Newsletter | 2024 | Jul - Aug | Volume 01

PATHWELtimes

BIMONTHLY NEWSLETTER

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

> *We live in a moment when the dream of equal opportunity is within reach*
>
> *Barack Obama*

WORLD THALASSEMIA DAY

PATHWEL Center of Hematology & BMT - Pakistan Thalassemia Welfare Society (Report on Page 3)

INSIDE THIS ISSUE

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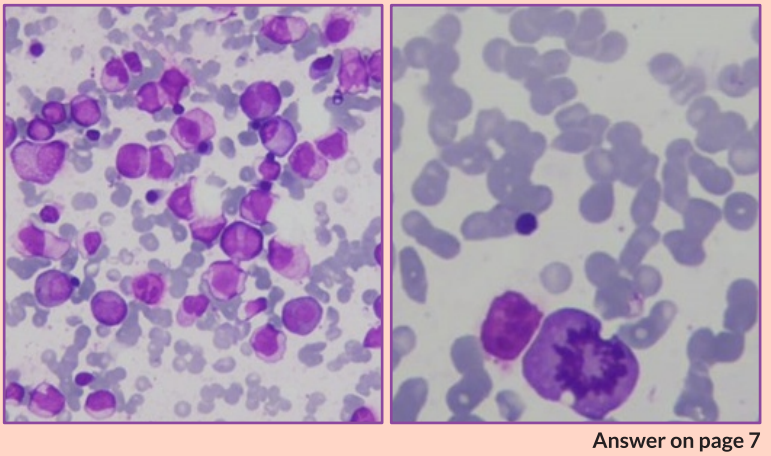
Picture Quiz *by Dr Sidra Barlas*

A 46-year-old female presented with a 4-week history of fever and generalized weakness. On physical examination she was of short stature and pale. There was no visceromegaly. Laboratory studies showed platelet count of 139 x 10^9/l, WBC count 5.9 x 10^9/l, and Hb 13.7/dl.

What is the diagnosis?



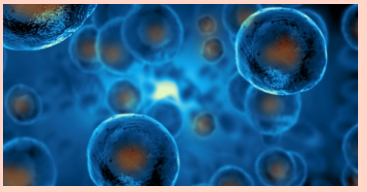
Answer on page 7

DONATE BLOOD SAVE LIFE

WORLD BLOOD DONOR DAY | 14 JUNE 2024

From Editor's Desk

WMDA
matching donors • serving patients



Dear Readers,

Human organ transplantation has been plagued with the scandals of human organ trade. This not only tarnished the image of the medical community but created adverse environment for a genuinely lifesaving treatment for many diseases. However, stem cell transplant and cellular therapy are different from other organ transplantation in many ways. The following is an excerpt of recently published article which raises an important issue with respect to payment for the stem cell donation.

"The cell and gene therapy (CGT) sector has witnessed significant advancement over the past decade, the inception of advanced therapy medicinal products (ATMPs) being one of the most transformational. ATMPs treat serious medical conditions, in some cases providing curative therapy for seriously ill patients. There is interest in pivoting the ATMP development from autologous based treatments to allogenic, to offer faster and greater patient access that should ultimately reduce treatment costs. Consequently, starting material from allogenic donors is required, igniting ethical issues associated with financial gains and donor remuneration within CGT. The World Marrow Donor Association (WMDA) Cellular Therapy Committee has provided recommendations based on expert views that support nonremuneration as the best way to ensure the safety and well-being of donors and patients alike in the CGT field. We recognize that the supporting regulations and guidance for cell and gene therapies are constantly evolving, and we will review our recommendations as the field advances and practices develop. Nevertheless, we believe that to achieve our goal of advancing the field while ensuring the protection of donors' rights and well-being, the safety of patients, non-remunerated donation is the way forward for now, for stem cell and cell and gene therapy".

In this article authors have reviewed key ethical principles in relation to donating cellular material for the CGT field. I hope that this would provide food for thought for you.

Take care.

Reference:
Remuneration of donors for cell and gene therapies: an update on the principles and perspective of the World Marrow Donor AssociationLina Hamad, Salmah Mahmood Ahmed, Eefke van Eerden et al; Bone Marrow Transplantation (2024) 59:580–586; https://doi.org/10.1038/s41409-024-02246-x

World Thalassemia Day

By Dr Sumyyia Abbasi & Ms Nigar Shah
PATHWEL Center for Hematology & Bone Marrow Transplant

Every year, 8th May is observed as World Thalassemia Day. The day provides us an opportunity to sensitize stakeholders and create awareness among masses regarding the importance of preventing thalassemia and how we can provide quality care for those affected by the disease. The theme for this year was "empowering lives, embracing progress, equitable and accessible thalassemia treatment for all".

This year Pakistan Thalassemia Welfare Society (PTWS) and the children with thalassemia marked the World Thalassemia Day with a heartwarming ceremony filled with performances, inspirational speeches, and a shared commitment to raising awareness about thalassemia. The program was held at the auditorium of Rawalpindi Medical University (RMU). We would like to thank the administration of RMU which was

Dr Tariq Fazal Chaudhry, MNA
Chief Guest

Maj Gen Suhaib Ahmed (R)
President, PTWS

Maj Gen Parvez Ahmed (R)
Medical Director, PATHWEL

Dr Jamal Nasir
Vice President, PTWS

Mr. Zamarrud Khan
CEO, Pakistan Sweet Homes

Dr Abdul Qayyum Awan
Member Executive Council, PTWS

Ms Asma Naz,
MPA

Maj Gen Qamar Un Nisa Ch. (R)
Consultant Hematologist, PATHWEL

Friends of Pakistan Thalassemia Welfare Society

forthcoming in offering us their full support.

The program was jointly hosted by Dr Sumyyia Abbasi and Ms Nigar Shah of PATHWEL. It started with recitation of Holy Quran followed by a vibrant opening act by the children, whose energetic performance set the tone for the day. The event was a joyous occasion, the tableaus and musical numbers not only entertained but also highlighted the hope and resilience that is central to the fight against thalassemia. The pride of parents was evident as they watched their children shine on stage. Their involvement underscored the crucial role families play in supporting those affected by thalassemia.

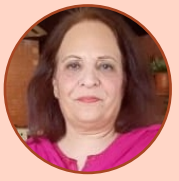
The presence of a large number of celebrities from civil society was very encouraging for us and our children. We were honored to have politicians, media personnels, showbiz personalities, social workers, distinguished doctors, donors, dignitaries from different walks of life, and members of the Executive Council of PTWS. The gathering was addressed by a number of distinguished guests who shared their insights and experiences.

Our special thanks to the Chief Guest Dr Tariq Fazal Chaudhry, MNA, who was kind enough to spare some time from his busy schedule to grace the occasion. We are also grateful to members of Islamabad Chamber of

Commerce for Women, members of Alkhidmat Foundation, Mr. Zamarrud Khan (Founder and CEO, Pakistan Sweet Homes), Dr Sadia (Asst director Pakistan Bait-ul-Mal), Ms Asma Naz (MPA), Maj Gen (Retd) Abid Latif Khan (CEO Hajira Hamza Foundation), Lt Gen (Retd) Kamal Akbar (super donor), and Mr. Hanif Khalid (chief editor daily Jung).

Together, we have taken another step forward in raising awareness and supporting those affected by thalassemia. Let us continue to work towards a future where thalassemia is better understood, managed, and ultimately eradicated.

World Blood Donor Day

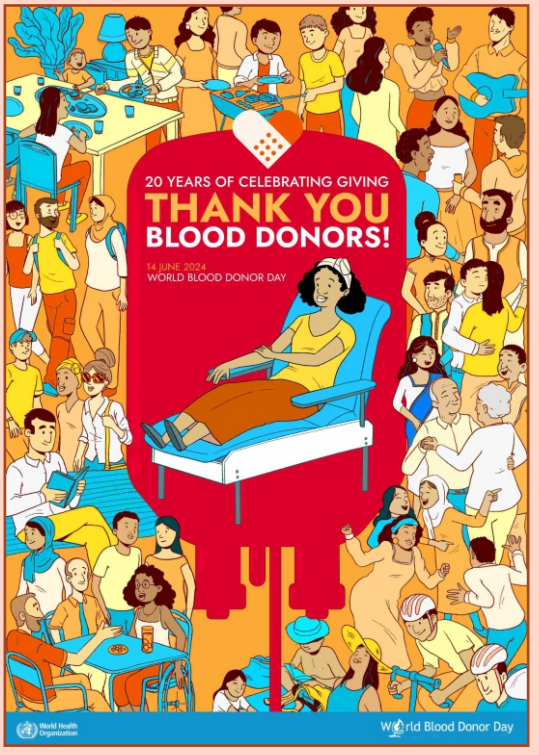


By Dr Zohra J Wazir
Chief Medical Officer Thalassemia Wing

Blood Donor Day is celebrated worldwide on 14th of June to pay tribute to those who donate blood voluntarily without any remuneration, saving lives of those who cannot get this precious commodity in shops.

This year is the 20th year of *blood donor day* honoring the birthday of Karl Landsteiner who discovered ABO blood group system.

PATHWEL celebrated the day with Rawalpindi Medical University (RMU) students' organization- Synergy. Students brought gifts and food for the children. They played different games and spent quality time with them.



Blood Camps' Diary

By Ms Nigar Shah
PRO & Camp Coordinator, PTWS

In May and June we organized number of successful blood collection camps. We are very grateful to all the blood donors and facilitators who helped us in organizing these camps.

Rawalpindi Bar Council | Date: 18 May 2024 | Venue: Rawalpindi Bar Council
The camp members and the visiting officials of PATHWEL were received by the office bearers and members of Rawalpindi Bar Council. We are thankful to secretary general Raja Shahid Zafar, vice president Ghulam Ali Siddiqui, Syed Zulfiqar Naqvi, Sardar Manzir Bashir, Nasir Jamal Siddiqui, Sardar Raqeeb Advocate, and Sardar Shahid Jameel Advocate for their support.



Galaxy College | Date: 24 May 2024 | Venue: Galaxy College, Rawalpindi
A blood donation camp was organized by Pakistan Thalassemia Welfare society at Galaxy College on 24 May 2024. Present on the occasion were Mr. Malik Haq Nawaz, Principal & CEO; Malik Faraz Awan, Major (R) Nasir Awan, and Bilal Afzal Abbasi.

Rawalpindi Law College | Date: May 29, 2024 | Venue: Rawalpindi Law College
A blood donation camp was organized by PTWS at Rawalpindi Law College. Dr Sumyyia Abbasi delivered motivational talks to the students for blood donation. The students were keen to participate in this camp. We collected 30 blood bags within 3 hours. Principal Sardar Ghazanfar Khan and VP Advocate Hasnat Ahmed visited the camp.



Madrassa Tul Fatmia | Date: 8 June 2024 | Venue: Madrassa tul Fatmia
A blood donation camp was organized at Madrassa tul Fatmia Rawalpindi. Present on the occasion were Mr. Murtaza Ali Burhani, member of executive council of PTWS; Peer Maulana, Mr Ali Asghar and other senior members. The community was motivated and very enthusiastic to donate blood.

Islamic International Medical College (IIMC), Riphah International University | Date: May 30, 2024 | Venue: IIMC

A blood donation camp was organized at Islamic International Medical College. One day before camp Maj Gen (R) Dr Parvez Ahmed, MD PATHWEL went to deliver a lecture on blood donation and create awareness about thalassemia and other blood diseases. The camp was facilitated by Brig (R) Professor Maqsood ul, Hasan, Vice Principal; Professor Amena Rahim, HOD Biochemistry; and Professor Shahzad Saeed.



Islamabad High Court Bar Association | Date: 6 June 2024 | Venue: Islamabad High Court

A blood donation camp was organized in collaboration with Islamabad High Court Bar Association. The appointment holders of the Bar spent time with the blood donors and appreciated efforts of PATHWEL team. Those present at the camp included President High Court Bar Riasat Ali Azad (Advocate Supreme Court), Gen Secretary Shafqat Abbas Tarar (Advocate Supreme Court), and Advocate Nadeem Akhtar (Joint Secretary).

Islamabad District Bar Association (Judicial Complex) | Date: 8 June 2024 | Venue: Islamabad District Bar Association

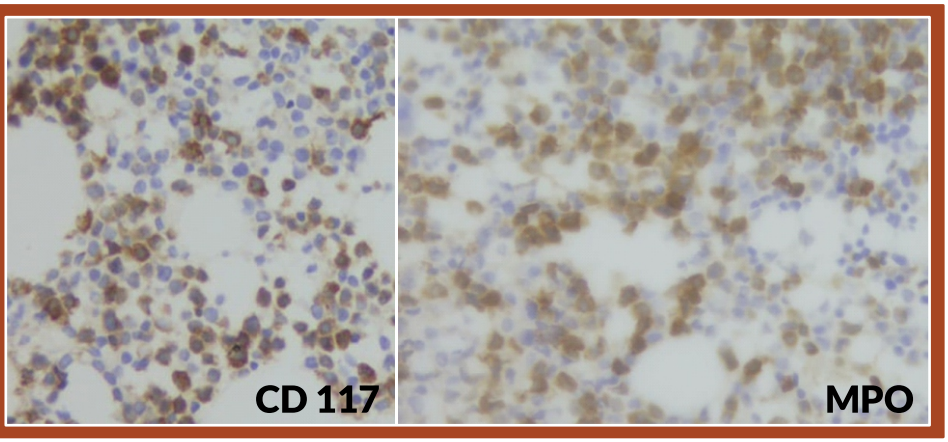
A blood donation camp was organized at Islamabad District Bar Association (Judicial Complex). The efforts of team PATHWEL and the spirit of blood donors was praised by the President High Court bar Riasat Ali Azad (Advocate Supreme Court), President District Bar Advocate Raja Shakeel Abbasi and Secretary Advocate Syed Ameer Hassan.



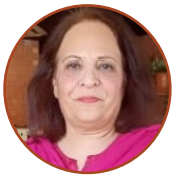
Picture Quiz Answer

by Dr Sidra Barlas

Acute Myeloid Leukemia with myelodysplasia related changes (AML – MRC). The blasts cells were positive for Cd 117 and MPO.



How to Live Better with Thalassemia?



By Dr Zohra J Wazir
Chief Medical Officer Thalassemia Wing

Children with thalassemia have reduced or no ability to produce hemoglobin so anemia develops leading to other complications. Here are some management tips which help children with thalassemia lead a near normal life and avoid complications.

1. Regular Blood Transfusions. Through regular transfusions one can overcome the deficiency of RBCs and hemoglobin. This helps in providing the patients with good oxygen and nutrients delivery to tissues and organs.

2. Folic Acid. This vitamin is necessary for cell production including blood cells. Due to cell destruction and rapid turnover, patients with thalassemia require folic acid supplement.

3. Avoid Iron Supplementation. The commonest cause of anemia in Pakistan is iron deficiency. Therefore, many patients are wrongly prescribed iron supplements, or they take them believing that iron is going to improve their Hb. On the contrary, thalassemic patients are iron overloaded due to frequent blood transfusions. And in fact, iron is poison for them.

4. Iron Chelation. There is no natural mechanism in the human body for removal of excess iron. Therefore, medicines are required to remove extra iron and avoid the organ damage caused by the iron deposition in the body tissues. These medicines are called iron chelators. Both oral and injectable iron chelators are available.

5. Hydration. Staying hydrated is important for everyone particularly for thalassemic patients. When the patient is hydrated, it maintains the blood volume and prevent increase in blood viscosity and complications related to dehydration.

6. Avoidance of Infections. Thalassemia patients are not immunocompromised but as they are receiving frequent blood transfusions and are exposed to healthcare facility environment, they are more prone to infections. It is prudent that all children with thalassemia should practice good hygiene, gets vaccinated, avoid meeting sick people and get proper treatment after infections.

7. Regular Checkups. Regular checkups are very crucial to maintain good hemoglobin levels, control iron levels and overall health of the children. Timely intervention for fall in Hb and rise in iron levels prevent complications and guarantees good health in the long run.

8. Genetic Counseling & Family Screening. Genetic counseling is very important and can help individuals understand the risk of passing their genes to their children. Families at risk can be screened and timely actions can be taken to avoid birth of children with thalassemia major.

9. Prenatal Diagnosis. Thalassemia is a genetic disorder which is preventable, so prenatal diagnosis is very important in thalassemia minor patients. Early pregnancies (at about 3 months gestation) can be tested for thalassemia major in the fetus. This test is called Chorionic Villus Sampling (CVS) and is available in the major cities of Pakistan. Therapeutic abortion can be offered to the parents and birth of a child with thalassemia major can be prevented.

10. Emotional Support. Thalassemia can drain the patients and their families emotionally that can be very challenging for everyone. Here comes role of the family, friends, support groups, and healthcare professionals which can improve the overall well-being and adherence to the treatment.

Patient of the Month

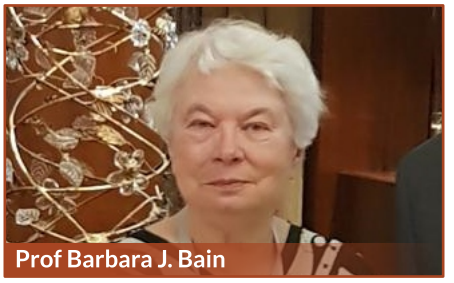
Areesha Naeem (17 Years)

That's how well we treat them at PATHWEL

Morphology Updates

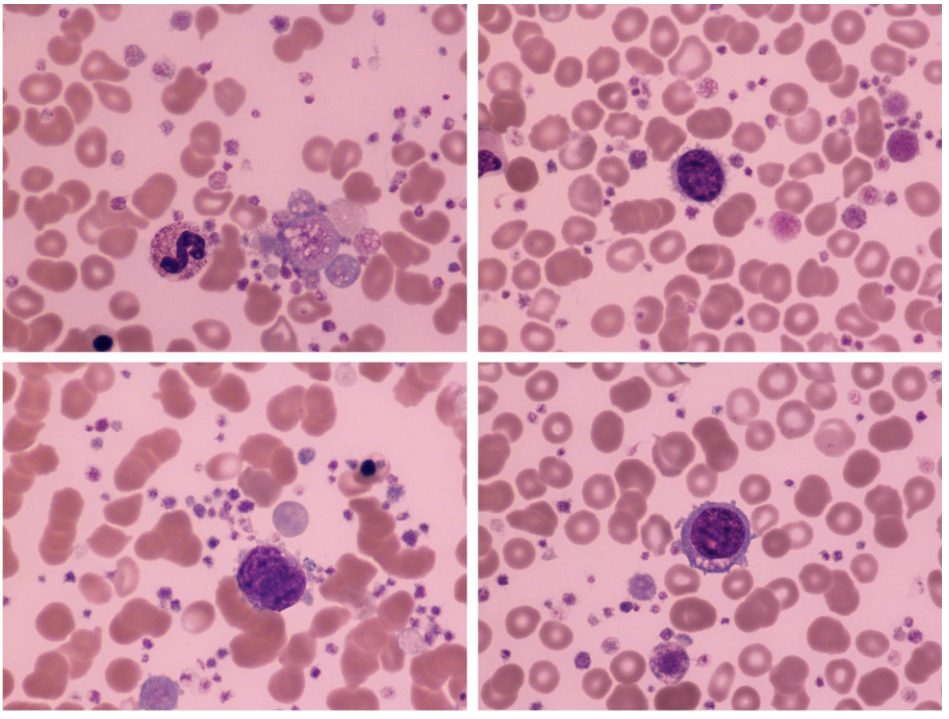
Circulating micromegakaryocytes in an asplenic patient with post-polycythemia myelofibrosis

Albert Borg[1] | Viviene Ballon[1] | Barbara J. Bain[1,2]
[1]Blood Sciences, Imperial College Healthcare NHS Trust, St Mary's Hospital, London, UK
[2]Centre for Haematology, Department of Immunology and Inflammation, St Mary's Hospital Campus of Imperial College Faculty of Medicine, St Mary's Hospital, London, UK
DOI: 10.1002/ajh.27213


Prof Barbara J. Bain

Micromegakaryocytes are usually only seen in the bone marrow of patients with myeloid neoplasms. They are rare in blood films. The images above are from a 55-year-old woman who presented with an upper gastrointestinal hemorrhage related to a bleeding peptic ulcer. She had a background diagnosis of JAK2-mutated polycythemia vera with progression to myelofibrosis. Mutations that had been demonstrated previously included JAK2 p.Val617Phe-variant allele frequency (VAF) 77%, ASXL1 p.Pro808LeufsTer10-VAF 35%, EZH2 p.-Arg690His-VAF 40%; p.Arg288Gln-VAF 12%.

Two months prior to this presentation the patient had suffered a traumatic splenic rupture requiring splenectomy to control acute bleeding. Spleen pathology showed a capsular breach consistent with the history of trauma and, in addition, extramedullary hematopoiesis in keeping with the known diagnosis of post-polycythemia myelofibrosis. This admission was complicated by aspiration pneumonia requiring intensive care admission for ventilatory support, and concomitant COVID-19. Blood count results at this time showed hemoglobin concentration 95 g/L, mean cell volume 98 fL, white cell count 25.1 10^9/L, platelet count 1967 10^9/L, and mean platelet volume 10.8 fL.



A blood film was markedly abnormal: leucoerythroblastic with prominent red cell changes (anisopoikilocytosis, dacrocytes, and ecchinocytes) with marked dyserythropoietic features (binucleated red cells, internuclear bridging, nuclear budding, abnormal hemoglobinization, and siderotic granules); the myeloid series was left shifted, and neutrophils were hypergranular, with pseudo-Pelger–Hu· nuclei. The most notable abnormalities, however, were marked thrombocytosis with giant platelets and multiple platelet aggregates (top left), and the presence of numerous circulating megakaryocytes with almost bare nuclei; some of the latter had ragged, almost villous, cytoplasm (top right) and others appeared to be budding platelets (lower images).

We attribute the presence of micromegakaryocytes to myelodysplasia associated with disease evolution in polycythemia vera with the large number of these cells in the peripheral circulation resulting from extramedullary hematopoiesis and hyposplenism.

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Reduced intensity versus myeloablative conditioning for MDS: long-term results of an EBMT phase III study (RICMAC)

Christian Niederwieser, Simona Iacobelli, Georg-Nikolaus Franke et al; Bone Marrow Transplantation; doi.org/10.1038/s41409-024-02282-7

Short-term outcome of myeloablative (MAC) and reduced intensity (RIC) conditioning in the prospective randomized international EBMT RICMAC study in patients with myelodyplastic syndrome (MDS) was comparable but longer follow up is lacking. Patients with MDS aged 18–65 years were randomized to receive MAC (N = 64) with busulfan/cyclophosphamide or RIC (n = 65) with busulfan/fludarabine followed by stem cell transplantation (HCT) from HLA matched or mismatched donor.

After a median follow-up of 6.2 (0.4–12.5) years, 10-year OS and RFS were 54.0% and 43.9% for RIC and 44.4% and 44.2% for MAC (p = 0.15 and p = 0.78), respectively. In a multivariate analysis, ECOG status and chemotherapy prior to HCT were independent risk factors for OS and RFS, ECOG and low cytogenetic risk for NRM and chemotherapy prior to HCT for RI. Patients with low cytogenetic risk had better OS [p = 0.002], RFS [p = 0.02], and NRM (p = 0.015) after RIC as compared to MAC.

The present analysis is based on the longest follow up in a randomized study for HCT in MDS. First, HCT leads to a long-term OS of 49% (95% CI: 38.3–60.1) at 10 years, irrespective of the preparative regimen and with similar results following RIC (FluBu2) and MAC (BuCy). Overall RI was around 25.4% (16.5–34.3) and NRM 30.4% (21.6–39.1) at 10 years without statistically significant differences between the two arms.

RIC showed a trend for better OS as compared to MAC early after HCT, but RFS was overlapping. In general, RIC protocols have been shown to have less morbidity compared to MAC. Chronic GVHD did not differ between the two arms. Overall, we report that low risk cytogenetic patients have the highest benefit with RIC for OS and RFS because of lower NRM. Therefore, RIC may be considered as equivalent to MAC in younger patients with MDS, but preferentially cytogenetic low risk patients should be treated with RIC.

Consensus definitions from ASTCT by Kharfan-Dabaja et al.

Anna Sureda, Paul A. Carpenter, Andrea Bacigalupo, et al: Bone Marrow Transplantation; doi.org/10.1038/s41409-024-02251-0
SOURCE: Harmonizing definitions for hematopoietic recovery, graft rejection, graft failure, poor graft function, and donor chimerism in allogeneic hematopoietic cell transplantation: a report on behalf of the EBMT, ASTCT, CIBMTR, and APBMT Open access: http://creativecommons.org/licenses/by/4.0/

Term	Definition
Neutrophil recovery	1st of 3 successive days with an absolute neutrophil count of ≥500/μL after post-transplantation nadir.
Platelet recovery	The first of 3 consecutive days with a platelet count of 20,000/μL or higher in the absence of platelet transfusion for 7 consecutive days.
Graft rejection versus graft failure	Graft rejection is an immune-mediated process, whereas graft failure represents a wider array of possibilities, including cell dosing, disease, infection, drugs, and an immune-mediated event.
Graft failure (primary) (according to cell source)	**PBSCs:** lack of achievement of an ANC ≥500/μL by day +30 with associated pancytopenia. **Unstimulated BM:** lack of achievement of an ANC ≥500/μL by day +30 with associated pancytopenia. **UCB:** lack of achievement of an ANC ≥500/μL by day +42 with associated pancytopenia.
Poor graft function	Frequent dependence on blood and/or platelet transfusions and/or growth factor support in the absence of other explanations, such as disease relapse, drugs, or infections
Secondary graft failure	A decline in hematopoietic function (may involve hemoglobin and/or platelets and/or neutrophils) necessitating blood products or growth factor support, after having met the standard definition of hematopoietic (neutrophils and platelets) recovery
Donor chimerism	**Full:** chimerism >95% for both myeloid and lymphoid lineages. **Mixed or partial:** chimerism 5%–95% for both myeloid and lymphoid lineages. **Absent:** chimerism as <5% for both myeloid and lymphoid lineages.

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Finding a balance in reduced toxicity hematopoietic stem cell transplantation for thalassemia: role of infused CD3+ cell count and immunosuppression

Barbara Meissner, Peter Lang, Peter Bader et al; Bone Marrow Transplantation (2024) 59:587–596; https://doi.org/10.1038/s41409-024-02219-0

We performed a retrospective analysis on 124 patients with transfusion-dependent thalassemia who were registered in the German pediatric registry for stem cell transplantation. All patients underwent their first allogeneic hematopoietic stem cell transplantation (HSCT) between 2011 and 2020 and belonged mainly to Pesaro risk class 1–2.

Four-year overall (OS) and thalassemia-free survival (TFS) were 94.5% ± 2.9% and 88.0% ± 3.4% after treosulfan-fludarabine-thiotepa- and 96.9% ± 3.1% (P = 0.763) and 96.9% ± 3.1% (P = 0.155) after busulfan-fludarabine-based conditioning.

Mixed chimerism below 75% occurred predominantly in treosulfan based regimens (27.5% versus 6.2%). OS and TFS did not differ significantly between matched sibling, other matched family and matched unrelated donor (UD) HSCTs (OS: 100.0%, 100.0%, 96.3% ± 3.6%; TFS: 96.5% ± 2.4%, 90.0% ± 9.5%, 88.9% ± 6.0%). However, mismatched UD-HSCTs performed less favorable (OS: 84.7% ± 7.3% (P = 0.029); TFS: 79.9% ± 7.4% (P = 0.082)).

We generated a scoring system reflecting the risk to develop mixed chimerism in our cohort. The main risk-reducing factors were a high CD3+ cell count (≥6 × 107/kg) in the graft, busulfan-conditioning, pre-conditioning therapy and low-targeted ciclosporin A trough levels. Acute GvHD grade III-IV in treosulfan-based concepts predominantly occurred in patients with UD and reduced GvHD prophylaxis but not in the context of high CD3+ cell doses.

Taken together, this information might be used to develop more risk-adapted HSCT regimens for thalassemia patients.

Splenic irradiation for myelofibrosis prior to hematopoietic cell transplantation: A global collaborative analysis

Nico Gagelmann, Gabriela S. Hobbs, Edoardo Campodonico et al; American Journal of Hematology; DOI: 10.1002/ajh.27252

Splenomegaly is the clinical hallmark of myelofibrosis. Splenomegaly at the time of allogeneic hematopoietic cell transplantation (HCT) is associated with graft failure and poor graft function. Strategies to reduce spleen size before HCT especially after failure to Janus kinase (JAK) inhibition represent unmet clinical needs in the field.

Here, we leveraged a global collaboration to investigate the safety and efficacy of splenic irradiation as part of the HCT platform for patients with myelofibrosis. We included 59 patients, receiving irradiation within a median of 2 weeks (range, 0.9–12 weeks) before HCT. Overall, the median spleen size prior to irradiation was 23 cm (range, 14–35).

Splenic irradiation resulted in a significant and rapid spleen size reduction in 97% of patients (57/59), with a median decrease of 5.0 cm (95% confidence interval, 4.1–6.3 cm). The most frequent adverse event was thrombocytopenia, with no correlation between irradiation dose and hematological toxicities. The 3-year overall survival was 62% (95% CI, 48%–76%) and 1-year non-relapse mortality was 26% (95% CI, 14%–38%).

Independent predictors for survival were severe thrombocytopenia and anemia before irradiation, transplant-specific risk score, higher intensity conditioning, and present portal vein thrombosis. When using a propensity score matching adjusted for common confounders, splenic irradiation was associated with significantly reduced relapse (p = .01), showing a 3-year incidence of 12% for splenic irradiation versus 29% for patients with immediate HCT and 38% for patients receiving splenectomy.

In conclusion, splenic irradiation immediately before HCT is a reasonable approach in patients experiencing JAK inhibition failure and is associated with a low incidence of relapse.

Hemlibra (Emicizumab) project; a significant step forward in hemophilia therapy

By Dr. Rafia Behzad

Hemlibra project was initiated in HTC Rawalpindi under World Federation of Hemophilia (WFH) pilot project. Thirteen patients were selected for the project. An awareness session for the patients and their attendants was held in Dec 2020. The session aimed to provide detailed information followed by a question-answer session. Consent was taken from all patients and their attendants.

Administration of Emicizumab injections began from 6th January 2021, while the maintenance dose was started on 10th February 2021. The project is currently on-going.

Dosing Schedule

- Loading dose of 3 mg per kg subcutaneously once a week for one month.
- Maintenance dose 3 mg per kg subcutaneously fortnightly.

Criteria for Patient Selection

a. Children under 12 years of age
   - Diagnosed WITH inhibitors
   - WITHOUT inhibitors, with ABRs of 8 or greater & past history of life-threatening bleeds (intracranial, intra-abdominal, pseudotumor)

b. Patients with Hemophilia (PWH) 12 years & above
   - Diagnosed WITH inhibitors
   - WITHOUT inhibitors on a case-to-case basis, and past history of life-threatening bleeds (intracranial, intra-abdominal bleed, pseudotumor)

Current Status

The Hemlibra (Emicizumab) project is successfully progressing with all the selected patients adhering to their treatment schedules. The program is closely monitored with regular follow-ups to ensure the safety and efficacy of the project.

Acknowledgement

We extend our heartfelt gratitude to the World Federation of Hemophilia (WFH) for their invaluable support and collaboration in making this project possible. Their contribution has been instrumental in advancing hemophilia care and improving the quality of life for our patients.

HEMLIBRA is a bispecific factor IXa- and factor X-directed antibody indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors. Source: https://www.hemlibra.com/

Retroperitoneal Hematoma in a 28-Year-Old Male Hemophiliac: A Case Report

By Dr. Rafia Behzad

Twenty-eight-year-old Ahsan Imtiaz, resident of Mirpur, was a known case of Severe Hemophilia A and presented to PIMS with a history of fall from stairs. His abdomen was tender and bowel sounds were sluggish. Abdominal ultrasonography showed fluid and mass in left hemiabdomen. CT Scan abdomen and pelvis demonstrated grade II renal injury, grade I splenic injury along with mild hemoperitoneum, and large left sided retroperitoneal hematoma with active bleeding at the time of scan and an approximate volume of 1087 ml.

Clinical Practice Guidance

Antithrombotic Treatment in Patients with Hemophilia: an EHA-ISTH-EAHAD-ESO Clinical Practice Guidance. Summary of Recommendations (Part-III)

Roger E.G. Schutgens, Victor Jimenez-Yuste, Miguel Escobar, et al; HemaSphere (2023) 7:6(e900); doi.org/10.1097/HS9.0000000000000900

Section 4: Heart Valves

How to manage valve replacement in PWH?

- We recommend bioprosthetic valves over mechanical valves to avoid life-long anticoagulation in PWH.
- Anticoagulation postoperatively is variable and can be administered, observing the suggested minimum trough factor levels as described earlier (in general, we recommend FVIII/IX levels >20 IU/dL).

Section 5: Venous Thromboembolism

Is routine thromboprophylaxis needed in PWH undergoing orthopedic surgery?

- Considering the low prevalence of postoperative VTE in PWH and the potential chance of bleeding complications, we do not recommend the use of routine pharmacological thromboprophylaxis in the perioperative period.
- We recommend an individual approach in surgery with high VTE risk.
- We recommend mechanical over pharmacological thromboprophylaxis if indicated.
- We recommend against extended duration of pharmacological thromboprophylaxis.

Is the recommendation for routine thromboprophylaxis in PWH different according to the hemostatic product that is used (bypassing agents/emicizumab)?

- We do not consider the routine use of pharmacological thromboprophylaxis for surgery in PWH patients using emicizumab or bypassing agents.

Section 6: Acute Neurology

What is the optimal antithrombotic management of transient ischemic attack in PWH?

- In PWH with a noncardioembolic transient ischemic attack (TIA) and factor levels <20 IU/dL, we recommend starting aspirin.
- In patients with severe hemophilia with a noncardioembolic TIA without clotting factor prophylaxis (FVIII/FIX <1 IU/dL), we do not recommend the use of antithrombotic medication.
- In PWH with a noncardioembolic TIA and factor levels >20 IU/dL, we recommend starting aspirin. In patients with high-risk noncardioembolic TIA, DAPT with aspirin and clopidogrel may be considered for a maximum of 21 days after the TIA, followed by long-term aspirin.
- We do not recommend the use of starting or adapting clotting factor prophylaxis merely to be able to start DAPT in the setting of a TIA.

What is the antithrombotic management of acute ischemic stroke in PWH?

- In PWH with acute ischemic stroke, we do not recommend intravenous thrombolysis.
- In anterior circulation ischemic stroke due to large vessel occlusion, fulfilling established eligibility criteria, we consider mechanical thrombectomy to be appropriate in PWH.
- In PWH with acute minor ischemic stroke (NIHSS score < 5), we recommend similar treatment to PWH and TIA.
- In PWH with acute, nonminor, ischemic stroke (NIHSS score > 3), we recommend starting aspirin.

Concluded

Initially surgical intervention via laparotomy was planned, but due to severity of his condition, the decision was made to adopt a conservative approach instead. He was given fluids, analgesia, antibiotics and blood products. He was transfused with a total of 8 units of RCCs and 12 units of FFPs in PIMS hospital.

HTC Rawalpindi provided complete FVIII cover during his stay in hospital. His retroperitoneal hematoma volume decreased to approximately 739.5 ml by day 10 and further reduced to around 688 ml by day 13. Ahsan was discharged from the hospital in a stable after 14 days. He visited HTC for review and was recommended for regular routine prophylaxis.

Thalassemia Major

(Part-3)

By Dr Tahira Zafar, Consultant Hematologist

تھیلیسیمیا میجر

(حصہ سوئم)

ڈاکٹر طاہرہ ظفر، کنسلٹنٹ ہیماٹولوجسٹ

We are starting page for information of blood diseases for our patients in Urdu. The first in this series of articles is on thalassemia major. This article is from a booklet written by Dr Tahira Zafar, Senior Consultant Hematologist. We are publishing this booklet in three parts.

۱۸۔ تھیلیسیمیا میجر کے بچے عام طور پر ۴ماہ کی عمر سے انتقال خون کے محتاج ہو جاتے ہیں۔ کبھی خون مناسب مقدار میں ملتا ہے۔ کبھی نہیں ملتا۔ ہر تیسرے چوتھے ہفتے یا اس سے بھی جلدی یہ بچے انتقال خون کے مراکز میں گھنٹوں کے حساب سے اپنی زندگی کے دن پورے کرتے ہیں ان کے والدین حسرت بھری نگاہوں سے ان کو دیکھتے ہیں۔ اور مایوسی اور لاچارگی کی زندہ مثال پیش کرتے ہیں۔ یہ مجبور والدین اپنے بچوں کو اس آزمائش سے گزارتیں ہیں اور بخوبی جانتے ہیں کہ ان کی معصوم اولاد ان کے پاس چند سالوں کیلئے اللہ کی امانت ہے۔ وہ اس کو ایک آزمائش، ایک امتحان، ایک فریضہ سمجھ کر اس میں سے گزر جاتے ہیں لیکن ان کے خیالات، مجبوری، بے بسی، دکھ اور کرب کی گہرائیوں کو کون سمجھ سکتا ہے کیا آپ سمجھ سکتے ہیں؟

۱۹۔ انتقال خون اس بیماری کا علاج نہیں ہے یہ ایک نامراد زندگی کو طول دینے اور والدین کی بے بسی اور حسرتوں میں اضافہ کرنے کا باعث ہے۔ انتقال خون سے جو بیماریاں لاحق ہو سکتی ہیں وہ بدرجہ اتم ان بچوں میں ہوتی ہیں۔ ان میں ہیپاٹائٹس بی اور سی، فولاد کی زیادتی، غدودوں کے فعل میں کمی اور دل کی بیماری سر فہرست ہیں۔ گویا کہ ایک لاعلاج بیماری کے علاج اور تگ ودو میں مریض کو جو فائدہ ہو نہ ہو چند دوسری بیماریاں بونس میں مل جاتی ہیں۔ ان بیماریوں کے علاج کے اخراجات، ان کے نقصانات، ان بیماریوں کا دوسرے افراد کو منتقلی، غرض یہ کہ علاج بیماری سے بدتر اور جلتی پر تیل کے مترادف ہے۔ یہ پہلے سے ایک اذیت ناک زندگی کو مزید اذیت ناک، بے معنی و بے مقصد بنا دیتا ہے۔

۲۰۔ تھیلیسیمیا میجر کے مریض عام طور پر سن بلوغت سے پہلے ہی فوت ہو جاتے ہیں جو بچے ۲۰ سال کی عمر تک زندہ رہتے ہیں وہ شادی کے لائق نہیں ہوتے۔ کیونکہ ان کے ہارمونز کا نظام نارمل نہیں ہوتا۔ ان مریضوں میں چونکہ بچے پیدا کرنے کی اہلیت نہیں ہوتی اس لئے یہ تھیلیسیمیا کو آئندہ نسل میں منتقل نہیں کر سکتے۔

تھیلیسیمیا میجر کے مریض بس اپنی جان پر ہی کھیل جاتے ہیں اور چند سالہ زندگی میں خون کے آنسو روتے اور رولاتے ہوئے یہ بچے والدین کو سسکتا اور تڑپتا چھوڑ کر خالق حقیقی سے جا ملتے ہیں۔

۲۱۔ تھیلیسیمیا میجر کے لئے جو مروجہ طریقہ علاج ہے۔ اس میں انتقال خون، تلی کا آپریشن، فولاد کی زیادتی کا تدارک وغیرہ شامل ہیں۔ ان میں سے کوئی بھی علاج مرض سے نجات نہیں دلاتا۔ یہ سب علاج مریض کی تکالیف کو کم کرنے۔ ان کی جسمانی حالت قدرے بہتر بنانے اور بیماری کی علامت کو کنٹرول کرنے کا ذریعہ ہیں۔ اس بیماری کو جڑ سے اکھاڑ پھینکنے کے لئے ایک نیا طریقہ علاج رائج ہوا ہے اسے (Bone Marrow Transplantation) یا (BMT) کہتے ہیں اس میں مریض کی ہڈی کے خراب گودے کو مکمل طور پر ختم کر دیا جاتا ہے اور اس کی جگہ کسی بھائی یا بہن کی ہڈی کا گودا نکال کر مریض میں ڈال دیا جاتا ہے اکثر و بیشتر یہ طریقہ کامیابی سے ہمکنار ہوتا ہے۔ لیکن یہ سو فیصد کامیاب نہیں۔ ناکامی کی صورت میں مریض کی موت واقع ہو سکتی ہے جن مریضوں میں یہ طریقہ کامیاب ہوتا ہے۔ ان کو دوائیں بھی لینا پڑتی ہیں۔ اور علاج اور بعد از علاج دوائوں کے مضر اثرات بھی برداشت کرنا پڑتے ہیں۔ اس علاج کی قیمت تقریباً ۱۵ لاکھ سے زیادہ ہے۔ نہ معلوم کہ غریب کہاں جائے۔ پتہ نہیں کہ کسی غریب تھیلیسیمیا میجر کے لئے معاشرے کے نزدیک زندہ رہنے کا حق بھی ہے کے نہیں؟

اوپر کے بیان سے یہ بات واضح ہے کہ تھیلیسیمیا مائیز اکثر و بیشتر خون کی ایک بے ضرر کیفیت ہے جو ان افراد میں کسی جسمانی ذہنی یا جنسی کمزوری کا سبب نہیں بنتی۔ آئندہ نسلوں میں تھیلیسیمیا میجر کی منتقلی کو ختم کرنے کیلئے یہ لازمی ہے کہ تھیلیسیمیا مائیز کے حامل افراد کے درمیان شادی کو روکا جائے۔ اس کے لئے ضروری ہے کہ تھیلیسیمیا جین کے حامل والدین اپنے بچوں میں تھیلیسیمیا کی کیفت کا پتا لگائیں جو کہ خون کے ایک ٹیسٹ ہیموگلوبن الیکٹروفوریسز سے باآسانی ممکن ہے اور شادی طے کرنے سے پہلے اس بات کا خیال رکھا جائے کہ تھیلیسیمیا میجر کے خطرے سے خاندان بھی محفوظ رہے اور ملک بھی اس مہلک بیماری سے پاک ہو جائے۔

یہ ہم سب کا قومی، سماجی، معاشرتی اور اخلاقی فریضہ ہے۔

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Half matched bone marrow transplant

By Dr. Khalil ur Rehman,
Junior Consultant and BMT specialist, PATHWEL

In December 2022, Obaid Ullah, 20 years of age, from Swat presented to local hospital with generalized body aches, fever and vomiting. At that time, CBC showed high WBC count of 269 x 10^9/l. Hb was 11g/dl, and platelets 40 x 10^9/l. The patient was referred to PATHWEL.

On presentation at our hospital, Obaidullah had stable vital signs. Physical examination revealed bilateral inguinal lymphadenopathy and Hepatosplenomegaly. Peripheral blood film showed 90% lymphoid blast cells. Flow cytometry was consistent with T-ALL (double Negative CD4+CD8). PCR for BCR ABL was negative.

Patient was started on UK ALL 2011 Regimen B induction on 20 December 2022. The patient tolerated chemotherapy well. Bone marrow examination on day 29 demonstrated iatrogenic hypoplasia with 3% blasts. There was complete morphological remission after consolidation.

Obaidullah had no fully matched donor available in the family. However, he was half matched with his sister Summaiya. Haploidentical stem cell transplant was planned and cranio-spinal plus testicular irradiation was given. Conditioning chemotherapy comprises of Thiotepa 10, Busulfan IV 9.6, and Fludarabine150 along with Post-transplant Cyclophosphamide 80.

Primed Bone Marrow harvest was the source of stem cells.
Transplant course was complicated by neutropenic fever, gut toxicity and mucositis grade II. There was transient grade III skin GVHD which responded to the adjustments in immunosuppression. Currently the patient is 10 months post-transplant, is off immunosuppression, GVHD free, relapse free and maintaining stable blood counts.