolescents and Young Adults: A Single-Center Experience from a Resource-Limited Setting in Pakistan

Zara tul ain, Zara tul Ain, Syed Waqas Imam Bokhari, Faisal Qayum, Usman Ahmad, Romena Qazi, Bushra Ahsan

Shaukat Khanum Memorial Cancer Hospital and Research Centre

Background:AML with t(8;21)/AML1-ETO (RUNX1::RUNX1T1) is classified as favorable-risk core-binding factor AML. However, real-world data on AYA patients from low- and middle-income countries remain limited, and relapse and treatment-related mortality continue to pose significant challenges.

Objective: To evaluate real-world clinical outcomes, including complete remission rates, patterns of hematologic and molecular relapse, ETO persistence, and survival (1-year overall survival and relapse-free survival) in adolescents and young adults (AYA) with AML1-ETO-positive acute myeloid leukemia treated at a tertiary cancer center in Pakistan.

Methods: This retrospective observational study included AYA patients (aged 18–23 years) with newly diagnosed AML1-ETO-positive AML treated at Shaukat Khanum Memorial Cancer Hospital and Research Centre between March 2020 and Januray 2026. All patients received standard DA 3+7 induction followed by high- or intermediate-dose cytarabine consolidation. FLAG-Ida was used as off-label salvage therapy. Primary endpoints were overall survival (OS) and relapse-free survival (RFS), reported as 1-year rates. Secondary endpoints included complete remission (CR) rate, early mortality, relapse patterns (hematologic and molecular), ETO/PCR persistence, and causes of death. Survival was estimated by the Kaplan–Meier method.

Results: Thirty patients were included (median age 19 years; 63% male). Overall CR rate was 86.7%. Four patients (13.3%) died before response assessment. Ten patients (33.3%) relapsed: hematologic relapse in 9, molecular relapse in 9, both in 8, and molecular-only relapse in 1. Persistent AML1-ETO/PCR positivity after consolidation was observed in 3 of 10 relapsed patients and showed a trend toward inferior RFS (log-rank p=0.077). Three patients underwent allogeneic stem-cell transplantation in second CR. At a median follow-up of 28.5 months among survivors, 14 patients (46.7%) remained alive.

One-year OS was 60.5% (95% CI 39.8–76.0%) and one-year RFS was 53.9% (95% CI 33.9–70.2%). Infection/sepsis accounted for 56% of the 16 deaths.

Conclusion: Despite a high initial remission rate consistent with international benchmarks for favorable-risk AML, the relapse rate and treatment-related mortality remained clinically significant in this AYA cohort from a resource-limited setting. Persistent molecular (ETO) positivity after consolidation may predict inferior outcomes and could help identify patients requiring intensified monitoring and consideration of allogeneic transplantation. Routine access to comprehensive co-mutation profiling remains limited due to cost constraints, underscoring the need for affordable molecular diagnostics to optimize risk stratification and outcomes in similar settings.

Keywords: AML1-ETO, RUNX1::RUNX1T1, core-binding factor AML, adolescents and young adults, AYA, resource-limited setting, Pakistan, molecular relapse.

Comparative Analysis of Mobilization Regimens and Their Impact on Stem Cell Yield and Engraftment Kinetics in Patients Undergoing Autologous Hematopoietic Stem Cell Transplant

Sidra Zafar, Hammad Javed, Mirium Farooq Baba, Tariq Ghafoor, Nighat Shahbaz, Mehreen Ali Khan, Tariq Kahatak, Jahanzeb Rehman, Raheel Iftikhar

Armed Forces Bone Marrow transplant Center, Rawalpindi

Background:"Successful autologous stem cell transplantation requires infusion of adequate dose of CD34+ stem cells. Stem cell mobilization methods include granulocyte colony stimulating factor (G-CSF) alone, G-CSG plus plerixafor or chemotherapy-GCSF mobilization. For patients at risk of mobilization failure.

Objective: The aim of this study is to compare outcomes of plerixafor vs non-plerixafor based mobilization regimens in various hematological malignancies.

Methods: The study was conducted at the Armed forces bone marrow transplant center, patients who underwent autologous stem cell transplant between 2020-2025 were included. Patients mobilized with plerixafor based protocol or without plerixafor-based protocol were both included. Clinical records were reviewed for demographic data, mobilization regimen, stem cell yield, and engraftment outcomes. Adequate stem cells yield was defined as ≥2×106 CD34+ cells/kg or ≥2×10^8 MNC/kg. Neutrophil engraftment was defined as an ANC ≥0.5 × 10^9/L for three consecutive days whereas platelet engraftment was defined as ≥20×10^9/L platelets without transfusion support. Ethical approval was obtained from the institutional review board, and informed consent was taken from all participants. Statistical analysis was performed using SPSS version 27.

Results:A total of 137 patients were included in the study who underwent autologous stem cell transplantation having amedian age 44.4(IQR 25.85) years, among them 66% were males and 34% were females. Multiple myeloma (54%) was the most common diagnosis followed by Hodgkin lymphoma (HL) (28.5%), Non-Hodgkin lymphoma (NHL) (8.8%) and Diffuse Large B-Cell Lymphoma (DLBCL) (8.8%). Plerixafor based mobilization was used in 72.3% of the patients in comparison to non Plerixafor based mobilization 27.7%. Mean neutrophil engraftment was achieved at 11.2±1.9 days while platelet engraftment was achieved at 15.5±9.3 days respectively. The Plerixafor group achieved higher CD34+ yields (5.34±3.36 vs. 4.15±1.72; p=0.003) and higher MNC doses (7.41±2.94 vs. 5.26±2.43; p=0.465). There was a trend towards early Neutrophil engraftment (p=0.613) in plerixafor arm, while platelet engraftment occurred earlier with Plerixafor (0.051). Engraftment patterns varied by diagnosis, with DLBCL showing the slowest platelet recovery (p value 0.001) and Multiple myeloma (MM) achieving the highest CD34+ cell dose (p value 0.033). Mean overall survival among the participants was 43.88 (95% CI 1253.97–1415.87) months while mean disease free survival was observed as 37 (95% CI 1030.63-1220.26) months across all disease groups.

Conclusion: Compared to non plerixafor based mobilization, plerixafor based mobilization significantly increased the stem cell yeild and accelerated the platelet recovery.

Keywords: Mobilization, Stem cells, kinetics, Neutrophils, Platelets, Engraftment

Definitive Radiotherapy and Systemic Coordination for Symptomatic Extramedullary Plasmacytoma of the Head and Neck: A Case-Based Review and GuidelinesAligned Management

Laraib Khan

JPMC,Karachi

Background: Solitary extramedullary plasmacytoma (EMP) of the head and neck is a rare plasma cell neoplasm lacking widespread systemic bone marrow involvement. Although highly radiosensitive, managing these lesions requires a meticulous multidisciplinary framework to rule out systemic progression and select localized dose fractionations that protect adjacent organs at risk (OARs).

Objective: To report a unique, clinically challenging case of an extraosseous head and neck plasmacytoma managed with modern image-guided radiotherapy (IGRT) and comprehensive staging aligned with current clinical practice guidelines.

Methods:A 58-year-old male presented with progressive cranial nerve symptoms and a localized, treatment-naïve submandibular soft tissue mass causing airway and swallowing discomfort. Core needle biopsy confirmed monoclonal plasma cell proliferation (CD138- positive, lambda light chain restriction). In accordance with clinical staging and imaging principles, a baseline workup—including whole-body FDG-PET/CT, a unilateral bone marrow aspirate/biopsy confirming

<10% clonal plasma cells, and serum free light chain (FLC) assays— ruled out active multiple myeloma. Treatment was delivered using advanced volumetric modulated arc therapy (VMAT) targeting the gross tumor volume (GTV) with a 0.5 cm clinical target volume (CTV) margin, avoiding adjacent OARs. A definitive dose of 50 Gy in 25 fractions (2 Gy per fraction) was administered to the involved site.

Results: The patient tolerated the course of radiation remarkably well, experiencing only transient Grade 1 acute mucositis that resolved completely two weeks post-treatment. Followup evaluation at three months—incorporating serial FLC monitoring and identical whole-body imaging techniques—demonstrated a complete radiological response with total regression of the submandibular mass. Clinical symptoms resolved entirely, and six-month surveillance confirmed no progression to multiple myeloma.

Conclusion: This case highlights the exceptional therapeutic efficacy of definitive, modern involved-site radiotherapy (ISRT) for head and neck extramedullary plasmacytoma. It underscores the necessity of rigorous baseline staging and precise target delineation to achieve durable local control while minimizing toxicity.

Keywords: Extramedullary Plasmacytoma, Radiation Oncology, Image-Guided Radiation Therapy, Head and Neck Neoplasms,

Improving Outcomes of Hematopoietic Stem Cell Ttransplantation in Transfusion Dependent Thalassemia: Lessons from Twenty-Five Years of Experience

Aamir Aslam Awan, Tariq Ghafoor, Tariq Azam Khattak, Haider Nisar Awan, Ayesha Bibi
Armed Forces Bone Marrow Transplant Center

Background: Pakistan exhibits one of the highest prevalence rates of transfusion-dependent thalassemia (TDT) globally. Approximately 5-8% of the population are carriers of the beta-thalassemia (BTM) gene, equating to an estimated 10-15 million individuals. It is estimated that 5,000-9,000 children are born with TDT annually. Thalassemia is the primary consumer of donated blood from blood banks. The survival rate for individuals with TDT is significantly lower than in under developed countries, primarily due to socioeconomic factors and limited access to consistent healthcare. Allogeneic hematopoietic stem cell transplantation (HSCT) remains the only curative treatment for transfusion-dependent thalassemia (TDT)and is performed worldwide with fully HLA matched related donor, offering the potential to eliminate lifelong transfusion requirements and associated complications.

Objective: To determine long term outcomes of allogenic bone marrow transplant in transfusion dependent thalassemia, identify factors that influence survival and common complications in resource limited setting.

Methods: Descriptive study conducted in armed forces bone marrow transplant center Pakistan from Oct 2001 to Dec 2025.Patient demographics, pre-transplant status, stem cell source, conditioning regimen and post-transplant outcomes were recorded.

Results:A total of 411 transplants were done, mean age of diagnosis was 10.80± 12.76 months and mean age at BMT was 6.0±3.1 years. There were 265 male patients and 145 females. 91 % patients had irregular chelation, 39 % patients had ferritin between 1000-2000 ng/dl, 55.4% had < 50 red cell transfusions, 14.40% were HCV +ve and 91.70% were CMV +ve. 259(63%) patients belonged to Pesaro risk group III. 375 (92%) donors were fully HLA matched siblings. Bu14Cy200ATG/TT conditioning protocol was used in 24.8% patients and FluBu14Cy160 conditioning was used in 75.2% patients. Bone marrow was the source of stem cells in 337 (82%) patients with median TNC 5.11±1.32 x 108/kg, median CD34 7.66±9.20 x 106/kg and median CD3 4.54±2.86 x 107/kg. Neutrophils and platelets engrafted on a median of day+ 14.56±3.63 and day+ 28.04±12.84 respectively. Neutropenic fever (83.4%), hypertension (79.6%), Mucositis/gut toxicity (49.2%), aGVHD (37.9%) and VOD (14.3%) were common complications. At a median follow up of 24 years, overall survival (OS) was 79.1% and disease-free survival was 68.1%. In univariate analysis, age more than 10 years ($p<0.001$), liver more than 5 cm below RCM ($p<0.001$), Pesaro grade IV ($p<0.000$) and VOD ($p<0.001$) significantly affected overall survival and disease-free survival. 15.3% patients had primary graft failure. Treatment related mortality occurred in 86 (20.92%) patients, infections (58%)-GVHD (14%) and VOD (11%) being common causes.

Conclusion: Good infection control, younger age and less blood transfusions before transplant, lower dose of ATG (5 mg/kg) and conditioning Flu120Bu16Cy160TG4.5-7.5 can improve overall survival.

Keywords: Transfusion dependent Thalassemia, Hematopoietic Stem cell transplant