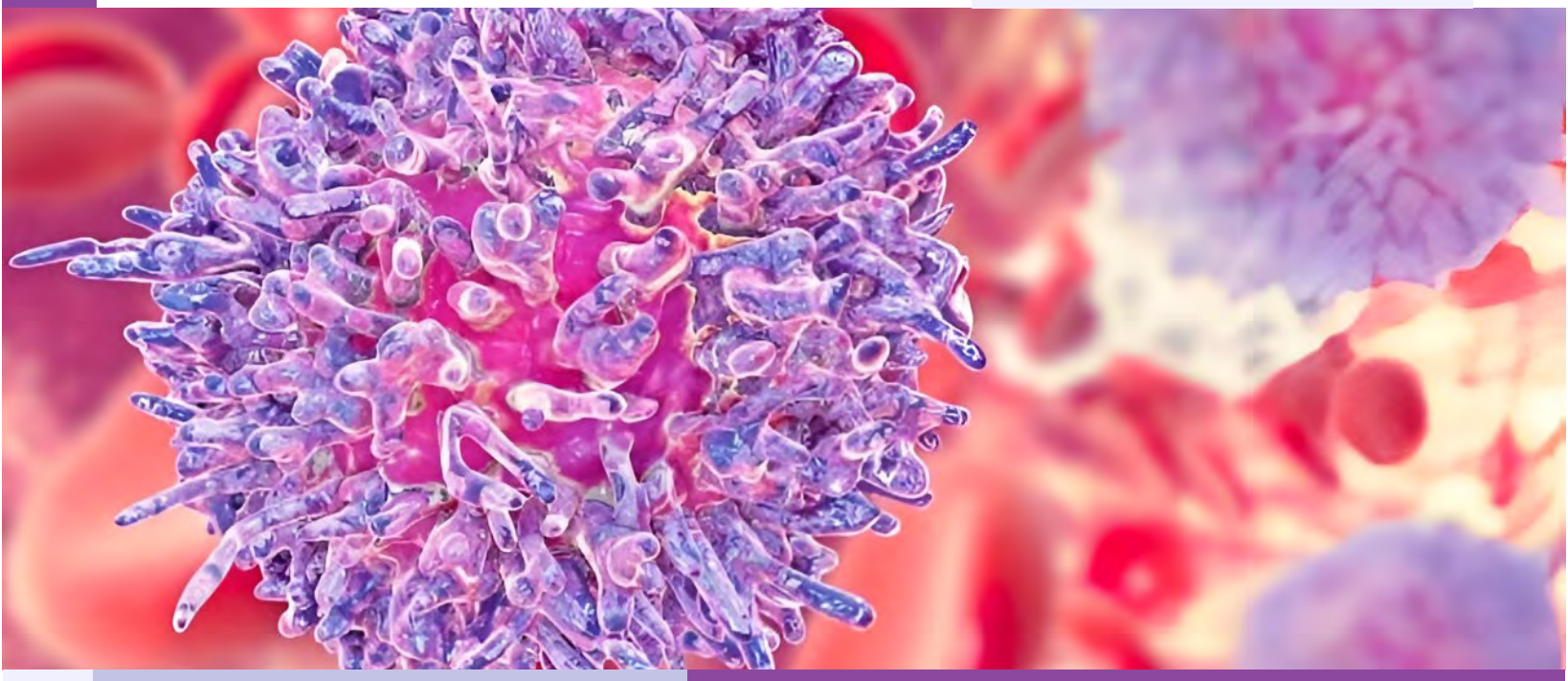
Newsletter | 2024 | May - Jun | Volume 01

PATHWELtimes

BIMONTHLY NEWSLETTER

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

Be a Hero Be a Donor



INSIDE THIS ISSUE

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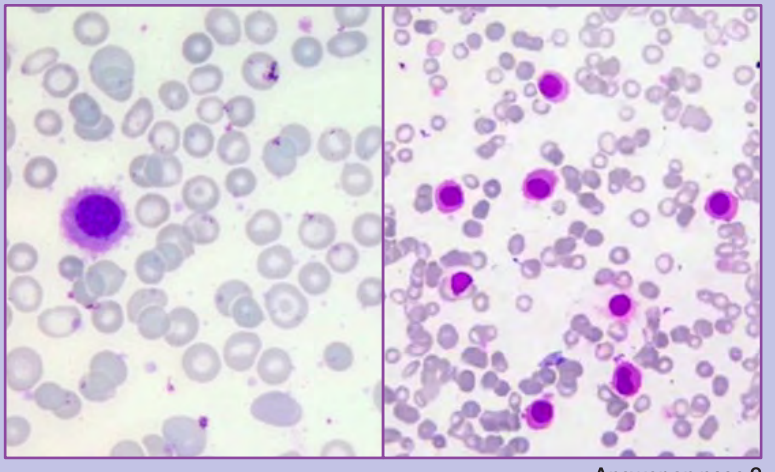
Picture Quiz *by Dr Sidra Barlas*

A 55-year-old man presented with a 4-week history of rectal bleeding, epistaxis, and weight loss. On physical examination he was pale with massive splenomegaly. Laboratory studies showed pancytopenia with Hemoglobin level of 4.8 g/dL WBC count 3.4 x 10^9/L, and platelet count 97 x 10^9/L. What is the diagnosis?



Answer on page 9

BE AWARE SHARE CARE
WORLD THALASSEMIA DAY | MAY 8, 2024

From Editor's Desk

Dear Readers,

The term Financial Toxicity became popular in medical literature after Zafar & Abernethy published an article in 2013. Initially the term was used in context with the costly cancer treatment but later it was also used by other specialties.

In Pakistan, clinical hematologists are quite familiar with the financial toxicities of the prohibitive cost of investigations and medicines used to treat patients not only with malignant but also with benign blood diseases. Many of the patients suffer the consequences of this toxicity and many lives are lost which could and should have been saved.

However, the connotation associated with financial toxicity implies that it is something like the medical toxicities that we see with the very toxic drugs used to treat cancers. As if it is something that is part of the treatment package and bound to happen over which we cannot exercise much control. This is unfortunate. Once it is realized that high cost of treatment is imposed on patients by a health care system that is fabricated to create profit, the financial toxicity becomes financial exploitation.

The clinicians, administrators, pharmaceuticals, regulatory authorities, and policy makers cannot absolve themselves of their responsibilities in addressing the physical and psychosocial repercussions resulting from the exorbitant cost of treatment. Everybody must play their role to bring down the prices of investigations and medicines. We, the doctors, have to lead the way by rationalizing our protocols and practices, and formulating guidelines for the resource constraint settings.

Take care.

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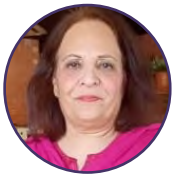
Eid Milan Party

Thalassemia Post



By Dr Zohra J Wazir
Chief Medical Officer Thalassemia Wing

Hyper Transfusion for Eid

Extramedullary hematopoiesis is one of the complications of thalassemia. Different sites like liver, spleen, lymph nodes and marrow spaces are involved. To reduce this process hyper transfusion regimen is used which permits normal growth and physical activity. Such transfusion suppresses erythropoiesis and gastrointestinal iron absorption, and inhibits extra medullary hematopoiesis, thus, preventing splenomegaly and skeletal changes.

Just before the start of Ramzan we arranged a few large blood donation camps to overcome the expected shortage due to fasting. We managed to collect a good number of blood bags and transfused 20-25 children daily to build their hemoglobin to more than 12 g/dL so that they can enjoy Eid with their families and friends.

Pre Eid get together

For girls, new clothes and putting mehndi on hands are a must for Eid. It is a cultural tradition that enhances the celebrations of Eid. Thalassemia staff created beautiful designs with mehndi on patients' hands and in return the kids made Eid cards for all of our Thalassemia staff.

Eid is a time for celebrations and festivities. Young doctors are always up for such occasions and the seniors also welcome a break from the psychologically and physically taxing routine of the hospital. We had an Eid Milan get together on 18 April 2024.
Present among others were Maj Gen (R) Qamar un Nisa and Dr Zohra J Wazir.

"Every child is a different kind of flower, and altogether make this world a beautiful garden" (Anonymous).

Our very cute patient Um e Habiba & Hadia Rani bring happiness in our ward with their beautiful outfits.

Visit of Dr Riaz Ahmed Chaudhry head of department of Surgery, MBBSMC, Mirpur, AJK visited the PATHWEL on 2nd April 2024. He met children with thalassemia and enquired about their health. Dir Riaz is brother of our senior consultant Maj Gen Qamar un Nisa Ch.

A blood Camp was held at SZABIST on 23 April 2023. A total of bags of blood were collected.

One of our registered patient Anaya Nasir, 7 years of age, underwent allogeneic bone marrow transplant on 25 May 2023 at PIMS Hospital. Her HLA matched sister donated the stem cells. Here is the latest picture of Anaya with her family. She is doing well and maintaining stable blood counts.

PATHWEL Stars

A young man with Severe Aplastic Anemia

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

Twenty-nine-year-old Abdul Wasay from Afghanistan, first presented with history of bruises, petechial rashes, pallor, and headache to another hospital in Peshawar in 2014. There he was diagnosed as a case of Severe Aplastic Anemia and was put on Cyclosporine.

Wasay had a fully HLA matched brother Abdul Sami and travelled to India with intention of getting a bone marrow transplant to cure his disease. In India, he found out that transplant is very expensive and started to work part time to arrange the money. Meanwhile his blood counts improved partially, and he remained on Cyclosporine for about 08 years but was never able to collect enough money to undergo bone marrow transplant. In Feb 2023, despite being on Cyclosporine, his blood counts dropped again. He then came back to Pakistan and found his way to PATHWEL for bone marrow transplant at an affordable price. By that time Wasy had received a total of 35 to 40 units of RCC transfusions and about 100 transfusions of platelets. At Pathwel, pretransplant workup was done and after conditioning chemotherapy (Flu120, Cy160 TG10), the patient underwent allogeneic bone marrow transplant on 2nd August 2023. GVHD prophylaxis was given with Cyclosporine. During the early post-transplant period the patient developed acute cholecystitis complicated by pancreatitis. There was also a brief period of neutropenic fever and mild Cyclosporine toxicity. Wasay achieved neutrophils engraftment on day + 11 and platelets engraftment on day + 15. Currently he is 9 months post-transplant, clinically stable, GVHD free, relapse free and maintaining stable blood counts.

Medical Trivia

Ginger, Cinnamon, Cumin Improve Glycemic Control

Nancy A. Melville; Medscape Medical News; March 18, 2024

According to a systematic review and meta-analysis of research, the spices and aromatic herbs of the Mediterranean diet that have significant benefits in improving glycemic health in type 2 diabetes are ginger, cinnamon, black cumin, turmeric, and saffron: with ginger, black cumin, and cinnamon having the strongest effects on fasting glucose. The meta-analysis also evaluated clove, thyme, and various other spices and herbs common in the diet but showed no other correlations with glycemic benefits.

Adults with type 2 diabetes, with data on fasting glucose and/or A1c and/or insulin, and involving any supplementation with black cumin, clove, parsley, saffron, thyme, ginger, black pepper, rosemary, cumin, cinnamon, basil, and/or oregano were included. Improvements in fasting glucose of were observed with cinnamon, turmeric, ginger, black cumin, and saffron. However, the most significant decreases in fasting glucose, between 17mg/dL and 27 mg/dL, occurred after supplementation with black cumin, followed by cinnamon and ginger.

Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits

10-Day Decitabine vs 3 + 7 Chemotherapy Among Older Chemotherapy-Eligible Patients With AML

Lübbert M, Wijermans PW, Kicinski M, et al. Lancet Haematol. Published online November 2023. doi: 10.1016/S2352-3026(23)00273-9

According to findings from a phase 3 trial, 10-day decitabine monotherapy demonstrated a better safety profile but did not improve overall survival compared with 3 + 7 chemotherapy among older chemotherapy-eligible patients with acute myeloid leukemia (AML).

In this trial, 606 patients with newly diagnosed AML, an ECOG status of ≤2, no prior treatment, and eligibility for intensive chemotherapy were enrolled. Patients were randomly assigned to receive either decitabine (n = 303) or standard 3 + 7 chemotherapy (n = 303). Patients in the decitabine group received this treatment at 20 mg/m2 for the first 10 days of the first 28-day cycle, followed by 28-day cycles of 5 or 10 days of decitabine. Patients in the 3 + 7 chemotherapy group received daunorubicin at 60 mg/m2 over the first 3 days, cytarabine at 200 mg/m2 over the first 7 days, followed by 1 to 3 additional cycles of chemotherapy. The study authors noted that HSCT was strongly encouraged to patients.

Results indicated that the 4-year overall survival was 26% in the decitabine group and 30% in the 3 + 7 chemotherapy group. Both groups had similar rates of on-protocol allogeneic HSCT. Grade 3 to 5 adverse events were observed in 254 patients in the decitabine group and 279 patients in the 3 + 7 group. The rates of grade 3 to 5 infections were lower in the decitabine group compared with the 3 + 7 group. Treatment-related deaths occurred in 35 patients in the decitabine group and 41 patients in the 3 + 7 group.

The authors concluded that, "Decitabine could be considered a better-tolerated and sufficiently efficacious alternative to 3 + 7 induction in fit older patients with acute myeloid leukemia without favorable genetics".

Daratumumab, Carfilzomib, Lenalidomide, and Dexamethasone With Tandem Transplant in Newly Diagnosed High-Risk Patients with Multiple Myeloma (MM)

Cyrille Touzeau, Aurore Perrot, Cyrille Hulin et al: blood; DOI:10.xxxx/blood.2024xxxxxx

Context of research

- High-risk (HR) cytogenetics is associated with poor outcomes in newly diagnosed patients with MM
- Dedicated studies are needed for this difficult-to-treat patient population
- The Intergroupe Francophone du Myelome (IFM) therefore designed the phase 2 study 2018-04

IFM 2018-04 phase 2 study (NCT03606577)

Key inclusion criteria:

- Age < 66
- Newly diagnosed multiple myeloma
- Transplant-eligible
- High-risk FISH : t(4;14), 17p Del, t(14;16)
- ECOG 0-2

Objectives:

- **Primary Objective:** Feasability
  primary endpoint : >70% patients receiving 2nd trasnplant
- **Secondary Objectives:** Safety, ORR, PFS, OS, stem-cell collection

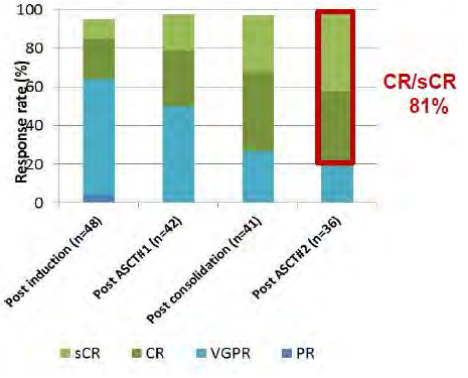
Dara, daratumumab; K, carfilzomib; R, lenalidomide; d, dexamethasone

Conclusions:

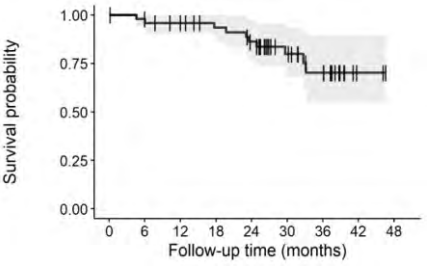
In newly diagnosed high-risk MM patients, an intensive program with quadruplet induction and consolidation plus tandem autologous transplantation was feasible. Treatment resulted in high rates of MRD negativity and 80% 30-month PFS.

Main findings

Response rates



Progression-free survival



Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits Tidbits

Pregnancy outcomes and iron status in beta-thalassemia major and intermedia: a systematic review and meta-analysis

Evangelia Vlachodimitropoulou, Hussain Mogharbel, Kevin H. M. Kuo, et al;
Blood Advances published online 1 February 2024; doi.org/10.1182/bloodadvances.2023011636.

Advancements in orally bioavailable iron chelators and MRI methods have improved life expectancy and reproductive potential in thalassemia major (TM) & thalassemia intermedia (TI). Pregnancy is associated with adverse maternal and neonatal outcomes, the frequency of which has not been well delineated. This systematic review aims to provide risk estimates of maternal and fetal outcomes in TM and TI and explore pregnancy's impact on iron homeostasis.

Fifteen studies (429 participants, 684 pregnancies) were included. Meta-analysis revealed a higher thrombosis risk in TI (3.7%) compared to TM (0.92%), unchanged from pre-pregnancy state. Heart failure risks in the earlier years appeared similar (TM 1.6% vs TI 1.1%), and maternal mortality in TM was 3.7%, but with current management, these risks are rare. Gestational diabetes and pre-eclampsia occurred in 3.9% and 11.3% of TM pregnancies, respectively. Caesarean section rates were 83.9% in TM and 67% in TI. No significant difference in stillbirth, small for gestational age neonates, or preterm birth incidence between TM and TI was observed.

In TM pregnancies, red cell requirements significantly increased (from 102 to 139 ml/kg/year, P = 0.001), and 70% of TI pregnancies required blood transfusions. As expected, increased transfusion alongside chelation cessation led to a significant increase in serum ferritin during pregnancy (TM by 1005 ng/mL; TI by 332 ng/mL, P < 0.0001). Deterioration in iron status was further reflected by an increase in liver iron concentration (from 4.6 to 11.9 mg/g dry weight, P < 0.0001), and myocardial T2-star (T2*) magnetic resonance imaging decreased (from 36.2 ± 2.5 ms to 31.1 ms) during pregnancy.

These findings emphasize the elevated maternal risk of iron-related cardiomyopathy during pregnancy and labor, stressing the importance of cardiac monitoring and postpartum chelation therapy resumption.

Targeting Molecular Measurable Residual Disease and Low-Blast Relapse in AML With Venetoclax and Low-Dose Cytarabine: A Prospective Phase II Study (VALDAC)

Ing Soo Tiong, Devendra K. Hiwase, Emad Abro et al: Journal of Clinical Oncology; doi.org/10.1200/JCO.23.01599

In this prospective phase II study, patients with AML at first measurable residual disease (MRD) or oligoblastic (5%–15% blasts) relapse were treated with venetoclax 600mg once daily on days 1to 28plus low-dose cytarabine once daily on days 1to 10in 28-day cycles. The primary endpoint was an MRD response in patients with MRD relapse and complete remission in those with oligoblastic relapse.

Patients received a median of four cycles. Among those with MRD relapse, 46% achieved MRD-negative remission by cycle two. In the oligoblastic relapse cohort, 73% of patients achieved complete remission. Response to treatment was observed at a median of one cycle. Overall, 44% of patients transitioned to stem cell transplantation. The 2-year overall survival rates were 67% and 53% in the MRD and oligoblastic relapse cohorts, respectively.

Early intervention with venetoclax plus low-dose cytarabine in patients with AML with early(MRD or low-blast) relapse appears safe and is clinically effective. Larger studies are warranted.

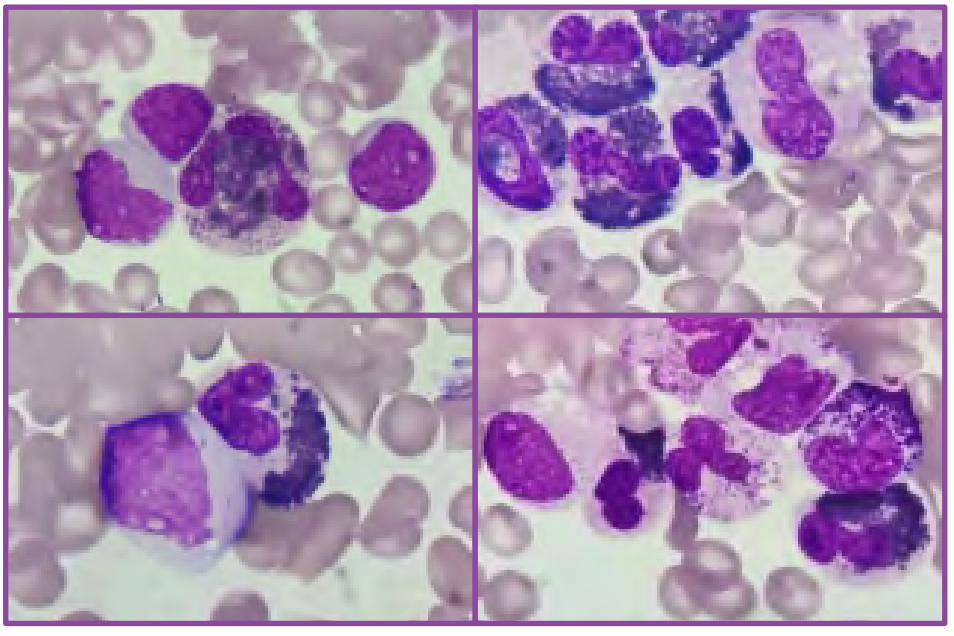
Morphology Updates

Pseudo-Chédiak–Higashi anomaly in acute myeloid leukemia

Biswadip Hazarika[1] | Barbara J. Bain[2]
[1] Department of Haematology, Batra Hospital and Medical Research Centre, New Delhi, India
[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.27114

A 13-year-old Indian boy presented with dysuria and intermittent fever for 6 weeks. Physical examination showed no specific abnormality. His blood count showed a white cell count of 26.8 109/L, hemoglobin concentration 109 g/L, mean cell volume 82.9 fL, and platelet count 24 109/L. His blood film showed marked neutrophilia and 26% blast cells; the neutrophils and eosinophils were packed with aberrantly staining, mainly purple granules, some of which were giant (all images 100 objective). No granules or Auer rods were detected in blast cells. Immunophenotyping showed the blast cells to express CD13, CD33, CD117, CD34, CD38, and CD7. There was no expression of myeloperoxidase, CD64, cytoplasmic CD3, or B-lineage markers. Cytogenetic analysis showed a normal male karyotype. There were no clinical features of Chédiak-Higashi syndrome. A diagnosis of acute myeloid leukemia (AML) complicated by the pseudo-Chédiak-Higashi anomaly was made. The patient responded to induction chemotherapy with abnormal granulocytes disappearing from the blood; the few neutrophils then present did not have abnormal granules. The patient was well enough to be discharged and was to seek further treatment elsewhere.

The pseudo-Chédiak-Higashi anomaly is well recognized but rare in AML. Usually the abnormal granules are found in blast cells, but occasionally they have been identified in promyelocytes and myelocytes.1–3 They stain variously, pink or purple. They are usually peroxidase-positive but not invariably.4 Auer rods are also not infrequently present. An association with t(8;21) has been reported in at least three patients,3,5,6 but no other consistent cytogenetic abnormality has been recognized. This patient is exceptional in that the granules were confined to mature granulocytes.



ORCID
Barbara J. Bain https://orcid.org/0000-0003-3077-4579

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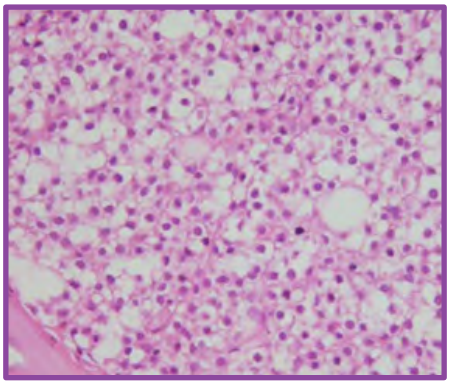
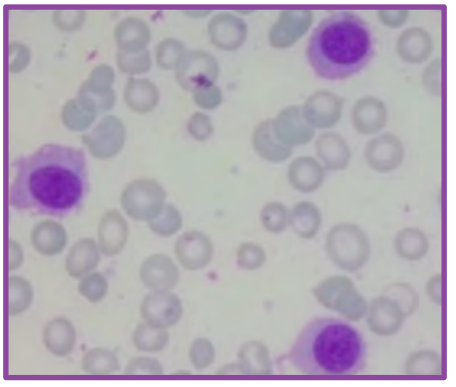
Picture Quiz – Answer

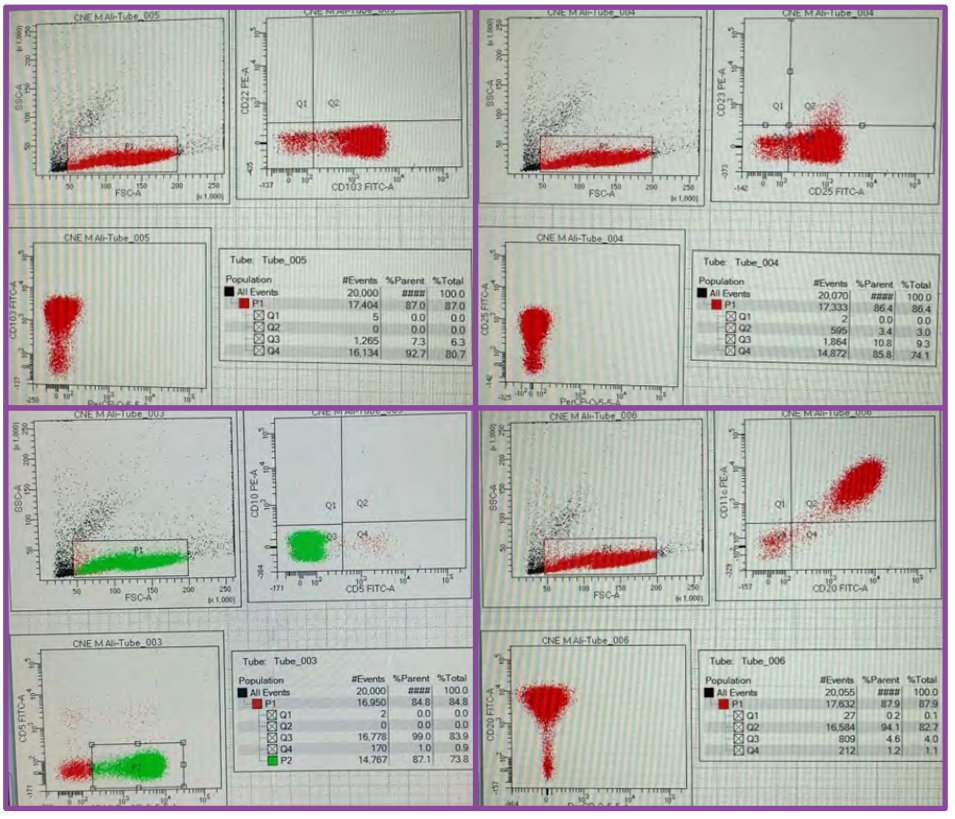
by Dr Sidra Barlas, Hematologist, Pathwel Center of Hematology & BMT

Hairy Cell Leukemia

Hairy Cell Leukemia (HCL) is a rare small, mature B-cell neoplasm that classically present with monocytopenia and involves predominantly the bone marrow and spleen. Marked splenomegaly is usually present.Hairy cells are lymphoid cells of small to medium size (10–20 mm in diameter). They have pale blue or blue-gray cytoplasm with circumferential, shaggy, irregular projections. The nucleus is often eccentrically placed and is oval or indented, with loose, spongy chromatin. Occasionally, the nucleus may be bilobate or dumbbell-shaped, a feature that is particularly evident in patients who have a true leukemic phase. Nucleoli are absent or inconspicuous.In virtually all patients with hairy cell leukemia, the bone marrow biopsy specimen demonstrates a diffuse or patchy interstitial infiltrate. This pattern of infiltration is apparent even at low magnification and contrasts with the focal nodules or aggregates of lymphoid cells with closely packed nuclei found in most other mature B-cell lymphoproliferative disorders. HCL has a distinctive immunophenotype based upon staining with antibodies to CD5 (negative), CD10 (negative), CD23 (negative), CD20 (abnormally bright), CD22 (abnormally bright), CD11c (abnormally bright), CD25 (abnormally bright), CD103 (positive), and CD123 (positive), CD200, Annexin A1, BCL1. Molecular studies show positive BRAF V600E mutation. Nearly 100% of cases are positive for BRAF V600E. Adverse prognostic indicators once diagnosis of HCL is made include unmutated IGHV and expression of the IGHV VH-34 (IGHV4-34+) immunoglobulin rearrangement.Treatment includes therapy with Cladribine, also historically responds well to purine analogues such as Pentostatin. Therefore, it is important to distinguish HCL from other small B-cell neoplasms that share similar morphologic and immunophenotypic features with HCL but may not respond to HCL-directed therapies.HCL-V (variant) atypically presents with leukocytosis, no monocytopenia and absence of CD25 and CD123. BRAF V600E mutation is also absent.Recent treatment guidelines include use of Moxetumomab pasudox (MP), especially in HCL failing treatment after purine analog therapy. MP is an immunotoxin directed against Cd22.







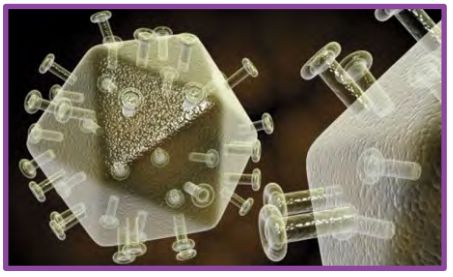
Cover Photo

Colored scanning electron micrograph of hairy cell.

Transplant TidingsTransplant TidingsTransplant Tidings

Addition of ruxolitinib to standard graft-versus-host disease prophylaxis for allogeneic stem cell transplantation in aplastic anemia patients

Xiaoyu Zhang, Xiaoli Zhao, Shulian Chen et al; Bone Marrow Transplantation; doi.org/10.1038/s41409-024-02266-7



Allogeneic hematopoietic stem cell transplantation (allo-HSCT) offers rapid hematopoietic and immune reconstitution for aplastic anemia (AA). As a non-malignant disorder, attenuation of GVHD remains a clinical priority in AA patients. Our study sought to investigate the safety and efficacy of the prophylactic use of ruxolitinib in allogeneic HSCT.

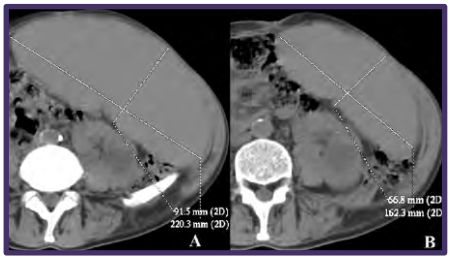
A total of 35 AA patients were retrospectively consecutively treated with allo-HSCT whereby ruxolitinib was added to the standard GVHD prophylaxis regimen (rux group). The addition of peri-transplant ruxolitinib did not impact the engraftment and graft function, while better recovery of CD4+ Tregs in the rux group was observed. Interestingly, the rux group demonstrated significantly lower incidence of bacterial/fungal infections (17.14% vs 45.71%).

Compared to the control group, the rux group exhibited significantly lower incidence of moderate to severe aGVHD (17.1% vs 48.6%) with a trend toward lower severe aGVHD (8.6% vs 20%) and cGVHD (26.2 vs 38.3). The rux group also demonstrated a trend toward higher GVHD and failure-free survival (GFFS: 85.7% vs 68.6%) and lower TRM (2.9% vs 14.3%).

Addition of ruxolitinib to standard GVHD prophylaxis regimen, thus, represents a safe and highly efficient method for the attenuation of GVHD with better outcome of allo-HSCT.

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

Nico Gagelmann, Gabriela S. Hobbs, Edoardo Campodonico et al; DOI: 10.1002/ajh.27252; Am J Hematol.2024;99:844–853.



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.

Transplant TidingsTransplant TidingsTransplant Tidings

Long-term follow-up of cancer and catastrophic diseases in hematopoietic stem cell donors: a comprehensive matched cohort study

Sung-Chao Chu, Chia-Jung Hsieh, Chi-Cheng Li, et al; Bone Marrow Transplantation; March 8, 2024

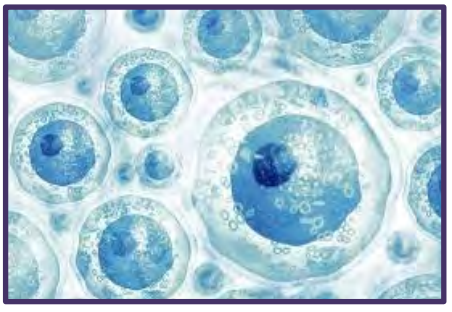
Hematopoietic stem cell (HSC) transplantation, using either bone marrow (BM) or peripheral blood stem cells (PBSC), is a well-established therapy for various hematologic and non-hematologic diseases. However, the long-term health outcomes after HSC donation remain a major concern for several potential donors. Thus, we aimed to conduct a matched cohort study of 5003 unrelated donors (1099 BM and 3904 PBSC) and randomly selected 50,030 matched controls based on age, sex, and resident area from the donor registry between 1998 and 2018.

The medical insurance claims of all the participants were retrieved from the Taiwan National Health and Welfare Data Science Center after de-identification. Our findings revealed no differences in the incidence of cancer, death, and catastrophic diseases between HSC donors and matched healthy participants during long-term follow-up. Kaplan–Meier curves depicting the cumulative incidence of cancer and overall mortality throughout the follow-up period also demonstrated similar outcomes between donors and non-donors.

In conclusion, our results indicate that HSC donation, whether through BM or PBSC, is safe and not associated with an increased risk of cancer, death, or catastrophic diseases. These findings provide valuable information for counseling potential HSC donors and for long-term management of HSC donor health.

Etoposide plus cytarabine versus cyclophosphamide or melphalan in busulfan-based preparative regimens for autologous stem cell transplantation in adults with acute myeloid leukemia in first complete remission: a study from the Acute Leukemia Working Party of the EBMT

Jaime Sanz, Myriam Labopin, Thomas Pabst et al; Bone Marrow Transplant. 2023 Nov;58(11):1197-1202. doi: 10.1038/s41409-023-02075-4



We retrospectively compared the impact of the conditioning regimen in adult patients with AML in first complete remission (CR1) that received high-dose myeloablative chemotherapy followed by autologous stem cell transplantation (ASCT) from 2010 to 2021 with either high-dose cytarabine, etoposide and busulfan (BEA), busulfan with cyclophosphamide (BUCY) or busulfan and high-dose melphalan (BUMEL) registered in the EBMT database.

Overall, 1560 patients underwent ASCT, of which 156, 1143 and 261 received BEA, BUCY and BUMEL, respectively. Compared to BUCY and BUMEL, BEA patients were younger ($p < 0.001$) and less frequently had NPM1 mutations ($p = 0.03$).

Transplant outcomes at 5 years with BEA, BUCY and BUMEL were: cumulative incidence of relapse 41.8%, 46.6% and 51.6%; non-relapse mortality (NRM) 1.5%, 5.2% and 7.3%; probability of leukemia free survival (LFS) 56.7%, 48.2% and 41.1%; and overall survival (OS) 71.3%, 62.3% and 56%, respectively. In multivariable analysis the BEA regimen showed significant improvement in OS compared to BUCY (hazard ratio [HR] 0.65; 95% CI, 0.42–0.83; $p = 0.048$) and BUMEL (HR 0.59; 95% CI, 0.37–0.94; $p = 0.029$).

In conclusion, high dose myeloablative combination chemotherapy with BEA offered improved outcomes compared to classical BUCY or BUMEL in patients with AML in CR1 undergoing ASCT.

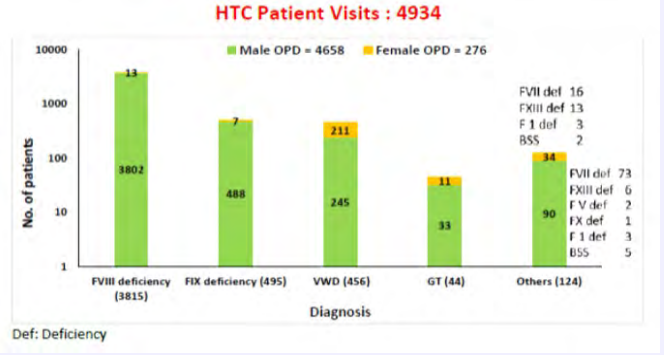
Hemophilia Treatment Center Rawalpindi in 2023

By Dr Tahira Zafar
Consultant Hematologist | Director, Hemophilia Treatment Centre

Key Highlights

An overwhelming number of 4,934 visited HTC Rwp including 3,815 Haemophilia A, 495 Haemophilia B, 456 VWD, 44 Glanzmann Thrombasthenia, and others patients. Following is a registry of patients for the year 2023.

- 101 new patients were identified and registered.
- Successfully running 3 welfare projects (Hifazat e Najam, Hifazat e Jan, Hifazat e Nisa) under HTC
- On-demand, prophylactic and home treatment
- Access to novel treatment (Emicizumab from World Federation of Hemophilia)
- Successful surgeries in 9 patients



Welfare Projects Under HTC; At a Glance

Hifazat e Najam

The project caters for patients who cannot afford to pay for Factors obtained from the parallel market. These patients are registered with (HPWS-Rwp) with family income below 30,000 /month. Families who have 2 or more PWBD to support, have a moderate to severe deficiency and in particular those with VWD, FVIII, FIX and FVII deficiencies, are preferred. To date, 160 patients are covered under Hifazat e Najam program.

Hifazat e Jan

Hifazat e Jan project is designed for patients with inherited bleeding disorders and life-threatening bleeds, non-availability of donated factor concentrates for use, and the inability to cover the costs of factor concentrates. HTC has enrolled 7 patients under this program.

Hifazat e Nisa

Hifazat e Nisa is a unique project which is meant for women with Von Willibrand Disease (VWD) and who can not afford to purchase factor concentrates. So far, 8 women have been registered under this category.

Hemlibra, a life changer for Ali Haider

Ali Haider suffered from severe Hemophilia A since he was a year old. His parents relocated from Gilgit (Northern Pakistan) with their three hemophilic kids to be closer to HTC Rawalpindi. Ali Haider visited HTC regularly due to his recurrent bleeds. Rifadin Injections (Rifampicin) were tried for his target joints (knees) but they had little effect. He had to take frequent leaves from school which led him to leave school. He became depressed and demotivated; his parents were helpless and wondered if their child would ever live a normal life.

His life turned around when he was selected for Hemlibra (Emicizumab) treatment which changed both his present and future. He has not bled since he had been on Hemlibra. Ali re-joined school and is a picture of happiness and hope for all Hemophilia patients and their families. Recently, he secured 88% marks in his Matric (Grade 10, National exam). The entire family is ever so grateful to HTC Rawalpindi for taking care of Ali & to WFH for providing treatment. Ali Haider's goal is to become a mathematician & be a productive & useful member of society. With the Hemlibra treatment, he has now the courage and hope to build a shiny future.

Clinical Practice Guidance

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

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

Section 2: Atrial fibrillation

What tool can be used for ischemic stroke risk assessment in PWH with AF?

- We suggest using the CHADS2 score for individual stroke risk assessment as a general guide in PWH, but we cannot recommend specific predictive thresholds. Thus, expert-provided balance of thrombotic and bleeding risk must be taken into consideration for PWH.

What tool can be used as bleeding risk assessment in PWH with AF?

- We consider PWH as being at high risk for bleeding in any bleeding score, regardless of factor level.

Is there a place for aspirin in the treatment of AF in PWH?

- In PWH with AF, we recommend against the use of aspirin over oral anticoagulation.

What is the role for alternative strategies in PWH with AF, such as left atrial appendix closure or pulmonary vein isolation?

- We consider left atrial appendix occlusion (LAAO) a feasible option in PWH not eligible to long-term anticoagulant treatment for AF. However, accurate selection of eligible patients should consider the risk of bleeding during follow-up and temporary adapted prophylaxis is warranted if baseline level is <20 IU/dL.

Section 3: Acute and Chronic Coronary Syndromes

Can systemic thrombolysis be given in PWH?

- We consider systemic thrombolysis to be relatively contraindicated in all PWH.

Is there an indication for pretreatment with antiplatelet therapy in PWH with acute coronary syndromes (ACS) before invasive (percutaneous cardiac intervention [PCI]) treatment?

- We do not recommend pretreatment with a P2Y12 receptor inhibitor in PWH with an ACS if an early invasive management is planned.

Is there an indication for clotting factor replacement in PWH before cardiac intervention?

- In PWH undergoing a cardiac intervention, we recommend clotting factor supplementation with a target FVIII/FIX peak level of 80–100 IU/dL before the procedure. We recommend additional bolus infusions to maintain trough levels according to the procedure.
- We recommend radial artery access over femoral in cardiac interventions.
- In PWHA on emicizumab without inhibitors undergoing a cardiac intervention, we recommend additional FVIII supplementation as in PWH without emicizumab.
- In PWHA on emicizumab with inhibitors undergoing a cardiac intervention, we recommend supplementation with rFVIIa and do not recommend the use of activated prothrombin complex concentrates (aPCC).

Which anticoagulant is preferred in PWH before and during PCI?

- In PWH with ACS where PCI is indicated, we recommend using unfractionated heparin (UFH) or bivalirudin over enoxaparin given their shorter half-lives.
- We recommend the use of UFH or bivalirudin only after replacement of clotting factor levels.

Is there a formal bleeding risk assessment tool for bleeds in PWH with ACS?

- We consider all PWH at higher risk for bleeding and therefore recommend they should be treated as such according to the existing guidelines. We recommend that the severity of hemophilia and the individual bleeding risk should guide the clinician, not a formal score.

What type of stent is preferred in PWH with ASC?

- We recommend a newer generation drug-eluting stent (DES) as these allow the shortest DAPT time without an increase in the risk of stent thrombosis.

What DAPT regimen is preferred in PWH?

- We recommend the use of clopidogrel over ticagrelor or prasugrel in PWH in need for DAPT due to its lower bleeding risk.
- We recommend short duration of DAPT (1 mo) after newer generation DES placement followed by long-term monotherapy with clopidogrel or aspirin.
- In inhibitor patients, we consider an individual approach depending on the use of emicizumab and other risk factors for bleeding.

(to be continued...)

Thalassemia Major
(Part-2)

By Dr Tahira Zafar, Consultant Hematologist

تھیلیسیمیا میجر
(حصہ دوئم)

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.

۱۱۔ تھیلیسیمیا مائیز اکثر و بیشتر کسی قسم کی علامت پیدا نہیں کرتا۔ ایسے افراد عام طور پر بالکل تندرست ہوتے ہیں اور اپنے تھیلیسیمیا سے بے خبر۔ یہ بے خبری کی ہی صورتحال ہے جو کہ انتہائی خطرناک ہے۔ کیونکہ اگر دو تھیلیسیمیا مائیز کے افراد بے خبری میں شادی کر لیں تو کبھی کبھار ان کو ایک انتہائی تلخ حقیقت خواب خرگوش سے جھنجھوڑتی ہے کہ نومولود کو تھیلیسیمیا میجر ہے۔ اس لئے اس بات کا ادراک انتہائی ضروری ہے کہ ظاہری صحت تھیلیسیمیا سے پاک ہونے کی قطعی ضمانت نہیں ہے۔

۱۲۔ اگر ہم رضاکارانہ طور پر اس بات کا عہد کر لیں کہ ہم اپنے معاشرے میں دو تھیلیسیمیا مائیز کی شادی نہیں کریں گے تو یہ معاشرہ تھیلیسیمیا میجر سے پاک ہو سکتا ہے۔ یہاں یہ بات قابل ذکر ہے اگرچہ تھیلیسیمیا میجر سے پاک معاشرے کا حصول ممکن ہے لیکن تھیلیسیمیا مائیز سے نجات ناممکن ہے یہ کیفیت ازل سے ہے اور ابد تک رہے گی۔ اس سے نجات ممکن نہین۔ اہمیت تھیلیسیمیا مائیز کے موجود ہونے یا نہ ہونے کی نہیں ہے۔ اصل بات یہ ہے کہ تھیلیسیمیا مائیز والے دو افراد اسپس میں شادی نہ کریں۔ تاکہ بچوں میں تھیلیسیمیا میجر منتقل نہ ہونے پائے۔

۱۳۔ تھیلیسیمیا کے بارے میں حتمی فیصلہ خون کے ایک عام اور سستے ٹیسٹ سے ہو سکتا ہے۔ اس ٹیسٹ کو (Hemoglobin Electrophoresis) ہیموگلوبن الیکٹروفوریسز کہتے ہیں۔ اگر تھیلیسیمیا مائیز کے کسی بھی فرد کے بہن بھائی اور رشتہ دار اس ٹیسٹ کو اخلاقی فرض اور سماجی ذمہ داری کے طور پر کروائیں تو معاشرہ بڑی حد تک تھیلیسیمیا میجر سے پاک ہو سکتا ہے۔

۱۴۔ ہیموگلوبن الیکٹروفوریسز خون کا ٹیسٹ ہے جس سے یہ چیز واضح ہو جاتی ہے کہ کسی فرد کو تھیلیسیمیا مائیز ہے یا نہین۔ اس ٹیسٹ میں ہیموگلوبن (A-2) کی مقدار چیک کی جاتی ہے یہ ہیموگلوبن نارمل لوگوں کے خون میں بھی موجود ہوتی ہے۔ ایک تندرست آدمی میں اس کی مقدار 3.5 فیصد ہوتی ہے۔ اگر اسکی مقدار 3.8 فیصد سے زیادہ ہو اور خاص طور پر اگر یہ 4 فیصد سے زیادہ ہو تو تھیلیسیمیا مائیز کی تشخیص ہو سکتی ہے۔

۱۵۔ ہیموگلوبن (A-2) کی مقدار پیدائش سے لے کر اختتام تک ایک جیسی رہتی ہے۔ اس میں وقت کے ساتھ ساتھ کسی قسم کی تبدیلی نہیں ہوتی۔ اگر کسی شخص کی ہیموگلوبن الیکٹروفوریسز میں ہیموگلوبن (A-2) زیادہ ہو۔ تو اس شخص میں تو تھیلیسیمیا مائیز ہے ہی۔ اس شخص پر اب ایک اخلاقی اور سماجی ذمہداری یہ آن پڑی ہے کہ وہ اپنے گھر کے ہر فرد کا (علاوہ ضعیف والدین کے) ٹیسٹ کروائے اور فرداً فرداً ہر ایک کے (Thalassaemia Status) کا پتہ چلائے تاکہ آئندہ نسل میں تھیلیسیمیا مائیز کے جوڑے کی شادی نہ ہو اور انکی اولاد میں تھیلیسیمیا میجر نہ ہونے پائے۔

۱۶۔ بسا اوقات معاشرے کی اقدار کو ملحوظ رکھتے ہوئے تھیلیسیمیا مائیز کے حامل افراد کے درمیان شادی ناگزیر ہو جاتی ہے۔ ان حالات میں درجہ ذیل صورتیں (Options) اختیار کی جا سکتی ہیں:۔

اگر اپنے بچے پیدا کرنے کی خواہش ہو یا غیر ارادی طور پر حمل کے دسویں ہفتے ایک خاص ٹیسٹ کروایا جا سکتا ہے۔ جس سے یہ پتا چل سکتا ہے کہ ماں کے پیٹ میں جو بچہ ہے اسے تھیلیسیمیا میجر ہے یا نہیں۔

اگر بچے کو تھیلیسیمیا میجر نہیں ہے تو اس حمل کو اختتام تک چلنے دیں۔ لیکن اگر بچے کو تھیلیسیمیا میجر ہے تو اس حمل کے بارے میں انتہائی ٹھنڈے دل سے غور کرنا چاہیے کیونکہ اس صورت میں جو بچہ پیدا ہو گا وہ ایک ایسی تباہی و بربادی کا پیغام لائے گا جسے وہی سمجھ سکتا ہے جو اس جسمانی، روحانی، مالی اور سماجی عذاب سے گزر چکا ہو۔ اور جس کو آہوں، سسکیوں، ذہنی اذیت، جسمانی بدحالی کا تلخ تجربہ ہو چکا ہو اس لیے ایک ایسے حمل کو جاری رکھنا جس میں تھیلیسیمیا میجر کی تشخیص ہو چکی ہو غیر مناسب ہو گا۔ اسلام میں بھی اس بارے میں ہدایت موجود ہے۔

۱۷۔ تھیلیسیمیا میجر خون کی ایک مہلک لاعلاج اور حسرت بھری داستان ہے۔ جس میں اذیت، مایوسی، آہوں، سسکیوں اور ٹھنڈی سانسوں کے علاوہ کچھ نہیں۔ چند سالہ زندگی جو کہ ان بچوں کا مقدر ہے۔ وہ کمزوری، بخار، یرقان، چہرے کی بے رونقی و بدنمائی، سیاہ رنگت، انجیکشن کی تکالیف، دوستوں کی بے رخی۔ تعلیم میں رکاوٹ اور مالی بدحالی سے رقم ہے۔ اس دردناک جسمانی اور روحانی کیفیت کا علاج ممکن نہین لیکن اس کا تدارک آپ کے اپنے ہاتوں میں ہے۔

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